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# Carbon Dioxide Insufflation During Colonoscopy

## A Randomised Controlled Trial

A thesis presented in partial fulfilment of the requirements for  
the degree of Masters of Philosophy (Nursing) at Massey  
University

Anne Cleland  
2009

# Abstract

## **Aim**

To determine that carbon dioxide (CO<sub>2</sub>), instead of air, insufflated during colonoscopy reduces pain experienced by patients post colonoscopy.

## **Method**

A randomised, double blinded, controlled trial with 205 consecutive consented patients referred for elective colonoscopy was undertaken at MidCentral Health Gastroenterology Department between July 2008 and January 2009. Patients were randomised to colonic insufflation with either air or CO<sub>2</sub>. A comparison of reported pain was undertaken using a 0 -10 point numeric rating scale at several time periods; intra procedure, 10, 30, and 60 minutes post procedure.

## **Results**

The results were analysed using the SPSS programme. CO<sub>2</sub> insufflation was used in 108 patients and air in 97 patients. Pain scores 10 minutes after were  $0.43 \pm 1.20$  for CO<sub>2</sub> and  $1.61 \pm 2.40$  for air ( $P < .0001$ ). 30 minutes after the procedure 90% of patients in the CO<sub>2</sub> group reported no pain, compared to 61% of the air group. CO<sub>2</sub> significantly reduced the amount of discomfort post colonoscopy at 10, 30 and 60 minutes.

## **Conclusion**

Those receiving CO<sub>2</sub> during colonoscopy experienced less post colonoscopy pain than those who received air insufflation. Carbon dioxide should be considered as the insufflating gas during colonoscopy.

## Acknowledgements

One chapter on the journey of my nursing career is about to close and I would like to thank all who have accompanied me and spurred me on.

The biggest thank you goes to my family. My husband Kevin who has persevered with having to go solo for many a time when I was preoccupied, I am deeply grateful. To my children Stacey, Jason and Matthew; thank you for being there to encourage me through out and never questioning that I would make it.

A special acknowledgment needs to go to my belated parents who passed on to me the motto *'Nothing ventured, nothing gained'* which has kept me going and will spur me to take the narrow road as the next chapter opens.

My deep gratitude goes to my supervisors: Professor Jenny Carryer who compelled me to embark on this challenging yet deeply rewarding academic journey. Her expectations of excellence were always communicated in a way that left me encouraged. Professor Steve LaGrow challenged me to tackle understanding areas that I never thought were possible

I express my extreme appreciation to my colleagues in the Gastroenterology Department whose unquestioning enthusiasm throughout the research was a huge encouragement. Without them and the many willing participants, this research could not have been done

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# Chapter One

## Background and Orientation to The Study

### 1.1 Introduction

A large number of people undergo a diagnostic and/or therapeutic colonoscopy in the Gastroenterology Department at MidCentral Health (MCH) every year (1000 in 2008/2009). Many patients experience discomfort during a colonoscopy, and in the hours following, from air distension as a consequence of the air insufflated during the procedure. Intra procedure the use of a short acting sedation (hypnovel) and analgesia (fentanyl) are used to manage this pain. After the procedure it is common for the retained air to cause distension. For some patients this can result in varying degrees of pain ranging from minor pain, some moderate and a few experience strong abdominal pains. Sumanac and his colleagues (2002) in their research claim that one hour post colonoscopy 45% of patients experience abdominal pain. Although statistics are not readily available at MCH, anecdotally pain/discomfort post colonoscopy is common. The reputation of colonoscopy as an uncomfortable and painful procedure is concerning. Focusing on post colonoscopy pain and finding a tool that will relieve this pain safely will be of huge benefit to the patient.

I have worked as a registered nurse in the Gastroenterology/ Endoscopy field since 1990, including 4 years in the USA. In the last few years I became interested in the area of post colonoscopy pain and observed efforts being made to find a method to reduce this pain.

Various interventions are used at MCH Gastroenterology Department in an attempt to alleviate the effects of air distension and cramping after a colonoscopy. Sedation and analgesia intra-procedure is offered, utilising intravenous hypnovel and fentanyl, which may have some residual effect on post colonic analgesia. However, the discomfort caused by intra colonic gas may extend beyond the period of the short acting effect of these two drugs. Nurses in gastroenterology (gastro) will try a variety of methods, to facilitate passing of air in patients post-colonoscopy. All patients are encouraged to `pass air`, then depending on the success of this and/or complaints of abdominal cramping pain, various positional methods are suggested; from lying on their right side, lying prone, get in the reverse trendelenberg position, to walking around. Panadol is also offered to patients during recovery. Despite various non-pharmacological and pharmacological interventions, post-colonoscopy pain is experienced and a concern to both patients and nurses.

A literature search using Medline, CINAHL (1980 – 2008) found a limited variety of interventions being trialled to relieve this pain. In looking into this area further, it seemed that internationally this may be a `forgotten area` of pain management in the endoscopy world. According to Steinberg and Howden (1997, p. 444) “traditionally endoscopists have sought to provide maximum comfort for patients undergoing colonoscopy but may have been less concerned with the level of patient discomfort following the procedure.” This response indicates how endoscopists, themselves, are highlighting that there is big focus on relieving pain

intra-procedure, but that this attention to patients' comfort needs to continue to post-procedure.

In comparing the variety of post colonoscopy pain relieving interventions used anecdotally, or discussed in published literature, it was felt that the use of carbon dioxide (CO<sub>2</sub>) to insufflate the colon held the most promise of a successful method to reduce post colonoscopy pain. The advantage of CO<sub>2</sub> is that it is rapidly absorbed by the colon lumen, enters the venous system, and excreted through the lungs (Church & Delaney, 2003). Cotton and Williams (2003) claim that CO<sub>2</sub> is absorbed 100 times faster than air and thus results in less distension and the associated pain.

Internationally there are a slowly growing number of endoscopy units using CO<sub>2</sub> instead of air to insufflate the colon during colonoscopy, which substantially reduces the pain experienced post colonoscopy. Despite this method being supported by randomised controlled trials (Bretthauer, Thiis-Evensen, et al., 2002; Church & Delaney, 2003; Stevenson, Wilson, Wilkinson, Norman, & Goodacre, 1992; Sumanac, et al., 2002) these researchers note that this method is still slow to gain popularity. Prior to this study this method was not yet being used in New Zealand. In conjunction with commencing use of a CO<sub>2</sub> delivery system, at MCH Gastroenterology Department, an investigation in its efficacy in the New Zealand setting was proposed by undertaking a randomised controlled trial (RCT).

## **1.2 The Aim of the Study**

The aim of the present study was to determine that carbon dioxide (CO<sub>2</sub>), instead of air, insufflated during colonoscopy reduces pain experienced by patients post colonoscopy. The amount of pain post colonoscopy reported by the treatment group receiving CO<sub>2</sub> will be compared with the control group receiving air.

## **1.3 The Hypothesis**

The following hypothesis was developed and investigated in this study:

Those receiving carbon dioxide (CO<sub>2</sub>) insufflation during colonoscopy will experience less post colonoscopy pain than those receiving air insufflation.

## **1.5 The Significance of the Study**

The incidence of colon cancer in New Zealand is one of the highest in the world according to the National Screening Unit (2007). Colonoscopy is the gold standard tool for both diagnosis and surveillance of the colon but the demand is outweighing the supply. Patients` referred for colonoscopies are entering a health service providing a diagnostic procedure, whose resources are stretched to capacity. When the patient does get to the top of the waiting list and undergo a colonoscopy, they may experience a painful procedure (intra and post).

Reports of a painful procedure and experience of this pain may negatively impact on future presentation. Mayer, et. al. (2001, p. 44) claim that neglected pain will erode a patient`s trust in the health provider. Tywcross (2002, p. 705) expands this

thought in explaining that “future medical interventions will be anticipated with greater anxiety if pain has not been managed effectively in the past.” If all efforts are made to reduce colonoscopy pain to a minimum with use of CO<sub>2</sub>, the patient is more likely to present for a procedure if it is known to involve minimal discomfort and then more likely to be compliant for future surveillance (Church & Delaney, 2003).

Although there is a growing trend internationally to use colonoscopy as a screening tool, this was not initially believed to be cost effective in New Zealand according to a Ministry of Health (MOH) report (2006). Nonetheless a report by Shaw, Cunningham and Sarfarti (2008)) informed the MOH on the feasibility of a screening program. Subsequently in May 2008 the present Minister and Associate Minister of Health announced that the Government is committed to setting up a bowel cancer screening programme in New Zealand as quickly as possible (2008). The screening tool will be faecal occult blood test which if positive will then lead to colonoscopy. The impact on the demand for colonoscopy is set to increase significantly. However even disregarding screening, a MOH National Screening Unit survey of ‘Colonoscopy capacity in New Zealand’ by Yeoman and Parry (2005) showed that the pressure of providing timely diagnosis for symptoms and surveillance colonoscopy is straining our Gastroenterology departments. This concerning trend is reflected locally at MCH. Finding a method that would not only make colonoscopy patients more comfortable, but may also aid the efficiency of the Gastroenterology Department would be very pertinent.

Undertaking a trial to explore if CO<sub>2</sub> significantly reduces post colonoscopy pain raises issues implicating Maori people that need to be addressed. The population of patients presenting for colonoscopy is predominantly pakeha. Few Maori people present for colonoscopy at MCH which suggests issues to be explored. Colonoscopy is undertaken predominantly as a diagnostic and surveillance tool for colorectal cancer. Maori people, according to the MOH report (2006), have a lower incidence of colon cancer than non-Maori. This same report goes on to mention that new information is surfacing suggesting that the incidence of colon cancer in Maori may actually be higher than initially thought and may *equal* non-Maori. More alarming, Maori mortality rate from colorectal cancer is higher than non-Maori, presumably due to late presentation. Also the Maori mortality rate, (in contrast to the decrease in mortality rate for non-Maori) increased between 1980-1999, possibly due to the disparity in access to services (Blakely, Ajwani, & Robson, 2004). Reducing post colonoscopy pain by using CO<sub>2</sub> may encourage colonoscopy compliance for diagnosis as well as future return for surveillance.

CO<sub>2</sub> use in colonoscopy was yet to be recognised and taken seriously in New Zealand. A randomised controlled trial of the use of this gas at the commencement of its use at MCH, but also in New Zealand, was considered to be of value. Not only would MCH patients' benefit, but also the outcome from patients in a New Zealand setting will have better generalisability to the wider New Zealand colonoscopy population and to other endoscopy units. Personal testimony holds a lot of strength to influence others. The use of CO<sub>2</sub> and a concurrent RCT at the outset would be a benchmark and an encouragement to other endoscopy

departments to consider using this gas and result in more patients in benefiting from the reduction of discomfort post colonoscopy.

## **1.6 Overview of the Study**

Chapter one introduces the background of the trial and its purpose, highlighting the aim and the hypothesis. This chapter goes on to discuss the significance of the trial in the field of New Zealand Gastroenterology practice.

Chapter two overviews the literature which was explored to establish a greater understanding of the surrounding issues, and to provide justification for the research.

Chapter three provides a description of the study design and methods. This includes an explanation of the preparation steps for the trial and overviews some of relevant ethical issues.

Chapter four outlines the results of the statistical analysis. The results are discussed in relation to relevant literature in chapter five; followed by a presentation of the limitations, implications for current practice and suggestions for future research.

Chapter Five concludes with the results. These results are discussed in relation to context along with further discussion covering the implications of the findings in

practice. The limitations of the trial and recommendations for future research are outlined.

The reference list was compiled using the referencing method of the American Psychological Association (1994) and the appendices display some of the supporting documents.

## **1.7 Summary**

Colonoscopy is the gold standard procedure for both diagnosis and surveillance of the colon. During the procedure it has been traditional to use air to insufflate the colon. There is a slow growing international practice for utilising CO<sub>2</sub> to insufflate the colon instead, which results in a reduction of pain experienced during recovery. This method had not been explored for use in New Zealand.

An experimental design using a randomised controlled double blind clinical trial was undertaken to determine the cause and effect relationship and establish if CO<sub>2</sub> insufflation reduces post colonoscopy pain.

This chapter introduced the background to the study, its aim and hypothesis. The significance of this research within the New Zealand setting is discussed. Finally an overview of the study is outlined, which leads into a literature review that is presented in the next chapter.

# Chapter Two

## Literature Review

### 2.1 Introduction

This chapter considers the relevant literature in relation to the use of CO<sub>2</sub> insufflation during colonoscopy to reduce post colonoscopy pain. Conceptualisation of this study involved identifying and exploring the current state of knowledge around the dependent variable, pain, and then understanding some of the independent variables involved.

As reducing peoples` experience of pain post colonoscopy is the overall focus of this study, post colonoscopy pain is examined. The type of pain involved is reviewed and the factors that influence this pain are considered. The extent of the problem is outlined, along with the risks associated with not controlling this pain.

A focus of the literature search was also to explore and critically analyse the current state of knowledge on methods available to relieve post colonoscopy pain. Five methods were highlighted in the literature search. These are discussed concluding with a clear case for the benefits and safety of CO<sub>2</sub> use. A literature search using Medline, CINAHL, Cochrane data bases (1984-2009), library resources and the Internet were used to access information.

## **2.2 Causes of post-colonoscopy pain**

Visceral pain is the specific type of pain that is commonly experienced following colonoscopy, but it needs to be reinforced that this pain originates in the process of what happens intra procedure. There are many factors that influence this post colonoscopy pain.

### **2.2.1 Visceral pain**

The colon is a visceral organ which evokes a variety of sensations, viscera being the internal organs within the abdominal cavity. Visceral sensations are an every day occurrence and vary from non painful sensations like a feeling of fullness to the urge to defecate as well as the sensation of pain (Bushnell, Strigo, & Duncan, 2003). Al-Chaer (2000) describes the sensations experienced by viscera as predominantly limited to pain and discomfort compared to the complex and wide range of sensations that the skin experiences. Further more visceral pain is commonly diffuse and poorly localized (Al-Chaer, 2000; Cervero & Laird, 1999; Devine, 2005).

The visceral nociceptors of the colon are not stimulated by normal everyday transport of material, air or the peristaltic movement of the colon, but are thought to be high threshold receptors. Transduction occurs with stimuli in the noxious range. The colon can be cut with minimal pain felt. However in contrast severe pain can be experienced with strong contractions, distension or ischaemia (Porth, 2005).

Miller and Alpert (2006) describe three causes of visceral pain; tension, inflammatory and ischaemic pain. Inflammation of the colon may stimulate a painful response and likewise with ischaemia. Visceral C nociceptors will be stimulated resulting in pain. Tension pain is commonly described as colic, which results from an increase of forceful colon contractions, over and above normal peristalsis. Tension pain can also arise from distension of an organ. It is this distension of the colon and/or strong colon contractions that are the common cause of post-colonoscopy pain (Lee, Wang, Chiu, Lin, & Huang, 2006).

### **2.2.2 Intra colonoscopy Pain**

The pain caused during a colonoscopy is predominantly a pain induced from both the endoscope stretching the colon and also from the air being induced, which can cause strong spasm (contraction) of the colon. This air insufflation during colonoscopy can cause painful abdominal distension (bloating) during and commonly continues to have an effect after the colonoscopy.

Patients with an existing abdominal condition, such as Irritable Bowel Syndrome (IBS), Diverticulitis, Inflammatory Bowel Disease (IBD), colon cancer and with previous abdominal surgery, may also experience added abdominal pain intra-procedure and post-procedure. Visceral sensitisation can be a factor in both IBD and IBS. Visceral sensitisation may occur when the colon experiences extended visceral stimulation, e.g. hypoxia and inflammation. Once sensitised, the nociceptors will respond to less noxious stimuli e.g. motility, resulting in pain

(Porth, 2005). Although initial studies suggested that visceral hypersensitivity was limited to the gut it is now thought to also include a central nervous system sensitisation component as well (Davis, et al., 2003; Moshiree, Zhou, Price, & Verne, 2006).

### **2.2.3 Post colonoscopy Pain**

Residual bowel gas from the colonoscopy causing distension and spasm is the main cause of the pain experienced post colonoscopy ( Lee, Vigil, & Leung, 2001; Lee, et al., 2006). Further expanded by Miller and Alpert (2006), discomfort also comes from distension of insufflated air within the colon and from the robust peristaltic contractions that are trying to expel the air. In one study most patients post colonoscopy had radiological colon distension; 39% had colonic diameter > 6cm and 18% of patients had > 10cm colonic diameter (Stevenson, et al., 1992). There are other causes of post-colonoscopy pain but these occur infrequently e.g. serosal tears with pneumatosis (Hilzenrat, et al., 2003) and colon perforation which is claimed by Pearl, McNally, Elster and DeNobile (2006) to be < 0.5% of cases, (including both overt perforation and micro perforation).

### **2.2.4 Factors determining post colonoscopy pain**

A study undertaken by Lee et al. (2006) of 1000 asymptomatic patients having colonoscopy, listed the following four points as the main factors determining post colonoscopy pain:

Duration of colonoscopy: The length of the procedure is directly linked with the presence of abdominal pain and also to the severity of the pain. It is assumed by Lee et al. (2006) that post colonoscopy pain is directly related to the amount of air used intra procedure. Factors, which may affect length of procedure, include technical difficulties, endoscopist skill and endoscopy manipulation was not measured. These latter factors are taken into consideration by Steinberg and Howden (1997, p. 444) who claim “Patient comfort during and after colonoscopy is influenced by several factors including the degree of technical difficulty, the duration of the procedure, and the level of expertise of the endoscopist”.

Female: Women are at higher risk of post colonoscopy pain. Lee et al. (2006) findings were similar to Saunders, Fukumoto, and Halligan (1996) which indicated that a deeper pelvis and decreased muscularity of abdominal wall predisposed women to difficult intubation of colonoscope. Various other reasons have been suggested; women have longer colons than men, leading to higher risk of colon looping and longer procedures (Saunders, et al., 1996; Saunders & Williams, 1996). As Hull and Church (1994, cited in Lee et al.,2006) mention there is more likelihood of women having had pelvis surgery predisposing to colon tortuosity. Hilzenrat et al. (2003) do not suggest being female, as such, as a risk factor. However they reported that, of the 20 % of patients in their study who experienced severe discomfort after their colonoscopy, more of these had previous abdominal surgery compared to those who had not experienced strong pain. Hilzenrat and his colleagues concluded that maybe this caused intra-abdominal adhesions resulting in reduced mobility of the colon.

Sedation / analgesia: The administration of pain relief and sedation during colonoscopy appears to provide some residual effect on post colonoscopy pain. A study by Lee et al (2006) showed patients receiving conscious sedation had on average a 32 minute delay of onset of pain after the procedure, but a shorter duration of pain of average of 121 minutes. Sedation/ analgesia did not have any effect on the presence and severity of abdominal pain. With the drive for being cost effective and facilitating faster discharge, it could be conceivable for patients to start experiencing abdominal pain after discharge.

Irritable Bowel Syndrome (IBS): Patients with history of IBS were not more likely to experience abdominal discomfort according to Lee et al (2006), but if they did experience pain it was more likely to be a prolonged episode. As mentioned earlier in this report it is now thought that these people have both a peripheral and a central sensitisation (Davis, et al., 2003; Moshiree, et al., 2006) causing hyperalgesia (reduced pain threshold and/or an exaggerated response to a painful stimulus) and also allodynia (prior non painful stimulus which now causes pain) (Moshiree, et al., 2006). Normal motility now causes pain. With the colonoscopic distension of air and subsequent spasm/ contractions this hyperalgesia and allodynia can result. Fukudo et al. (2002) extend this by suggesting that not only is visceral hypersensitivity occurring but also an abnormal intestinal reflex. This effect was shown in their study where repeated distension of the distal colon below sensory threshold induced an exaggerated motility of the colon in IBS patients. The study undertaken by Lee et al. (2006) summarized in the above four points was undertaken with asymptomatic patients only. The effect of patients who

present pre procedure with abdominal pain was not investigated. A further factor determining post-colonoscopy pain was highlighted by Lugay, Otto, Kong, Mason and Wilets (1996) namely intra-procedure complications, which will now be discussed.

Intra procedure complications: Intra procedure `occurrences` like abdominal pain, reduced oxygen saturation, hypertension and hypotension along with bradycardia were the common occurrences in a study undertaken by Lugay et al. (1996). Of their 405 patients, 69% of patient who had problems intra procedure also experienced problems post procedure with abdominal pain being the most common. The percentages of people experiencing complications intra procedure in the Lugay et al study may have changed since 1996. Nevertheless the outcome of this study adds to the four points made above (duration, female, medication and IBS) which indicates that factors starting during procedure time may impact on the incidence of pain post procedure.

### **2.3 The Extent of the problem**

It is common knowledge amongst gastroenterology nurses at MCH that patients regularly experience uncomfortable abdominal bloating post procedure. It is generally felt that any discomfort, after the procedure, is quickly relieved by passing air. Nevertheless, in some cases, pain is more of a problem and the occasional patient needs an extended recovery period due to strong abdominal pain. That patients at MCH are not alone with this problem of post colonoscopy

pain was confirmed by the comments of nurses questioned on this topic at a `Lower North Island Gastro Nurses Meeting` in October 2006. No statistical evidence of the extent of the problem of post colonoscopy pain is available at MCH at present. A new `gastroenterology nursing record` form is now developed which includes more accurate assessment and evaluation of pain relief methods as well as documentation of a follow up phone call 24-72 hours post procedure, asking if the patient has experienced continuing pain. This documentation will provide the means to clarify the local extent of post colonoscopy pain.

Internationally there is varying statistical evidence of the prevalence of post colonoscopy pain. A study by Lee et al. (2001) found that 59% of patients experienced bloating post colonoscopy; 14% of these reported this bloating to be moderate to severe. This study went on to record the patients reporting pain as a separate group and within this group there were only 3 patients out of 65 patients who experienced painful bloating. Abdominal bloating occurred, despite efforts to decompress the colon with the colonoscope intra procedure. Initially results identified a reduction of bloating, but bloating returned to 45% at 24-48 hours post procedure. Reports of pain 24-48 hours afterwards did not reach statistical significance. This study seems to indicate that minimal pain was experienced post procedure and that bloating could be experienced, even to the point of severe, without it being described as painful.

In contrast, other researchers confirm the prevalence of post colonoscopy pain / discomfort. Bretthauer et al. (2002) reported that 40% of 125 patients complained

of pain in the first few hours after colonoscopy reducing to 20% at 24 hours. A 48-53% incidence of abdominal pain post colonoscopy (with sedation and without) ranging from mild to severe, was reported by Lee et al. (2006), with 16% of these experiencing moderate pain and 0.9% describing their pain as severe. Hilzenrat, Fich and Odes (2003) even described a rather extreme statistic of “20% in whom severe abdominal discomfort develops after colonoscopy” (p.57). The extent of the problem is described by Newcomer, Shaw, and Williams (1999) in which 4% of people post colonoscopy take an unplanned day off work with abdominal pain and bloating being the main reason. Despite the wide range of reported incidence of people experiencing pain post colonoscopy, the evidence internationally demonstrates that post colonoscopy pain is a common problem.

#### **2.4 Importance of managing post colonoscopy pain:**

Gas distension is stated by Lee et al. (2006) as not usually harmful. Lee et al. (2001) elaborates and says that although abdominal distension is not usually dangerous, there can be some concern that excessive air can exacerbate chronic obstructive pulmonary disease, cause hypoxia in the elderly and even cause colon perforation or colon ischemia. Reducing retained air in the colon post colonoscopy will lower the risks of complications but also the associated discomfort and potentially reduce financial costs associated with longer hospital stays (Tasso, 2004). Most importantly from a gastroenterology perspective, reducing the pain post colonoscopy will aid patient satisfaction, encouraging the return of people for colonoscopy in the future.

## **2.5 Methods to relieve post colonoscopy pain**

The only interventions being used to treat post colonoscopy pain at MCH were non pharmacological methods. The main method used was encouraging the patient to adopt a variety of positions to encourage the passing of flatus and to ease abdominal discomfort. The literature search focused on what methods were currently being investigated internationally. The following are five methods found during the literature search ending with a method of insufflating the colon with carbon dioxide.

### **2.5.1 Decompression of the Colon:**

In order to relieve colonic distension and improve patient comfort after colonoscopy total decompression of the colon was tried by Lee et al. (2001). At the completion of their colonoscopy, 100 patients had the colonoscope reintroduced back to the caecum and then air was removed as the colonoscope was withdrawn. This decompression improved initial post colonoscopy bloating with 25% of decompression group experiencing bloating compared to 41% of control group. However 24 - 48 hours after the procedure the benefits of total decompression were temporary and the percentage of participants reporting bloating in the decompression and control group were 45% and 47% respectively. Lee et al. (2001) suggested that this might have been from air that had moved up into the small intestine. They concluded with the suggestion that total decompression was not worth doing on a regular basis.

In support of this, a study undertaken by Stevenson et al (1992) of abdominal films, showed 93% of patients had small bowel air one hour post colonoscopy, with 61% experiencing moderate to extreme distension. Decompression of just the *lower* colon prior to withdrawal of the endoscope is a common technique used by some endoscopist although the benefit of this may be limited by the effect of further air distension higher up.

Likewise, for the same reason as above, passing a flatus tube in patients experiencing post colonoscopy pain (which has been tried historically at MCH) may not be successful. In favour of the use of rectal tube placement, Steinberg and Howden (1997) carried out a trial with positive outcomes. At 30 minutes post procedure the satisfaction 10 point rating scale was 9.1 in the flatus tube group and 5.7 in the control group. The limitations of this study were that it was not blinded, restricted to men, only 67 patients and 10 patients exhibiting strong abdominal pain post procedure were taken out of the trial. In contrast, Hilzenrat et al. (2003) trialled the use of a rectal tube with 157 men and women post colonoscopy, and did not find any significant improvement in terms of abdominal bloating and discomfort at discharge or 24 and 48 hours later. Decompression methods either with the colonoscope or a flatus tube to reduce the subsequent distension, show limited usefulness.

### **2.5.2 Anti cholinergic Medication**

Traditionally an intramuscular or intravenous form of cholinergic blocker; an antispasmodic e.g. buscopan has been used very successfully to relax the gastrointestinal tract for symptomatic IBS. For the purpose of relaxing intestinal muscle; some endoscopists also use this drug during colonoscopy examinations.

The systemic effect of this drug drives its careful administration and limited use. The common side effects can be cardiac palpitations, dry mouth, difficulty urinating, orthostatic hypotension, eyesight impairment and anaphylactic reaction (Asao, et al., 2003; Mui, et al., 2004). Anti cholinergic drugs are contraindicated for use in patients with heart disease, prostatic hypertrophy, and narrow angle glaucoma (Asao, et al., 2003).

There is mixed opinion on the usefulness of anti cholinergics for colonoscopy intra procedure or post. Mui et al (2004) considered the use of intravenous hyoscine N-butylbromide (buscopan) during colonoscopy and concluded that hyoscine N-butylbromide impeded colonoscopy insertion, caused an increase in patient discomfort and caused greater hemodynamic instability. Depending on consultant preference at MCH, intravenous buscopan is used to cause a 5 -10 minute colonic relaxation effect intra procedure, to aid colonoscope advancement when there is a lot of spasm. However it is not considered a method to reduce colon cramping post colonoscopy because of its short action and potential systemic effects.

### 2.5.3 Peppermint Oil

Peppermint oil is a herbal medicine which has been found to have a local action of inhibiting contraction of smooth muscle of the gastrointestinal tract (Yamamoto, et al., 2006). The major component of peppermint oil is menthol and although its action is not completely clear, it is thought to alter the calcium ion transport in the smooth muscle receptors (Liu, Chen, Yeh, Huang, & Poon, 1997). Menthol is rapidly absorbed and excreted almost entirely in the urine (Hiki, et al., 2003). It is thought to be helpful in reducing pain associated with IBS, also endoscopic and radiological examinations (Asao, et al., 2003; Asao, et al., 2001; Hadley & Gaarder, 2005; Hiki, et al., 2003; Yamamoto, et al., 2006). It has a similar effect as the antispasmodic action of buscopan, but in contrast, it has minimal side effects (Asao, et al., 2003).

The side effects of peppermint oil are thought to be anal burning (when high concentrations are used), and epigastric pain (when there is early release of oral peppermint capsules resulting in relaxation of the lower oesophageal sphincter). In a study by Asao et al. (2001) peppermint oil was deposited into the colon during colonoscopy. Of the 409 patients no reported adverse effects to peppermint oil were noted, during or afterwards. Rectal biopsies were also taken with no pathologic changes noted.

Due to peppermint oil's rapid absorption and its local action in the colon, it needs to be directly deposited there. Asao et al. (2003) study used either an enema tube or

gave peppermint oil via the barium, during a double-contrast barium enema. There was an equal effect, but fewer side effects, than noted with buscopan. Another method of ensuring its action in the colon is by way of the endoscope. Asao et al. (2001) proposed a method of intraluminal administration of peppermint oil using a hand pump apparatus via the endoscope, in order to reduce over active contraction to aid visualization during colonoscopy. They found that in their sample size of 445 patients (409 in treated group and 36 in control group); within 20 seconds there was strong colonic relaxation. They did not know how long the effect lasted for, but it was probably longer than 20 minutes because the sigmoid was relaxed and without spasm at completion of the colonoscopy. Amounts of 30ml of peppermint solution were injected via a hand held pump apparatus at least 3 times during the colonoscopy.

Administering peppermint oil intra procedure using the endoscope may have some effect post colonoscopy to reduce spasm, but its usefulness is limited. There is no certainty as to the duration of its effect. Also it is a time consuming method of injecting large quantities of solution intra procedure. The use of antispasmodics intra procedure is an endoscopist preference. Antispasmodics have been suggested by some studies to assist colonoscopy (Marshall, et al., 1999; Saunders, et al., 1996). In contrast others suggest that the use of antispasmodics intra procedure may actually impede endoscope advancement by reducing muscle tone (Mui, et al., 2004). The use of an antispasmodic agent during colonoscopy is controversial.

Oral peppermint capsules are an alternative method to get peppermint oil into the colon e.g. colpermin. These latter are capsules that are 0.2 ml of peppermint oil surrounded by gastrointestinal resistant hard gelatin capsule. Colpermin's effect starts in the small intestine and has been used in symptomatic relief of IBS (Liu, et al., 1997). A pharmaceutical web site called Rxmed claims that a study was undertaken showing that colpermin dissolution rate was 143 +/- 14.8 minutes. Colpermin could be a useful tool but the dissolution time makes for a restriction in its action for the immediate alleviation of post colonoscopy pain (RxMed, 2005), but may have a role when given to patients experiencing post colonoscopy pain to assist them *after* discharge. As a result of this literature search the use of peppermint oil capsules as a pain relief option for post discharge is now suggested on the colonoscopy discharge instruction. The utilisation of peppermint oil however has limited usefulness and does not address the route cause of post colonoscopy pain.

#### **2.5.4 Paracetamol**

When benchmarking other gastro units in New Zealand and also from the researchers experience in the United States, MCH was not alone in analgesia not being offered on a routine basis post colonoscopy. Use of non pharmacological therapies that support analgesics are often under utilised and can enhance analgesia (Sherwood, McNeill, Starck, & Disnard, 2003). In contrast to this approach the Gastroenterology department at MCH have historically used only non pharmacological methods and a pharmacologic approach was not being used.

A search of the literature for analgesia with minimal side effects resulted in looking at the efficacy of paracetamol to relieve post colonoscopy pain. According to White's (2002, p. 580) review on the management of pain after ambulatory surgery; "Of the non opioid analgesics, acetaminophen is potentially one of the most useful, yet vastly underused in the ambulatory setting." Removing the air and the subsequent distension needs to be a main focus in relieving post colonoscopy pain, but a combination with an analgesic like paracetamol (acetaminophen) needs to be considered. Paracetamol has been the cornerstone for pain management for the last 40 years and continues to be so. It is considered to a first line analgesic for most acute and chronic conditions because it is effective, well tolerated, cost effective and when used within therapeutic doses, it is safe (Knaggs, 2006; Whelton, 2005).

The action of paracetamol since its introduction in 1960 has been unclear. However in recent days there is growing evidence to suggest that not only does it have a peripheral action of inhibiting inflammatory mediators but a greater central action too. This central nociceptive mechanism is still not established but the potential mechanisms for this have been suggested as including; inhibition of a central nervous system COX-2, inhibition of susceptible to paracetamol COX-3, and modulation of inhibitory serotonergic pathways (Power, 2005; Whelton, 2005). Nevertheless regardless of the exact mechanism of paracetamol analgesic action with a peripheral action at the distended colon or with its central action, paracetamol could be used to relieve the pain in conjunction with other methods to alleviate the air distension (Raffa, 2001).

Since this literature investigation MCH now offers paracetamol post colonoscopy to patients who are experiencing abdominal pain, when they are awake and responsive. It is also suggested on the discharge instructions as a choice, along with peppermint oil, to alleviate continued discomfort. Paracetamol as a pharmacological option will have an action of inhibiting the pain pathway, but the air distension of the colon is still occurring. The cause of the pain is still there so a method to alleviate this root cause of post colonoscopy pain could have huge benefits for the patient.

### **2.5.5 Carbon dioxide Insufflation**

The utilisation of carbon dioxide (CO<sub>2</sub>), instead of air, to insufflate the colon was highlighted in the literature. The benefit was claimed that CO<sub>2</sub> absorbed far more rapidly than air and consequently reduced the distension quickly. There are a number of published trials which showed that when CO<sub>2</sub> is used instead of air to insufflate the colon during colonoscopy, post-colonoscopy pain is reduced (Bretthauer, Thiis-Evensen, et al., 2002; Church & Delaney, 2003; Sumanac, et al., 2002).

The use of CO<sub>2</sub> instead of air to insufflate the colon during colonoscopy is not a new discovery. It was first recommended by Becker (1953, cited in, Bretthauer, Thiis-Evensen, et al., 2002) as a method to reduce the risk of colon explosion during electrocautery. This was supported by Rogers (1974) and Williams (1986). The outcome of these studies was not only a safe environment for polypectomy but

the CO<sub>2</sub> benefits of minimising distension were gradually appreciated. Hussein and his colleagues (1984) found that x-rays 30 minutes after colonoscopy on all 40 patients who had received CO<sub>2</sub> showed no residual air compared to excessive distension in 19 out of 20 who had received air insufflation. Phaosawasdi, Cooley, Wheeler and Rice (1986) looked at the success of barium enema post failed colonoscopies. Patients who had received CO<sub>2</sub> intra colonoscopy were noted to be more comfortable than patients who had received air.

One of the early randomised controlled trials looking at the use of CO<sub>2</sub> in reducing post-colonoscopy pain was Stevenson, Wilson, Wilkinson, Norman, & Goodacre (1992). In their RCT of 56 patients they found no statistical difference in intra procedure pain but significantly less pain in patients 6 and 24 hours after colonoscopy. They also looked at the amount of air distension in the colon radiologically at one hour post colonoscopy. Of the CO<sub>2</sub> group 96% had minimal retained gas where as the air group showed 18% with a colon diameter of >10cm and 57% were >6cm in colonic diameter. These latter results confirmed the findings of Hussein et al. (1984) which are discussed in a previous paragraph. This RCT undertaken by Stevenson and colleagues had limitations due to the small numbers, but it served well to start the slow acceptance of the benefits of CO<sub>2</sub> use during colonoscopy.

It is only in the last few years that a growing number of RCTs have added weight to this claim of reduction of pain with use of CO<sub>2</sub>. Bretthauer and his colleagues in Denmark looked at carbon dioxide use in 202 patients having flexible

sigmoidoscopy (Bretthauer, Hoff, et al., 2002). Of the patients receiving CO<sub>2</sub> (N=97) 84% had no pain an hour later. In contrast to this, 64% of the air group (N=105) experienced no pain. These researchers went on to undertake a RCT with 240 unsedated patients who reported that more than 90% of CO<sub>2</sub> group (N=121) reported no pain post procedure. This was compared to the air group (N=119) where 40% reported pain in the hours post colonoscopy. This later study randomised whole sessions to either CO<sub>2</sub> or air to avoid unblinding the gas changing between patients (Bretthauer, Thiis-Evensen, et al., 2002).

This outcome was again reflected in a similar trial undertaken by Sumanac et al (2002) in Canada looking at 97 sedated patients. At one hour post colonoscopy 7% of CO<sub>2</sub> group (N=49) had pain in comparison to 45% of the air group (N=51). They took supine abdominal X-ray pictures one hour post colonoscopy which reinforced this outcome by showing that 71% of air group had colonic distension of > 6cm in contrast to only 4% of CO<sub>2</sub> group. These researchers also acknowledged the ease of insufflation of CO<sub>2</sub> with a recently available commercial gas delivery system (provided by the manufacturer who paid for the statistical analysis).

Church and Delaney (2003) added their voices to the RCT results and confirmed, with 247 patients that their CO<sub>2</sub> group (N=123) had a statistically significant drop in pain levels compared to air (N=124) at 10 minutes post procedure. Pain scores from a 10 point analogue scale were  $2.1 \pm 0.2$  for air group and  $0.9 \pm 0.2$  for the CO<sub>2</sub> group. Maybe greater statistical significance may have been apparent if data

was collected again at one hour (like some of the other CO<sub>2</sub> RCTs). This trial was blinded to patient only.

More recently Bretthauer and his colleague (2005); this time with sedated patients (in contrast to their earlier studies), confirmed again the outcome of a reduction of pain with CO<sub>2</sub> use. They showed at 1 hour post colonoscopy, using a 100mm (VAS), that air patients (N=51) experienced a mean score of 23mm, where as CO<sub>2</sub> group (N=52) had a score of 4mm.

After colonoscopy a significant amount of air is usually retained within the colon. Air then has to pass out the intestinal tract and exit by way of the rectum. It is this residual air causing distension and spasm that is the main cause of pain experienced post colonoscopy (J. G. Lee, et al., 2001). The advantage of CO<sub>2</sub> is that it is rapidly absorbed by the colon lumen (Bretthauer, Thiis-Evensen, et al., 2002). Cotton and Williams (2003) claim that CO<sub>2</sub> is absorbed 100 times faster than air. This results in less distension at the end of the colonoscopy and less associated pain.

This use of CO<sub>2</sub> has been investigated for its reduction in pain experienced, but also its safety in regards to CO<sub>2</sub> retention. The question of CO<sub>2</sub> being rapidly absorbed into the body and excreted via the lungs resulting in arterial CO<sub>2</sub> retention and subsequent acidosis has been investigated. Bretthauer et al (2002), in a RCT on the use of CO<sub>2</sub>, focused not only on pain, but also measured end-tidal

CO<sub>2</sub> (ETCO<sub>2</sub>) as an indication of retained CO<sub>2</sub> (pCO<sub>2</sub>). They found the increase of ETCO<sub>2</sub> in *unsedated* patients was not statistically significant.

These researchers then continued in 2005 with an RCT that focused on the levels of CO<sub>2</sub> in *sedated* patients, who are in theory more likely, because of impaired respirations, to retain CO<sub>2</sub> (Bretthauer, et al., 2005). Once again these researchers found that the increase in ETCO<sub>2</sub> with *sedated* CO<sub>2</sub> patients was *not* statistically significant and interestingly the increase that was revealed, although still insignificant, was higher in *sedated* patients of both air and CO<sub>2</sub> groups. This suggested that the level of sedation is the primary cause of CO<sub>2</sub> retention, not the use of CO<sub>2</sub>. Excluded from their research were known CO<sub>2</sub> retainers and patients with severe chronic obstructive respiratory disease (CORD).

The literature is consistent regarding the safety of CO<sub>2</sub> insufflation. Dellon, Hawk, Grimm and Shaheen, in a systematic review of the use of CO<sub>2</sub> during gastrointestinal endoscopy claimed, “in nine RCTs and six other studies in which safety was assessed, CO<sub>2</sub> was not retained and no adverse pulmonary events related to CO<sub>2</sub> insufflation were seen “(2009, p. 844).

Many researchers thought that CO<sub>2</sub> was slow to be utilised, despite obvious patient benefits, mainly due to the technical difficulties of delivering this gas (Church & Delaney, 2003). The use of CO<sub>2</sub> internationally is slowly growing since there is now a commercially available CO<sub>2</sub> delivery system, which has been on the market internationally in the last few years but only recently available in New Zealand.

The call to use CO<sub>2</sub> has been echoed by many researchers including the internationally renowned authors of an endoscopy technique text book, `Practical Gastrointestinal Endoscopy: The Fundamentals`, who state; “ Few colonoscopists, regrettably, use CO<sub>2</sub> insufflation, although it has much to commend it from the patients` point of view (Cotton & Williams, 2003, p. 106).” Domagk and his colleagues recently commented that air is still used in 90% of the endoscopy centres internationally (Domagk, et al., 2007). According to personal communication with M Bennett, Olympus national sales manager, it presently has widespread use in Western Australia but not used in New Zealand (personal communication, April 3, 2007). Since undertaking this research there is now growing interest in New Zealand.

The use of CO<sub>2</sub> is not a recently discovered and untested hypothesis in fact it has been in use in some centres for many years. The benefits of the effect of CO<sub>2</sub> in reducing post colonoscopy pain was strengthened by the testimony of personal communication (email), from Dr G Forbes, Head of Gastroenterology and Hepatology, Royal Perth Hospital where he and all their endoscopists have been using this method. He claims “We’ve been using CO<sub>2</sub> for colonoscopy insufflation probably for 5 years now. It’s clearly led to a reduction in the amount of post colonoscopy abdominal distension and pain...I strongly recommend you to make the change” (personal communication, August 22, 2007). As mentioned earlier, CO<sub>2</sub> insufflation has now widespread use in Western Australia.

## 2.6 Summary

This chapter demonstrated the issues around the dependent variable, pain that some people experience during and after colonoscopy. Some of the independent variables that influence the experience of pain post colonoscopy were discussed. The importance of managing this post colonoscopy pain was explored. A focus on a range of methods to relieve colonoscopy pain including pharmacologic agents highlighted that although panadol and peppermint oil may be helpful in reducing discomfort, it is the use of CO<sub>2</sub> that may fix the root cause and shows the most potential in making the biggest difference. It was highlighted that despite numerous trials which show that CO<sub>2</sub> is of benefit, there are many places in the world which still do not use it including New Zealand.

In conclusion to this chapter some personal communication was shared which added insight into the relevance of this study. A Gastroenterologist strongly commended, as experienced from his practice, the use of CO<sub>2</sub> to reduce patient discomfort post colonoscopy (G Forbes, personal communication, August 22, 2007).

The observations from this literature search are examined in the present study by means of a randomised controlled double blinded clinical trial which is discussed in the following chapter.

# Chapter Three

## Methodology and Methods

### 3.1 Introduction

My goal was to research an area of practice that was causing concern; this being the pain that some patients experience post colonoscopy. Limited interventions were being used to reduce this pain. The previous chapter described the search undertaken to find a method being used or trialled to relieve this pain. This search highlighted the use of CO<sub>2</sub> in some endoscopy units around the world.

There were already several randomised controlled trials (RCT) that had been done in the last 20 years that all showed a statistical improvement in pain with the use of CO<sub>2</sub> compared to air. With undertaking the present trial it was decided to do a replicated trial. Exact replication in any one trial was not chosen but what resulted in this trial was a combination of the methods used in previous similar trials. A systematic review focusing on the evidence from RCTs looking at the use of CO<sub>2</sub> insufflation during endoscopy found that meta analytic techniques could not be done due to the “wide range and heterogeneity of studies (Dellon, et al., 2009, p. 2)”. Despite this variance all the studies still showed a clear improvement of pain with the use of CO<sub>2</sub>.

CO<sub>2</sub> for the purpose of insufflation in colonoscopy had never been used in New Zealand. It was thus decided to explore its use in New Zealand. At the outset of the use of CO<sub>2</sub>, a randomised controlled trial looking at the cause and effect of CO<sub>2</sub> use during colonoscopy was commenced July 2008 in the Gastroenterology Department where the researcher worked. In order to measure a cause and effect and test a therapeutic intervention a RCT is the gold standard (Jolley, 2004).

In this chapter the methodology is outlined and then the study design is expanded.

### **3.2 Methodology**

Quantitative research methodology was chosen. Experimental research is quantitative research; taking the objective/ positivist assumptions and doing research that answers questions in a measurable way. Quantitative research is focused on testing a hypothesis and discovering cause and effect relationships that can be analysed using statistical measures (Axford, et al., 2004). Harris (2004) explains that quantitative research is about a scientific approach of measuring empirical entities (existing in the world and observed via the senses). In the context of this research the ability to show that a treatment intervention (air or CO<sub>2</sub>) works, is essential to evidence based practice.

### 3.3 Method

The design used was a double blinded, randomised controlled trial comparing the effects of CO<sub>2</sub> insufflation to air insufflation on pain score ratings at (time intervals) post procedure. This allowed the hypothesis to be tested and cause and effect to be examined.

The experiment took place in a clinical setting; a Gastroenterology Department in the lower North Island of New Zealand. The independent variable is the type of gas used for insufflation (CO<sub>2</sub> and air). The dependent variable was the pain score expressed by the participant post colonoscopy.

The consenting participants were randomly assigned to the control group that received the standard gas (air) or to the experimental group that received CO<sub>2</sub>. A double blind study was chosen to reduce bias from the researcher, gastroenterologist, research assistants and participants. A self reported numeric rating scale (NRS) was used to measure the intensity of pain experienced during the procedure and post procedure at 10, 30, 60 minutes and 24 hours (the 24 hour time period data was not included in the final analysis).

Intravenous sedation and analgesia was given during the procedure at the discretion of the endoscopist. Commonly 2-5mg of intravenous (IV) hypnovel are used and 25-100mcg of IV fentanyl. Occasionally 10-20mg of IV buscopan is also used to reduce spasm of colon.

### **3.3.1 Trial Preparation**

There was considerable preparation prior to commencing the trial. The necessity of specialised equipment to deliver the CO<sub>2</sub> resulted in a process to obtain this equipment and ensure its safe use. Trial methods needed to be clearly understood by all 16 department staff (referred to hereon as research assistants). Communication with the Pharmacy Department, eliciting their support and involvement was part of the trial preparation. Pain management issues needed to be addressed by the research assistants. This involved increasing a knowledge base, reviewing basic pain assumptions and training in pain assessment skills to ensure pain scores data were collected appropriately. The details of the steps involved in the preparation for this trial are described as follows.

#### **3.3.1.1 CO<sub>2</sub> Delivery System**

The use of CO<sub>2</sub> to insufflate the colon during colonoscopy had not been used in New Zealand previously so the equipment required to deliver this gas for endoscopy was not available in New Zealand prior to the trial commencing. A company, which is the major supplier of endoscopy equipment nationally, was approached and they offered to obtain this equipment from an international source. Two endoscopy units in Perth, Australia were contacted and photos of the equipment involved were obtained. A choice was made to replicate the equipment used by these Australian hospitals for many years (with wide spread use throughout Western Australia), rather than wait for the automated- commercial CO<sub>2</sub>

regulator. Although now available, the automated CO<sub>2</sub> regulator for colonoscopy was not on the market in New Zealand at the time of commencing the trial.

Standard practice for colonoscopy is for air to be delivered into the colon via a bottle attached to the endoscope. This is also the receptacle to hold water (`water bottle`). Both this air and water then passes intermittently through the endoscope at the control of the endoscopist pressing a button on his hand piece of the endoscope. The Olympus CO<sub>2</sub> delivery system required drawing CO<sub>2</sub> from a gas cylinder, which had a two stage regulator, and a flow meter which controlled the flow. This gas was then delivered to a CO<sub>2</sub> `water bottle` (MAJ902), then on into the endoscope (appendix 16 for photos).

The request was made for the CO<sub>2</sub> delivery system in November 2007. The equipment arrived in May 2008. The focused training of the research assistants was not commenced until this equipment was on site, and the reality of the trial was then tangible.

### **3.3.1.2 Safe handling of Medical Gas**

Once CO<sub>2</sub> gas equipment was delivered the safe handling of this medical gas needed to be addressed before we started using it. The CO<sub>2</sub> tank supplier provided in-service on safe handling of this gas for all the Gastroenterology nurses. Handling of tanks was taught along with the education on CO<sub>2</sub> itself (Material safety Data Sheet was stored in department, see appendix 9). The researcher

followed this by further reinforcement of safe handling skills at the department nurses meeting. When the trial started the researcher provided one on one support for the nurse who was in the procedure room setting up and managing the CO<sub>2</sub> equipment during that endoscopy session. This support was given until all nurses were confident with the equipment set up and also management of blinding.

### **3.3.1.3 Training Research Assistants**

This research was undertaken in the Gastroenterology Department involving all staff. This included four endoscopists, seven nurses, two reception staff, one care assistant and two endoscope technicians. These staff all had roles to play in ensuring the trial design was carried out according to the agreed research protocol.

All of the research assistants received training in the trial methods before commencing. Training was provided formally at several of the nurses meetings. Individual training was given to all the other staff (reception, care assistant, technicians and endoscopists) on a one to one basis. One of these staff members who would be key to ensuring appropriate access/sampling of the population group to be undertaken was the receptionist. Her role in sending out the appointments, information letters and consent appropriately was crucial. I continued to support and oversee the roles of all the research assistants throughout the trial.

To reinforce the verbal explanations a written handout explaining everyone's roles and the trial method was given to all involved staff (appendix 4). Each person needed to be clear on their own role and also on each others roles. I was aware that, with the number of research assistants involved, communicating the trial protocol needed to be very clear. Over the six month period I was not always able to be present, but I became confident that trial methods were continued thoroughly even when I was not overseeing things directly.

#### **3.3.1.4 Pain management**

Pain management issues were addressed leading up to the trial by instigating both formal and informal discussions. These discussions were important as the ultimate goal of the research was to offer a treatment for all colonoscopy patients to reduce pain post procedure and so pain management issues needed to be brought to the forefront.

The researcher provided a training session for the nurses on the topic of `Pain; the 5<sup>th</sup> Vital Sign` (appendix 7). This covered pain physiology and pathophysiology, pain assessment skills and a discussion on the different assumptions on pain that may influence our pain assessment. This discussion was aimed to help highlight to the nurses the importance of patients self report of pain and to not let our assumptions influence the outcome.

A year before, the trial a new gastroenterology nursing record (appendix 8) had been developed. This allowed the recording of pain scores, data that had not been captured previously. This documentation tool would be used as the trial data collection tool. The nurses had been using this tool for about six months before the trial commenced. This facilitated the collecting of pain scores to become normal routine. Thus it was easier during the trial period to ensure adherence by the research assistants (nurses) to collect the data at the designated times because undertaking pain assessment and documenting was already common practice.

### **3.3.1.5 Testing the Procedure**

Carrying out a pilot test to ensure that potential problems can be anticipated and rectified before starting is suggested by Cone and Foster (2006). The decision was made to carry out a preliminary test of two real patients consenting to get CO<sub>2</sub> unblinded. The goal of this was that as we had not yet used the CO<sub>2</sub>, the technicalities of use of the delivery system would be smoothed prior to the first trial participant. CO<sub>2</sub> was delivered smoothly to both the patients in the preliminary test and we were reassured that the technical aspects of the delivery system were under control.

Both these patients had a positive experience with minimal pain experienced post procedure, but one in particular had a *very* good outcome with the CO<sub>2</sub> use. Jane (pseudonym) has crohns disease and has had numerous colonoscopies over the years. She commonly experienced considerable abdominal pain, cramping and

bloating after colonoscopy and so was naturally very anxious every time she came for this procedure. The previous endoscopist had been unable to get the endoscope around to the caecum due to colon tortuosity and the pain experienced. This procedure was now months later, and as she had been symptomatic, it was another attempt to view the whole colon.

The procedure was technically difficult and took one and a half hours opposed to the average 30 minute procedure, however this time there was success from the endoscopists perspective as the caecum was reached and the terminal ileum was intubated with the scope. There was active crohns visible in the small intestine which now explained the exacerbation of her symptoms in the last few months. Jane could now be treated more appropriately.

There is a clear association with the length of the procedure (amount of gas insufflated) and abdominal pain (Lee, et al., 2006). Added to this Jane was someone with a past history of a painful recovery post colonoscopy. We were thrilled to see Jane sitting up having a cup of tea feeling comfortable only five minutes after the procedure and remaining comfortable until discharge. A follow up phone call the next day confirmed that she had not had any abdominal pain or bloating over the 24 hours afterwards. Her story can be an example of the benefits of the use of this gas and an illustration of the human side of undertaking a clinical trial. The technical aspects of the pilot test with the two patients had gone smoothly and it had been encouraging to see first hand an indication of the benefit of CO<sub>2</sub>

### **3.3.2 Pharmacy Support**

CO<sub>2</sub> is a medical gas (appendix 9) and is covered under the medicines act. This RCT was then in effect a clinical trial. The Pharmacy department was consulted when seeking hospital approval for undertaking the trial. They were very positive about supporting the trial in a tangible way. I consulted with them on the trial methods. Pharmacy helped with organising the randomisation envelopes by using an excel program to obtain random numbers for 120 women and 120 men. Slips of paper stating the gas to use (air or CO<sub>2</sub>) were placed inside the envelopes. They held the master copy, of what gas each number received, till the end of the trial.

### **3.3.3 Recruitment and Selection of Patients**

Quantitative researchers are focused on being able to generalise their results therefore there is great effort to seek a sample that is reflective of a broader group or population. This population group is described by Polit and Hungler (1999, p. 180) as the `target population` and the `accessible population` as to who is available to be studied. In this RCT the accessible population would be all patients who have colonoscopy at MCH and then with random sampling a representative group of the accessible population would be drawn.

The description of the sampling frame for this RCT was

- New patients with symptoms referred for colonoscopy and also patients for surveillance colonoscopy (for reasons of past history of colon cancer,

adenomas, very strong family history of colon cancer or inflammatory bowel disease).

- Age span for referral is wide, with high numbers of over 60 yrs, no children under 14.
- Sex of the population base is both male and female.
- Ethnicity: Predominantly pakeha with a minority of other ethnicities including Maori, and Chinese immigrants (statistics of ethnicities not available).

Trial participants were recruited from the waiting list for elective colonoscopy at MidCentral Health. They were invited by mail to take part in the trial in conjunction with their planned colonoscopy. The Gastroenterology receptionist mailed out the information and consent forms, included with their appointment information. To allow prospective trial participants time to read the information sheet, think about it, seek advice and ask questions, the invitation to be a part of the trial was only sent to prospective colonoscopy patients who were booked at least two weeks in advance of their appointment. No invitations were sent to `in patients` or to acute/urgent patients who were booked at short notice.

The information sheet gave a phone number for them to call the principal researcher with any questions (appendix 1) The consent form (appendix 2) was included with information sheet and this was brought with them for their appointment if they chose to participate. When the patient presented for their colonoscopy one of the Gastroenterology nurses confirmed their consent or non-

consent. This nurse proceeded to carry out a health assessment, answer any questions and as appropriate confirm trial suitability.

#### Exclusion Criteria

- Age under 16 and age over 90
- Inability to understand participant information
- Patients with severe chronic obstructive pulmonary disease (COPD).  
Insufflation at a rate that exceeds the normal rate of expiration could result in retention of CO<sub>2</sub> and subsequent acidosis. This is discussed fully later.
- Refusal to participate

Some of the above exclusion criteria information on a prospective patient was not available prior to the appointment being sent. The receptionist books patients from a printout off the waiting list with demographic information only available. The receptionist sent out trial invitations to patients within the age criteria. The exclusion criteria as stated above were stated in the information sheet (appendix 1). On presenting for their appointment the participant's suitability for inclusion in the trial was assessed by one of the nurses.

Experimental research and in particular RCTs are typically undertaken under controlled conditions. Therefore Heard and Harris pose the question to be considered about the generalisability of this type of study against other settings (Heard & Harris, 2004). In contrast the setting of the present trial is undertaken in a

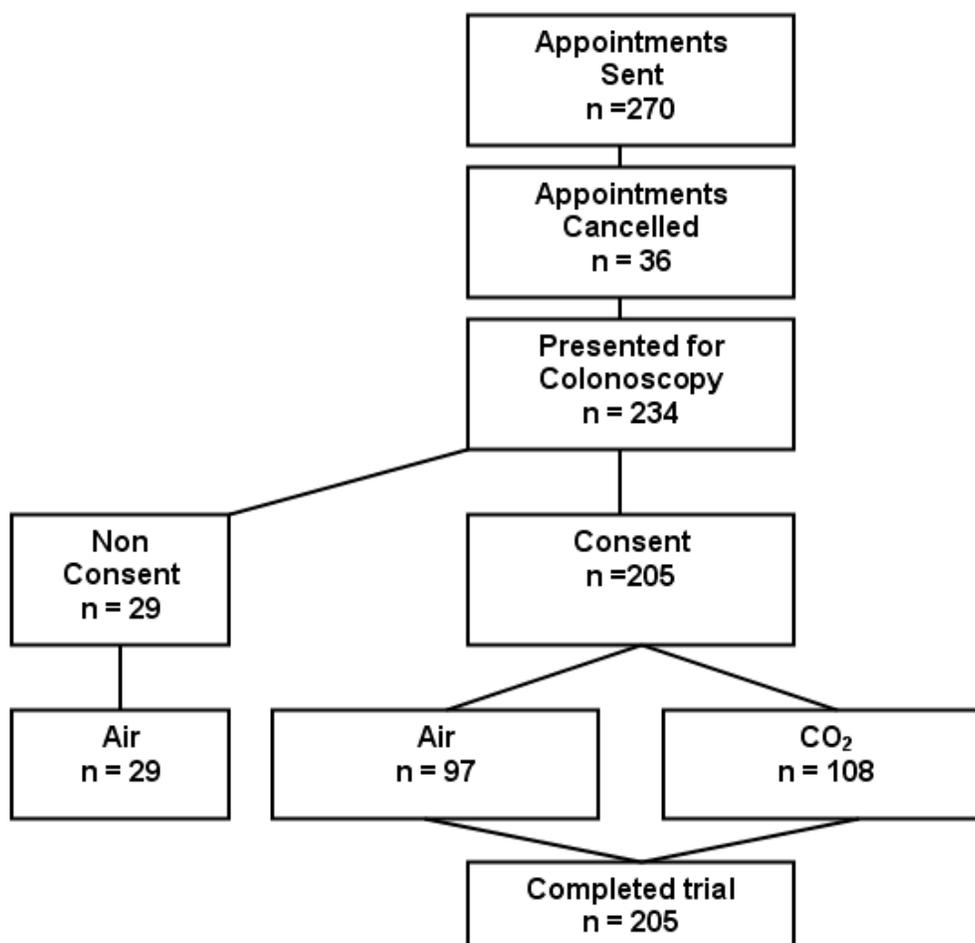
clinical setting with real patients having their elective colonoscopy and not in a laboratory. This clinical setting and the type of patients may be reflective of patients presenting for colonoscopy at other centres in New Zealand.

### **3.3.4 Sample Size**

Sample size can be calculated using a statistical formula called power analysis. Using a less formal method, the size can be based on previous published results (Schofield, 2004). After discussion with a statistician the latter method was chosen. 240 patients for randomisation was chosen to achieve a 90% power to detect a significant difference in NRS between air and CO<sub>2</sub> group based on published trials (Bretthauer, Hoff, et al., 2002; Bretthauer, Thiis-Evensen, et al., 2002; Church & Delaney, 2003; Sumanac, et al., 2002). This number allowed a drop out rate of 40. Statistical significance was defined as  $p \leq 0.05$ .

During the 6 month trial period, 270 colonoscopy appointments were sent along with invitations to be part of the trial. Thirty six of these appointments were cancelled by the patient; therefore they were not available for the trial. Reasons for cancellation included; no longer needed colonoscopy, postponement to a later date (that put them out of the timeframe for trial) and 5 did not turn up for their appointment. Thus 234 prospective participants presented for colonoscopy. Of these, 29 chose not to participate. A total of 205 patients consented to the trial. No one was excluded. The outcome of the randomisation was that 108 patients received the CO<sub>2</sub> and 97 had the standard treatment of air. See table 3.1

Table 3.1: Flow of participants through the trial



### 3.3.5 Randomisation

The Pharmacy department arranged the randomisation envelopes. An excel computer programme was used to allocate numbers to envelopes. Envelopes (120) were numbered for men and 120 for women. Inside the envelope it was stated on a slip of paper either the experimental `CO<sub>2</sub>` or `Usual` (the control air group).

The experience of pain is thought to be influenced by gendered aspects of sex (Lee, et al., 2006; Saunders, et al., 1996). Thus the randomisation envelopes were separated into male and female so that equal numbers of each sex could be watched for. At a statistician's advice; it was anticipated that if there were signs of inequality of sex, methods of manipulating the numbers would need to be considered. As the trial progressed it appeared this manipulation was not necessary. Final statistics showed; female (n = 111) male (n= 94). A statistician advised this was considered relatively even for statistical analysis. The randomisation envelopes were placed into boxes labelled male and female in the procedure room.

As patients arrived for their colonoscopy they were allocated a nurse (patient nurse) who assessed them for their trial consent or not. The patients who declined trial participation received the same care as consenting patients, but proceeded to receive the standard treatment of air insufflation during colonoscopy. For those consenting, as part of the usual assessment that all patients receive, trial suitability was reviewed and any further questions were answered. A comprehensive health assessment form was completed (appendix 8).

The patient's nurse informed the nurse in the procedure room of the prospective participant. The nurse in the procedure room for that endoscopy session opened the next male or female, numbered envelope and organised the administering of the appropriate gas. The patient's name was recorded against the corresponding numbered list. At the end of the trial, the master randomisation list held by

pharmacy was then matched to the numbered trial list, showing who had received air or CO<sub>2</sub>.

### **3.3.6 Control**

Control ensures manipulation of the independent variable and restraining of the extraneous variables. Peat (2002) explains that in the case of experimental research, randomised sampling is used to control threats to internal validity. Peat reinforces this by stating “Of all study designs, randomised controlled trials provide the highest level of evidence for the effects of an intervention and for causation (p. 23).”

In this study the extraneous variables that may influence the outcome measure or dependent variable of pain were controlled by the randomisation of patients to the control or experimental group. Confounding variables like sex, age, reason for referral, tolerance to pain, health conditions such as irritable bowel syndrome, previous abdominal surgery, endoscopist technique, dosage of analgesia and sedation used, all of which may have effected the out come of pain ( Lee, et al., 2006), were controlled by randomisation.

The medications used intra procedure may have residual effect on post colonoscopy pain although the reduction of intracolonic gas appears to extend beyond the effect of the analgesia. Further more, Lee et al (2006) showed that the incidence of discomfort post colonoscopy was comparable with both sedated and

unsedated patients. The possibility of extraneous effect of analgesia and sedation on post colonoscopy pain was controlled by randomisation in the present trial.

All department endoscopists agreed to be part of the trial. The four Gastroenterology department endoscopists carried out most of the trial procedures, respectively 30.7 %, 29.3 %, 19.5% and 16.6 %. Three of the endoscopists had extensive experience ranging from 10 to 25 years with a fourth having had 1 year's experience. Additionally three registrars, under direct supervision, also performed 5.9% of the trial procedures. The confounding variable of endoscopist technique (which may have influenced the length of procedure, amount of gas insufflated therefore indirectly influencing post procedure pain), was controlled by the randomisation of patients.

The trial was `double blinded` as a means of improving objectivity and controlling against bias. The term usually refers to the blinding of patient and the physician (or researcher) so that they are unaware of what treatment is being used. In this RCT, the patient, endoscopist, and the nurse providing patient care and collecting data, were all `blinded`. The only person unblinded was the nurse in the procedure room for that session who was responsible to technical set up of the equipment. These efforts were made to reduce the chance of influencing the patients` report of pain during and after the procedure.

The following explains the procedure to ensure blinding: The procedure room nurse opened the sealed envelope prior to the patient entering the room and noted

which gas was to be used. This envelope was then discarded. Air or CO<sub>2</sub> was surreptitiously turned on, keeping the patient, nurse and doctor blinded to what gas was being used. The patient's name was documented on a numbered list with the corresponding envelope number. The CO<sub>2</sub> tank (with the regulator and the flow meter) was placed at the side of the endoscopy tower away from the patient and endoscopists (appendix15). The flow meter was kept covered. The air operating switch on the endoscopy processor was kept covered. There is an optional CO<sub>2</sub>/water button (MAJ 502) which can be used on the endoscope for CO<sub>2</sub> delivery, but is easily recognisable, so the standard air/water button was used. The procedure room nurse was not involved in patient care pre and post procedure and did not collect the pain score data.

### **3.3.7 Data Collection Instruments**

The data collection instruments that were used enabled the testing of the hypothesis and also recorded the main characteristics of the sample and relevant aspects of the participant's health status (Polit & Hungler, 1999). The tools of data collection used were the Gastroenterology Nursing Record (appendix 8) and the 0-10 Numeric Rating Scale (NRS) that measured the dependent variable of pain.

### **3.3.8 Gastroenterology Nursing Record**

The `Gastroenterology Nursing Record` was used to document; the participant's medical history, demographics, health assessment, progress and interventions throughout the continuum of the colonoscopy episode (appendix 8). This documentation was chosen for its comprehensiveness and ease of use as it was already the documentation tool in standard practice for colonoscopy.

The constructs of interest for the research were recorded onto the Gastroenterology nursing record. As Polit and Hungler (1999, p. 315) suggested, in addition to the main variable of pain, information about other variables was gathered. These were demographic detail, reason for referral, procedure start time, time to caecum, procedure finish time, arrival into recovery time, discharge time, NRS scores, interventions during the procedure, polypectomy and intra procedure interventions performed. The researcher later transposed these constructs of interest onto an excel spread sheet. Then as per normal practice the Gastroenterology nursing record was filed into the patients notes.

### **3.3.9 Numerical Rating Scale**

The 0-10 numeric rating scale (NRS) was used to measure patients' abdominal pain at numerous time points that included intra and post procedure to test the hypothesis that carbon dioxide minimises post colonoscopy pain. The time periods recorded were intra-procedure (0), and post-procedure at 10, 30, 60 minutes and 24 hours. The first 4 time periods pain score data was collected prior to discharge.

The 24 hour data was obtained by phone call to the participant the next day. Prior to discharge it was explained to each participant that they would receive a follow up phone call the next day. The 24 hour pain data was later chosen not to be included in the final analysis as only 50% of participants were contacted (reducing the power) and some of this data was flawed.

This NRS was communicated to the participant, starting prior to the procedure by verbalising, “Can you tell me if you are in pain or discomfort? Zero to 10, with 10 being the worst pain you could experience and zero being no pain”. The score self reported by the patient was then documented on the Gastroenterology nursing record. The nurses explained the NRS to the participants prior to the procedure to facilitate the early understanding of this scale. These pain scores were recorded as interval level data.

A number of the published RCTs looking at CO<sub>2</sub> in endoscopy used a handout given to the patient to measure the pain intensity level on a Visual Analogue Scale (VAS) (Bretthauer, Hoff, et al., 2002; Bretthauer, et al., 2007; Bretthauer, Thiis-Evensen, et al., 2002; Domagk, et al., 2007). The VAS uses a 10cm line with “no pain” at the left end and “the worst pain imaginable” at the right. The patient is asked to mark the spot that represents the pain they are experiencing (McGuire, Kim, & Lang, 2004; Polit & Hungler, 1999).

There are a number of reasons why the verbally administered NRS was used as the measurement tool in preference to using the VAS:

1. The NRS is a way of measuring pain intensity that is supported by the hospital. It is in common use and therefore it was appropriate to promote its use. The nurses were already familiar with this tool. Subsequently the results are understood and can be compared in the wider hospital. After the trial finished the nurses carried on collecting the same data. This research was undertaken in the clinical setting and the reality of this meant use of the pain measurement tool already validated in this location.
2. The tool is valid, reliable and sensitive. The validity of a 0-10 point NRS was confirmed with cancer patients with an average age of 54.8 years and who had used an average of 87 mg of morphine daily (Paice & Cohen, 1997). The sensitivity of both the VAS and the NRS was similar when comparing post operative pain intensity by Breivik et al (2000). They expand this point to claim that choice between the VAS and the 0-10 NRS can be made on subjective clinical reasons as was done in the present study.
3. The ease of administration is one of the main reasons cited for its use (Breivik, et al., 2000; Paice & Cohen, 1997). No special form was needed for patients to fill out. Paice and Cohen (1997, p. 89) go on to claim that "Verbal administration also allows those individuals who are visually or physically disabled, as well as those patients communicating by telephone to quantify their pain intensity." It was felt for the present research that the NRS format was less intrusive and easy to use on patients who are recovering from the effects of a sedation and analgesia. Added to this they may not be wearing glasses and thus have

reduced visual acuity. Also the verbally administered NRS allowed pain score data to be obtained by telephone at 24 hours post procedure.

It is also suggested that the elderly may have difficulty with conceptualising their pain on a line as in the use of the VAS (Kremer, Atkinson, & Ingelzi, 1981; Paice & Cohen, 1997). Added to this, Paice and Cowen's research (1997) participants showed a strong correlation between difficulty in filling out a VAS and with opioid use. Thus for the present study with a mean age of trial participants being 62 years and including gathering data while patients are under the effect of sedation/analgesia, further supported the use of NRS rather than VAS.

There are numerous studies considering various aspects of the use of NRS but none found related to its use in endoscopy. Prior to undertaking a trial on whether CO<sub>2</sub> reduced post colonoscopy pain some researchers looked at sensitivity in pain rating scales (Skovlund, Bretthauer, Grotmol, Larsen, & Hoff, 2005). They compared the VAS with a 4-point verbal rating scale and concluded that the VAS was consistently more sensitive. These researchers acknowledged that the limitations to generalisability were that their patients were all aged between 50-64 years and received no analgesia/ sedation. In contrast, the age range of the participants of the present trial was 16-89 years, with an average age of 64, and sedation was used. Further research in the pain rating scales, particularly the NRS, for endoscopy would be valuable.

### 3.3.10 Statistical Methods

This was an experiment so the researcher used inferential statistics to draw conclusions from the result. The statistical analysis tests the null hypothesis, which states that there is no difference between the two groups (air and CO<sub>2</sub>). The alternative hypothesis is that there is a difference between the two groups.

The standard value of 0.05 for the significance level was set as a result of discussion with a statistician prior to commencing the study. The significance level is the probability that the test will show a significant difference between the two treatment groups when in fact there is no difference and the null hypothesis is true. If the P value calculated by the test is < .05 significance level, this indicates that the difference is too unlikely to have occurred by chance alone and the null hypothesis is rejected i.e. the probability that there is less than 5% chance that the obtained result is incorrect.

The researcher applied theory about the use of CO<sub>2</sub>, which influenced a directional hypothesis; expecting the variable of pain to be reduced with CO<sub>2</sub> use. Further supporting this directional hypothesis was the existing studies that revealed strength in using CO<sub>2</sub>. However despite this it could not be assumed that the findings opposing the directional hypothesis were virtually impossible, as a reason for using a one tailed test (looking at only one end of the distribution). Therefore the possibility was allowed that the treatment group may have a worse effect than the control group and the conventionally used two-tailed test was used. It is

generally assumed in statistical reports that a two-tail test was used unless otherwise stated (Munro, Jacobsen, & Braitman, 1997; Polit & Hungler, 1999).

The statistical analysis was performed using SPSS 17.0 software (SPSS Inc., Chicago, Illinois, USA). Differences in mean NRS scores were analysed by ANOVA for repeated measures. Chi-squared test for independence was used to explore the relationship between categorical variable. Parametric continuous data was compared with independent samples t-test. The proportion of individuals reporting no pain on NRS was compared at each point using the chi-squared test. Statistical significance was defined as  $p < 0.05$ . Two tailed tests were used.

### **3.4 Ethical Issues**

Approval to conduct the present study was received from Central Health and Disability Ethics Committee. The section of chapter three, outlining the methods used, indicates how ethical issues were dealt with in process of the trial.

The present research was a clinical trial and so it was necessary to assure participants that in the event of suffering from physical harm as a result of the trial, that the New Zealand Accident Compensation Corporation may be available to provide compensation. The detail related on this was outlined in the information sheet provided to prospective participants (appendix 1).

An important ethical issue to be considered was the timing of when a potential trial of CO<sub>2</sub> use could be considered. MCH Gastroenterology Department was convinced by the literature and international experience, to commence using CO<sub>2</sub> to insufflate the colon during colonoscopy and in so doing was the first Endoscopy unit in New Zealand to use this form of insufflation. If undertaking a RCT to compare CO<sub>2</sub> to air insufflation in relieving post colonoscopy pain was to be carried out, it needed to be at the commencement of CO<sub>2</sub> use. If a trial was considered after the use of CO<sub>2</sub> had become standard practice then withdrawing something that was proven to significantly relieve pain would have been an ethical issue. Undertaking a RCT in the New Zealand setting was thought to hold weight in convincing other endoscopy units to use CO<sub>2</sub> and the timing of a trial at the beginning of its use was crucial.

### **3.5 Dissemination of Results**

The researcher is compelled to ensure the outcome of the research is communicated to all the stakeholders in the field. The international community has struggled to accept the outcome of the previously reported CO<sub>2</sub> trials so the results of this research will add to the field of knowledge in regards to CO<sub>2</sub> use in colonoscopy.

The result of this trial has been sent to each participant along with informing them of the gas that was used in their procedure (appendix 3). The research report will be disseminated to major stakeholders at MidCentral Health. Reporting a description of the study and a summary of findings has been undertaken at the

regional Gastroenterology Nurses Meeting July 2009 and at nursing meeting at MCH, October 2009. A presentation was given at the National Gastroenterology Scientific Meeting, November 2009. Research out comes will also be published in the National journal for New Zealand Nurses Organisation Gastroenterology Nurses Section `the Tube`. Publication in a medical journal will be considered.

### **3.6 Summary**

The method of a randomised controlled, double blinded, clinical trial to investigate the effectiveness of using CO<sub>2</sub> insufflation, to reduce post colonoscopy pain was outlined in this chapter. The rational for undertaking this research was reflected on. The design and conduct of the trial was presented. The steps to prepare for the trial were described. This included outlining the process involved in training of all department staff in pain management issues, trial methods and safe gas handling. A patient's experience with a pilot study to test the procedure was described, highlighting the human aspect of the trial. Ethical issues were covered which included emphasis on the present timing of the trial. The outcome of the trial needed to be shared with the wider community. In conclusion the steps to undertake dissemination of the results were introduced. The trial results are presented in the next chapter.

# Chapter Four

## Result of the Experiment

### 4.1 Introduction

A mixed between subjects analysis of variance (ANOVA) was conducted to assess the impact of the two different interventions (air and CO<sub>2</sub>) on participants pain score at 4 different time periods; 0 (intra procedure), post procedure at 10, 30 and 60 minutes. Follow up scores that were obtained at 24 hours post procedure from those who were home were not included in the final analysis due to low numbers contacted (N= 104); reducing the power, and the flawed nature of this data. An independent groups test was conducted to assess the impact of the interventions.

This section outlines the results of the present study; commencing with a sample description, which includes information about the characteristics of the treatment groups. In the remainder of the chapter the results related to the hypothesis are presented.

### 4.2 The Sample Description

The following factors were considered to have an effect on the dependent variable and would impact the two groups being considered equal; age, gender, length of procedure time, procedure complications, intra procedure interventions (e.g. polypectomy) and amount of sedation and fentanyl use.

The sample was made up of 205 participants with a mean age of 61.61 (SD = 14.40). One hundred and eleven were female (54%) and 94 male (46%). Polyps were removed for 42.2% of participants. The mean duration of the procedure was 26.43 minutes (SD = 15.59). The mean dosages of each of the drugs used during the procedure was 3.8 mg (SD = 1.30) for hypnovel (sedation), 82.7 mcg (SD = 29.65) for fentanyl (analgesia) and 15.5 mg (SD = 5.0) for buscopan (muscle relaxant). There were no statistically significant differences between the groups on any of these variables. See table 4.1 below.

Table 4.1:

Age, sex, duration of procedure, polypectomy rate and dosage of medication for sample and groups.

	Total			CO2			Air			t	P
	N	Mean	SD	N	Mean	SD	N	Mean	SD		
<b>Age, years</b>	205	61.6	14.40	108	61.33	15.79	97	61.93	12.75	-.294	.766
<b>Duration,mins</b>	205	26.43	14.59	108	25.30	13.23	97	28.04	16.33	-1.214	.226
<b>Hypnovel,mg</b>	204	3.8	1.30	107	3.8	1.2	97	3.8	1.3	-.151	.880
<b>Fentanyl,mcg</b>	204	82.7	29.65	107	82.9	29.4	97	82.4	30.0	.113	.910
<b>Buscopan,mg</b>	27	15.5	5.0	17	14.1	5.07	10	18.0	4.2	-2.14	.052
	N	%		N	%		N	%		$\chi^2$	P
<b>Male</b>	94	45.9		51	47.2		43	44.3		.075	.784
<b>Female</b>	111	54.1		57	52.8		54	55.7			
<b>Polypectomy</b>	87	42.4		47	54		40	46		.036	.851

### **4.3 Basic Assumptions**

The assumptions underlying the mixed between-within subjects analysis of variance were assessed. The assumptions of sphericity, homogeneity of variance and equality of covariance matrices were found to be violated (appendix 5). Fin and Matttson (1978, p. 83) claim that “In practice behavioural data rarely meet the assumption of compound symmetry”. In an intervention study sphericity is not expected. When this assumption has been violated multivariate results should be reported (Munro, 1997). As a result the wilks` lambda statistic will be reported for main effects for time and interaction effects for time by group (appendix 6, Multivariate table).

### **4.4 Main Effect for Group**

A main effect was found for type of intervention (table 4.2). With CO<sub>2</sub> being more effective than air. The mean pain score over the four time periods was 1.2 (SD = 1.53) and ranged from 0 to 8 for CO<sub>2</sub> and a mean of 2.1 (SD = 2.26) and ranged from 0 to 10 for air ( $F(1, 202) = 17.36, p < .001, \text{partial } \eta^2 = 0.079$ ). This constitutes an effect of moderate size (i.e. Effect size of partial eta squared of .01 = small effect, .06 = moderate effect and .14 or greater = a large effect (Cohen, 1988, pp. 92-97)) in the effectiveness of one of the interventions on pain scores. Those in the CO<sub>2</sub> group had on average less pain than the air group (table 4.3 and appendix 6 for the tests of between subjects effects).

Table 4.2:

Main effect for group and time and intervention effect for group by time

Effect	Wilks Lambda	df	F	P	Partial Eta Squared
Main Effect for Group	N/A	1	17.36	.000	0.079
Main Effect for Time	0.414	3	94.1	.000	0.585
Interaction Effect	0.948	3	3.64	.014	0.052

#### 4.5 Main Effect of Time (Within the groups across time)

A significant main effect was found for time, with a large effect size (Wilks Lambda = 0.414,  $p < .001$ , partial eta squared = .586). (Table 4.2). The pain scores across the four time periods decreased markedly across time. The mean pain was 4.34 intra procedure (0 minutes), 0.99 at 10 minutes, 0.67 at 30 minutes and 0.43 at 60 minutes (table 4.3). There was a difference in pain scores from time across times which was greater than chance alone.

Table 4.3:

Pain scores by group over time

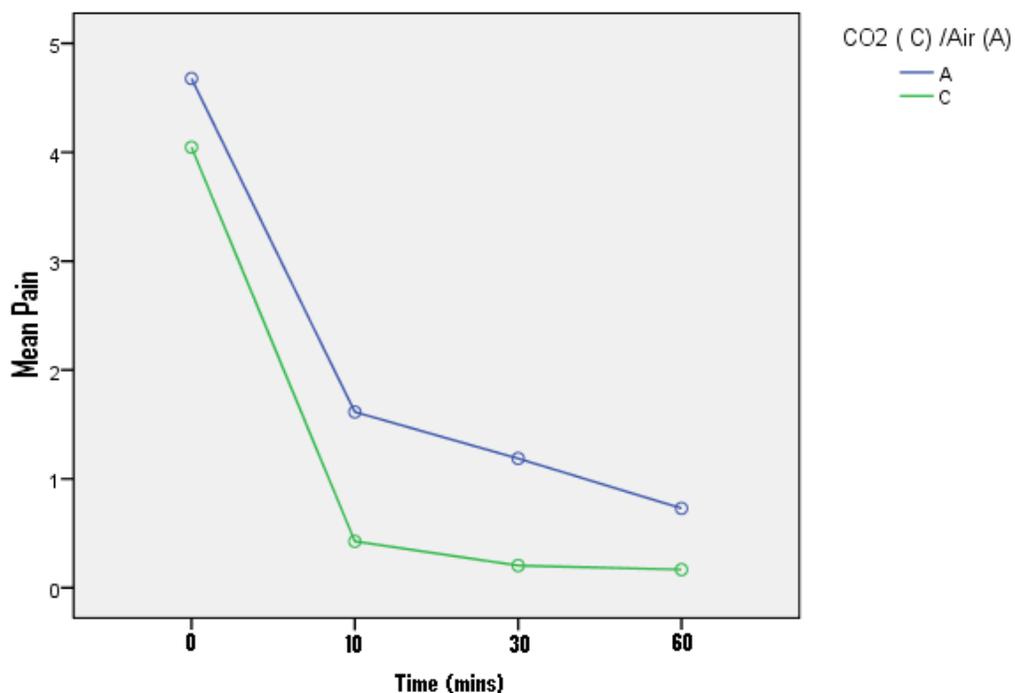
	CO2 ( C ) /Air (A)	Mean	Std. Deviation	N	t	P
Pain Score @ 0 min	A	4.68	3.342	96		
	C	4.05	3.257	108		
	Total	4.34	3.304	204	-1.26	.868
Pain Score @ 10 min	A	1.61	2.359	96		
	C	0.43	1.209	108		
	Total	0.99	1.931	204	-4.41	< .001
Pain Score @ 30 min	A	1.19	1.975	96		
	C	0.20	0.806	108		
	Total	0.67	1.553	204	-4.55	< .001
Pain Score @ 60 min	A	0.73	1.373	96		
	C	0.17	0.859	108		
	Total	0.43	1.162	204	-3.45	< .001

#### 4.6 Interaction Effect (between groups across time)

An interaction effect was found between the groups across time of a moderate effect size. (Wilks' Lambda = .948,  $p = .014$ , partial eta squared = 0.052). See table 4.2. The pain scores for those in the CO<sub>2</sub> group decreased faster across the four time periods than they did for those in the air group. (See figure 4.1).

Figure 4.1:

Mean pain scores by group over time



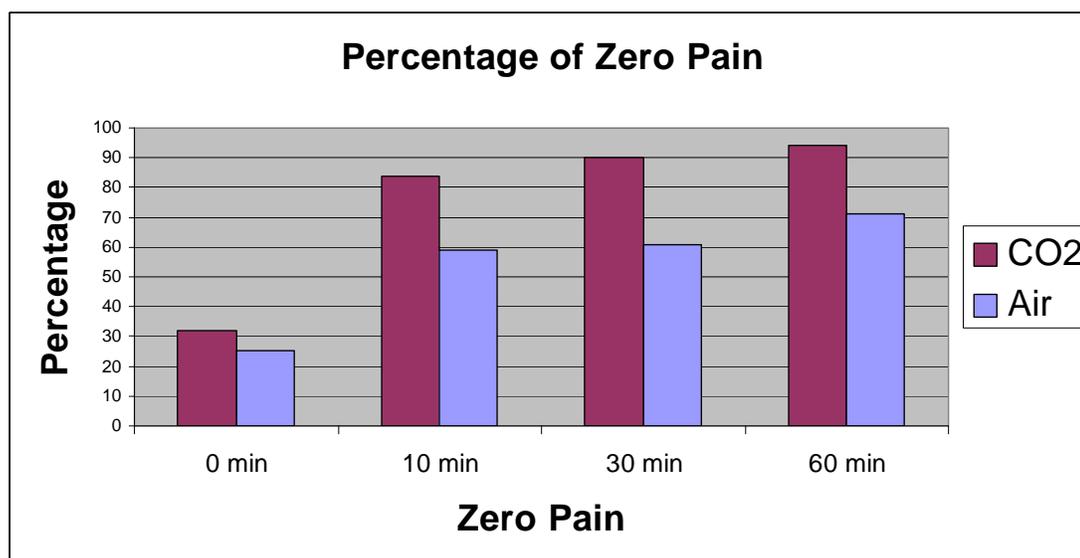
## 4.7 Zero Pain

The proportion of participants in both groups reporting *no pain* on the NRS was compared at all four time periods (table 4.4 and figure 4.2). A significant difference between the groups was noted with those in the CO<sub>2</sub> group reporting a greater proportion of zero pain score at each of the three times assessed following intervention.

Table 4.4 Zero pain scores by group over time

	CO <sub>2</sub>		Air		$\chi^2$	p
	N	%	N	%		
<b>0 Pain at 0 Min</b>	34	31.5	24	24.7	.836	.361
<b>0 Pain at 10 Min</b>	91	84.3	51	58.8	15.3	<.001
<b>0 Pain at 30 Min</b>	96	89.7	59	61.5	20.8	<.001
<b>0 Pain at 60Min</b>	101	93.5	68	70.8	16.8	<.001

Figure 4.2 Percentage of zero pain scores over time



## 4.8 Summary

The results related to the hypotheses were presented. The main effect between groups and within groups across time showed that those who received CO<sub>2</sub> insufflation reported less pain than those who received air insufflation. A significant interaction effect between groups across time showed that pain scores for those in the group who received CO<sub>2</sub> decreased by a greater amount and more rapidly than for those in the air group, over the three time periods following the procedure. There was no statistical difference in pain scores between the groups intra procedure.

# Chapter Five

## The Discussion

### 5.1 Introduction

The results of this study will be summarised and discussed in relation to context. This is followed by further discussion covering the implications of the findings in practice. The limitations of the trial and recommendations for future research will be outlined.

### 5.2 Findings

This study directly tested the hypothesis that: *Those receiving carbon dioxide (CO<sub>2</sub>) insufflation during colonoscopy will experience less post colonoscopy pain than those receiving air insufflation.* That hypothesis was accepted because there was a statistically significant difference of the pain scores post procedure recorded for those who received CO<sub>2</sub> insufflation, compared to those who received air insufflation. The participants who received CO<sub>2</sub> insufflation experienced less pain post colonoscopy than those who received air insufflation, therefore the null hypothesis was rejected and the research hypothesis that those receiving CO<sub>2</sub> during colonoscopy would experience less post colonoscopy pain than those receiving air insufflation was accepted.

There was no statistical significant difference of pain scores between both groups intra procedure ( $p = .868$ ). However at 10, 30, and 60 minutes post procedure the pain scores for those who received CO<sub>2</sub> were less than that for those who received air insufflation ( $p < .001$ ). An alternative visualisation of the pain score results was undertaken by investigating the proportion of participants reporting no pain on NRS. Again a significant difference was found at all three time periods post procedure ( $p < .001$ ). At 30 minutes post procedure 90% of those who received CO<sub>2</sub> had no pain in comparison to 61% of those who received air. Added to this, post procedure the pain scores of those insufflated with CO<sub>2</sub> dropped faster than for those insufflated with air.

The mean pain score over the four time periods was significantly less for those who received CO<sub>2</sub> (1.2) than for those who received air (2.1). These scores are relatively low in both groups and the range did not vary greatly, yet the range was greater for those in the air group at all three times post procedure (appendix 16). An examination of the distribution of the scores indicated that a greater number of those who received air insufflations experienced moderate to strong pain post procedure than those who received CO<sub>2</sub>. At 10 minutes post procedure 4 of those who received CO<sub>2</sub> insufflation reported pain ranging from 4 to 10, compared to 21 of those who received air insufflation (appendix 16). This reinforced anecdotal evidence that with air insufflation some people experience moderate to strong abdominal pain post procedure. In the present trial this was less common among those who received CO<sub>2</sub>.

### 5.3 Findings in Context

The results of the present trial are consistent with findings of all the other published trials. There was no significant difference in pain scores between the CO<sub>2</sub> group and air group *intra procedure*. In contrast the results *post procedure* at 10, 30, 60 minutes showed that those who received CO<sub>2</sub> insufflation reported less pain than those who received air insufflation. (Bretthauer, Hoff, et al., 2002; Bretthauer, et al., 2005; Bretthauer, Thiis-Evensen, et al., 2002; Church & Delaney, 2003; Stevenson, et al., 1992; Sumanac, et al., 2002) Bretthauer et al. is a major investigator in the use of CO<sub>2</sub> insufflation with involvement in 6 of the 9 RCTs undertaken.

The present trial was a systematic replication of earlier studies. This study randomised participants to the groups while most randomised the intervention by group. (Bretthauer, Hoff, et al., 2002; Bretthauer, et al., 2005; Bretthauer, Thiis-Evensen, et al., 2002).

Church and Delaneys RCT was blinded to participant only (2003). All the other previous RCTs were double blinded. The present trial was also double blinded, which included not only participant and endoscopist, but also the nurse looking after the patient.

The use of VAS was the most commonly used pain intensity measuring tool in the previous trials, although a 5 and 10 point likert scale has also been used (Dellon, et

al., 2009). In the present trial the use of the numeric rating scale (NRS) to measure pain, appears to be distinctive. As discussed in chapter three, this measurement scale appeared to be the best choice for this clinical trial setting and in reality it appeared to work well. The methods of the present trial that included using the NRS measuring tool has replicated the outcome of all the other trials

## **5.4 Limitations**

The limitations of the study are discussed under three headings

### 1. Pain score data at 24 hours post procedure.

The study design included measuring pain with a NRS at 24 hours post procedure, which would have strengthened the study by providing evidence of a longer term effect. However in the end this data was not included in the analysis because of limited numbers of participants contacted and the flawed nature of the data.

The method to gather the 24 hour pain score data was unreliable. This data was collected by the nurse phoning the participant the next day. Prior to discharge it was explained to each participant that they would receive a follow up phone call. Only 50% (N=104) of participants were contacted (either at home, work, or on a cell phone) so the power was considerably reduced. A phone method allowed the use of the same measuring tool (NRS) as all the other 4 time periods. The power of this data would have been increased by a stronger plan to get hold of as many participants as possible.

The data collected at 24 hours was also flawed. The time this phone call was made was not consistently at exactly 24 hours. There were also inconsistencies in the questions asked. Pain was assessed, but the NRS was not always used. There needed to be clearer instructions given to the research assistants on exactly what data needed to be collected at this time point. In addition, it may have been helpful to have collected data on the participants' pain over the previous 24 hours not just *at* 24 hours. A question that may have been considered was “with zero being no pain and 10 being pain as bad as you can imagine, what was your pain at its worst in the last 24 hours?”

Due to the small sample size at the 24 hour measuring period and the inconsistency in gathering this data, the power was greatly reduced and the data was flawed. Consequently the 24 hour pain score data was not included in the analysis.

## 2. Generalisability

The accessible population of this research needs to be considered carefully before generalisation is made to other centres within New Zealand and internationally. Some of the trial population characteristics (equality of sex, average age of 61 years) and the endoscopy methods (moderate sedation/analgesia, use of endoscopist in training) may transfer to other settings in New Zealand. Although anecdotally there was a low percentage of Maori participants, a limitation to this study was that the participants' ethnicity was not recorded, limiting generalisability to this ethnic group. The generalisability of the present research is strengthened

with its replicated design, undertaken in a new setting, with new subjects, which showed an outcome consistent with the previous RCTs.

### 3. Experimental effects

The researcher cared for some of the participants during their colonoscopy process and gathered some of the pain score data. Efforts were made to limit direct involvement in participant care but some involvement was unavoidable. Every attempt was made to remain neutral with no discussion of my status as principal investigator. Any subconscious effort to influence participants or the research assistants, to demonstrate that the hypothesis was correct, was limited by being blinded to what gas was used till after the whole trial was completed.

## **5.5 Implications of findings:**

The out come of the trial has implications for practice in the following four areas.

### 1. Use of CO<sub>2</sub> insufflation for colonoscopy is now common practice at MCH.

The Gastroenterology Department at MCH was convinced by the present trial that showed those who received CO<sub>2</sub> insufflation reported less discomfort post procedure than the patients who received air insufflation. Since the completion of the trial in January 2009, CO<sub>2</sub> insufflation is now common practice for colonoscopy with subsequent minimal reports of pain from patients.

## 2. CO<sub>2</sub> insufflation for other endoscopy procedures

The implication of reduction in pain for CO<sub>2</sub> use in colonoscopy could also be considered for other endoscopy procedures. Researchers have not only investigated CO<sub>2</sub> use in colonoscopy but also other endoscopic procedures. There are published trials investigating CO<sub>2</sub> insufflation in flexible sigmoidoscopy, endoscopic retrograde cholangiopancreatography (ERCP) and double balloon enteroscopy all supporting the reduction of pain post procedure (Bretthauer, Hoff, et al., 2002; Bretthauer, et al., 2007; Domagk, et al., 2007). In addition to colonoscopy, CO<sub>2</sub> use during ERCP is being considered at MCH.

## 3. Use of CO<sub>2</sub> nationally

The primary supplier of endoscopy equipment nationally, Olympus, recently released an automated CO<sub>2</sub> delivery system (UCR) into the New Zealand market. There are now a growing number of endoscopy units planning to trial the equipment. At least six endoscopy units have since purchased the delivery system from Olympus (Inmed Medical supply an insufflator called CoEfficient 2). It is not known if *all* the endoscopists within these departments are using this method; however there are certainly indications of the spread of this insufflation technique and the prospect of more than just MCH colonoscopy patients benefiting from reduced post procedure pain.

It was a common theme from past authors that despite what seemed like convincing research, CO<sub>2</sub> insufflation was not in widespread use (Church & Delaney, 2003; Sumanac, et al., 2002). Psaosawasdi et al (1986) claimed that only

15 of 146 hospitals in Illinois used CO<sub>2</sub>. The authors of a recent published systematic review (Dellon, et al., 2009) mention that it appears that this insufflation method is still not in common practice in the United States of America (USA). As mentioned previously, it was not in use in New Zealand prior to undertaking the present trial.

Various reasons have been suggested as to why the use of this gas has not been put into practice. Firstly specialised equipment was not initially available but has since been on the market in the last few years (Sumanac, et al., 2002). An associated cost with this equipment may be a deterrent. It is suggested that the benefits of this gas may not be considered important enough to warrant purchasing new equipment (Dellon, et al., 2009). The reasons for the reluctance to use CO<sub>2</sub> are perhaps varied and not clear. Further investigation needs to address the international extent of whether CO<sub>2</sub> insufflation is in use or not, and the factors contributing to lack of adoption.

The use of CO<sub>2</sub> insufflation in colonoscopy is common practice for most of endoscopy units of Western Australia. Communication with G Forbes a Gastroenterologist in Perth, Australia revealed that they had been using this gas in endoscopy for five years (personal communication, August 22, 2007). I hypothesised that the adoption of a new technique may be accelerated within close geographical/networking areas by word of mouth and benchmarking. I anticipated that undertaking a RCT at the beginning of CO<sub>2</sub> use in New Zealand might impact its use throughout New Zealand. It was therefore not a complete surprise to note

that since undertaking the present trial there was growing interest in CO<sub>2</sub> insufflation nationally.

4. Prospective national increase in colonoscopy rate.

The present research may be timely as currently there is a Ministry of Health task force focusing on facilitating a national colorectal cancer screening program. With the prospect of increasing colonoscopy numbers (at MCH and nationally), the use of CO<sub>2</sub> insufflation may impact on not only patient satisfaction and future compliance, but may also have an economic impact.

It is suggested that one of the benefits of this gas is that it may shorten recovery time, facilitate earlier discharge with subsequent reduction in costs. The present research was limited in investigating the recovery time because the collecting of pain score data at one hour meant the nurses ensured their trial participants were not discharged any earlier. The hypothesis that CO<sub>2</sub> insufflation shortens admission time is yet to be investigated.

The impact of air insufflation is on patients after 24 hours, is not fully known but may include reduced costs associated with next day absenteeism. Jonas and his colleagues' report that of 110 participants 17% of patients required more than 24 hours to recover from screening colonoscopy (Jonas, Russell, Sandler, Chou, & Pignone, 2007). Newcomer, Shaw, and Williams (1999) claimed that 4% of people post-colonoscopy took an unplanned next day off work due to abdominal pain and bloating as the main reason. A later study by Ko et al claimed that 20% of their

subjects took 2 or more days to fully recover to normal activity including work (2007). Little is known about the impact of colonoscopy on MCH patients after discharge.

## 5.6 Future Research

This research increased understanding but also highlighted areas that suggest further research:

1. Investigation of the impact of colonoscopy (with both CO<sub>2</sub> and air use) on patients post discharge. The following questions could be considered: “with zero being no pain and 10 being pain as bad as you can imagine, what was your pain at its worst in the last 24 hours?” What is the length of time to return to normal activity post colonoscopy? What is the next day absenteeism rate?
2. Investigation is required into CO<sub>2</sub> use in the higher risk populations with significant pulmonary disease. In the meantime for this group of patients, air should be used, otherwise in depth respiratory monitoring including Pco<sub>2</sub> measurements is recommended. The current literature supports that CO<sub>2</sub> is safe in the population with no serious underlying respiratory problems.
3. Investigation to enquire if CO<sub>2</sub> insufflation shortens admission time?
4. Investigation on the extent of CO<sub>2</sub> insufflation internationally and factors contributing to lack of adoption.

## 5.7 Summary

In this chapter the results of the research are discussed in relation to the hypothesis. The hypothesis was supported by the results which showed that CO<sub>2</sub> insufflation resulted in less reported pain than those who had received air insufflation. These results were discussed in relation to the published literature. The present research was a systematic replication of previous studies. The use of the Numeric Rating Scale stood out as unique aspect of the method. Despite this difference, the present trial replicated the outcome of all the other published trials.

The limitations were evaluated. The power for the 24 hour pain score data was reduced and the data was flawed, so it was not included in the final analysis. There was discussion emphasising caution regarding the generalisability of the trial to other New Zealand endoscopy units. The efforts to reduce the experimental effects of having the researcher involved in caring for the participants were highlighted.

The implications of the research findings on clinical practice were presented. CO<sub>2</sub> insufflation for colonoscopy is now normal practice at MidCentral Health and consideration is being given to application of CO<sub>2</sub> for other endoscopy procedures. At the beginning of this trial, CO<sub>2</sub> for colonoscopy was not being used in New Zealand; neither was there a delivery system available to support this use. Now there is an automated system available on the New Zealand market and a number of endoscopy units have since purchased this system, with others considering this method. It was suggested that the present research may be timely, as a

prospective national growth in colonoscopy numbers is expected, due to a national colorectal cancer screening programme being set up.

Finally recommendations for further research which arose from the discussion in this chapter were outlined.

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Appendix 1 (Massey University letter head went here)

## ***Does Carbon Dioxide Insufflation During Colonoscopy Minimize Post Colonoscopy Pain?***

### **INFORMATION SHEET FOR PATIENTS**

**You are invited to take part in a research project while undergoing your planned colonoscopy**

My Name is Anne Cleland. I am a registered Nurse in the Gastroenterology Department at MidCentral Health, and I am studying towards my Masters of Nursing at Massey University. In keeping with my commitment to improving the services of Gastroenterology and also in order to satisfy my degree requirement I am carrying out a study on the use of Carbon dioxide during colonoscopy. I am supported by Dr Andrew Herbert and the other department doctors and nurses. This study has been given ethical approval by the Central Regional Ethics Committee.

During a colonoscopy all patients receive air into their colon, which can sometimes cause abdominal pain or discomfort after the examination. Internationally the use of carbon dioxide gas (CO<sub>2</sub>), instead of air, has been found to reduce this abdominal pain after the examination. The aim of this research is to find out if this is true in our New Zealand setting.

### **Recruitment and Involvement**

240 patients, receiving a colonoscopy appointment are being invited to participate in this trial. You will need to be between the ages of 16 years and 90 years and have a good understanding of English.

If you choose to be a participant bring the enclosed trial consent form with you when you arrive for your colonoscopy. You will receive either air or gas during your colonoscopy. Neither the doctor carrying out the colonoscopy examination, nursing staff nor you will know which gas is used during your examination. Only the endoscopy assistant will know the type of gas used. Soon after the procedure and before you are discharged your nurse will ask if you are experiencing any abdominal pain. The next day a nurse will contact you about any discomfort that may have occurred after discharge.

Your participation is voluntary. If you choose not to consent to this trial then your planned colonoscopy will be performed with the use of air as usual and please be reassured that your care will not be affected in any way. Your nurse and endoscopist will be working on ensuring your procedure is as comfortable as possible as they normally do.

### **Safety of this trial**

The studies that have already been undertaken on the use of CO<sub>2</sub> have looked carefully at the safety of this gas and there have been no side effects found. CO<sub>2</sub> gets absorbed into the colon lining and eventually gets exhaled by the lungs. Carbon dioxide will not be given to you if you have a severe chronic obstructive lung disease. Use of CO<sub>2</sub> in colonoscopy is commonly used in parts of Australia. It is also the standard gas used during some surgery. If you choose to take part in this trial the risks involved are the same as a standard colonoscopy and are outlined on the back of the yellow form enclosed.

### **Compensation**

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

If you have any questions about ACC, contact your nearest ACC office or the investigator.

### **Confidentiality**

Your name or any identifying detail will be not be used in any reports on this study. During the study period, all data will be kept in a locked filing cabinet in my office. After completion of the research, December 2008/early 2009, data will be stored at the Massey University School of Sciences for 10 years and then destroyed.

### **Results**

At the completion of the research a summary of the trial findings will be available for participants or their families. I will write a research report which will be available for those who wish to read it and study findings will be submitted to health service journals.

**Contacts**

Please read carefully the instructions on the *yellow form* that you have received about your forthcoming colonoscopy. If you have any questions about the procedure itself ring the Gastroenterology Department as instructed on the yellow form.

If you have any questions or concerns regarding *this invitation*, or about your rights as a participant in this study, you may wish to contact a Health and Disability Advocate, telephone 0800 42 36 38. Alternatively you are welcome to contact myself using the phone number provided. You are most welcome to bring a support person with you when you attend your colonoscopy appointment. A member of the Palmerston North Maori Unit is also available to support you if you wish, telephone 06 3508210

Principal Researcher  
Anne Cleland  
Registered Nurse, Gastroenterology  
MidCentral Health  
06 3508665 or 06 3290845  
Anne.Cleland@midcentral.co.nz

Researcher Supervisor  
Dr. Jenny Carryer  
Professor of Nursing  
Massey University  
06 3569099  
[J.B.Carryer@massey.ac.nz](mailto:J.B.Carryer@massey.ac.nz)

Appendix 2 (Massey letter head went here)

## ***Does Carbon Dioxide Insufflation During Colonoscopy Minimise Post Colonoscopy Pain?***

### **CONSENT FORM**

**This consent form will be held for a period of ten (10) years**

- I have read the Information Sheet and have had the opportunity to discuss this study. My questions have been answered to my satisfaction, and I understand that I may ask further questions at any time.
- I understand that taking part in this study is voluntary ( my choice) and that I may withdraw from the study at any time and this will in no way affect my health care.
- I understand that my participation in this study is confidential and that no material, which could identify me, will be used in any reports on this study.
- I understand that the investigation will be stopped if it should appear harmful to me
- I understand the compensation provisions for this study.
- I have had time to consider whether to take part.
- I know who to contact if I have any questions about the study.

I agree to participate in this study under the conditions set out in the Information Sheet.

**Signature:**

**Date:**

**Full Name - printed**

Appendix 3 (Massey letter head went here)

## ***Does Carbon Dioxide Insufflation During Colonoscopy Minimise Post Colonoscopy Pain?***

Dear .....

**Thank you for taking part in this research. While undergoing your recent colonoscopy you received.....**

My Name is Anne Cleland. I am a registered Nurse in the Gastroenterology Department at MidCentral Health. Starting mid July 2008 and finishing mid January 2009 I carried out a study (Randomised Controlled Trial) on the use of Carbon dioxide during colonoscopy. I was supported by the other department doctors and nurses. There is evidence internationally that the use of carbon dioxide gas (CO<sub>2</sub>) to insufflate the colon instead of air can reduce abdominal pain after the examination. The aim of this research was to find out if this is true in our New Zealand setting.

### **Recruitment and Involvement**

You were one of 205 patients who consented to take part in the trial. All the participants randomly received either air or gas during the colonoscopy. Soon after the procedure and before you were discharged your nurse asked if you were experiencing any abdominal pain. The next day a nurse may have contacted you about any discomfort that may have occurred after discharge.

### **Results**

The outcome of the research showed that after the colonoscopy there was a clear reduction of pain experienced by the people who received CO<sub>2</sub>. As a consequence, CO<sub>2</sub> insufflation during colonoscopy is now the standard method used at MidCentral Health. I will write a research report by December 2009 which will be available for those who wish to read it and study findings will be submitted to health service journals. Your name or any identifying detail will be not be used in any reports on this study.

Once again, thank you very much in taking part in this trial. You have been involved in improving the experience of colonoscopy for MidCentral Health patients and also nationally as the use of CO<sub>2</sub> is now being considered by other hospitals in New Zealand.

Regards

Anne Cleland, RN

Principal Researcher  
Anne Cleland  
Registered Nurse, Gastroenterology  
MidCentral Health  
06 3508665 or 06 3290845  
Anne.Cleland@midcentral.co.nz

Researcher Supervisor  
Dr Jenny Carryer  
Professor of Nursing  
Massey University  
06 3569099  
[J.B.Carryer@massey.ac.nz](mailto:J.B.Carryer@massey.ac.nz)

## Appendix 4

**Carbon Dioxide Insufflation during Colonoscopy Minimises Post Colonoscopy Pain: A Randomised Controlled Trial**

Gastroenterology Department Research 2008

Anne Cleland, RN

The purpose of this trial is to establish that carbon dioxide (CO<sub>2</sub>), instead of air, insufflated during colonoscopy reduces pain experienced by patients post colonoscopy. A randomised, double blinded controlled trial with consecutive consented patients referred for elective colonoscopy will be undertaken at MidCentral Health Gastroenterology Department. Patients will be randomized to either colonic insufflation with air or CO<sub>2</sub>. A comparison of pain will be undertaken. During colonoscopy, air is the standard gas used to insufflate the colon. This commonly results in distension of the colon and subsequent pain. CO<sub>2</sub> is claimed to be an effective and safe gas to achieve insufflation, but with its rapid absorption, results in significant reduction in pain post colonoscopy. Improving the patient experience in regards to pain will contribute to better public acceptance of colonoscopy, maximise compliance for diagnostic and surveillance colonoscopy and reduce recovery time.

Dear

Thank you for being willing to take part in the carbon dioxide (CO<sub>2</sub>) trial that our department is planning to undertake. We will commence trial early in July. I will let you know the exact starting date soon. We will enrol 200 patients, to ensure statistically significant statistics. (15% difference in pain score between air and CO<sub>2</sub>). This may take 3-4 months to complete.

To assist this trial please read the following enclosed information that explains the trial method and process that will need to take place to keep the trial `rigorous`. Also attached is a copy of the patient information and consent form. Please ask myself or Dr Herbert if you have any questions. I am anticipating that there will be minor aspects of the trial that will need to be adjusted as we make a start. We will do a dummy run in the next week or two to try to iron out the practical issues before the first patient.

Undertaking a trial of a method to potentially relieve patients pain will be of huge benefit to not only our patients, but will benefit yourself as you become involved in research. The department itself will gain as we are the first in the country to use CO<sub>2</sub> and the trial will therefore impact nationally. Who knows, if the trial methods are rigorous, we can report internationally too!

Thank you, in anticipation, for your part in achieving this

Signed

## Roles for the CO2 trial:

(Please be familiar with yours and others. Ensure pt confidentiality at all times)

Ask Anne Cleland or Dr Herbert if you have any questions

### Reception/booking clerk:

- Sending information letter and consent forms (see attached) along with colonoscopy appointment to all out patients that have at least 1-2 weeks to think about taking part (ie no IPs and no acutes arranged at short notice). Take note of exclusion criteria ie do not send trial forms to anyone younger than 16 and older than 90 or to anyone known to you that will not understand English. (The nurses will double check this when the pt arrives).
- Forward phone calls to Anne, or take messages as appropriate, for patients that have questions about the trial.

### Medical Secretary:

- Forward trial questions to Anne as above.
- Anne will be taking Gastro nursing record and loading some detail (data collected) into computer before they come to you for filing in notes. Trial consent forms will not go in notes. They will be stored (by Anne) in a locked cupboard in charge nurses office.

### Patient Nurses:

- At time of pt assessment confirm pt participation or exclusion. Keep consent form on clip board. Reassure pt and answer any questions they may have. If they haven't already signed consent form and want to do so now this is ok.
- Assess suitability of pt for trial as per exclusion criteria ie pts with severe COPD, inability to understand English, < 16 or > 90 yrs. Ask Endoscopist for advice as necessary.
- Inform theatre nurse of trial participant consent **prior** to pt going into room.
- You will need to remain `blind` to what gas is being used so there is no risk of influencing the pt when asking their 0- 10 pain score.
- Record pts self report pain score @ 10, 30 and 60 minutes post colonoscopy. **Ask Pts : "Can you tell me if you are in pain or discomfort? Zero to ten, with 10 being the worst pain you could imagine and zero being no pain."** Explain to the patient *prior to their procedure* about your plan to ask them about any pain/discomfort they may or may not have.
- Ensure participants understand they need to be contacted in 24 hours and phone details are confirmed.
- Ensure Anne gets all gastro nursing records of trial pts prior to them going into pt notes. The trial data (Pts demographics, pain scores and gender) will be entered onto computer program for analysis later.

**Doctors:**

- Carry on your endoscopist practice as usual!
- You will need to be `blind` to what gas is being used.

**Endoscope Technicians:**

- Ensure that a clean CO2/ water bottle is available every day.

**Theatre Nurse:**

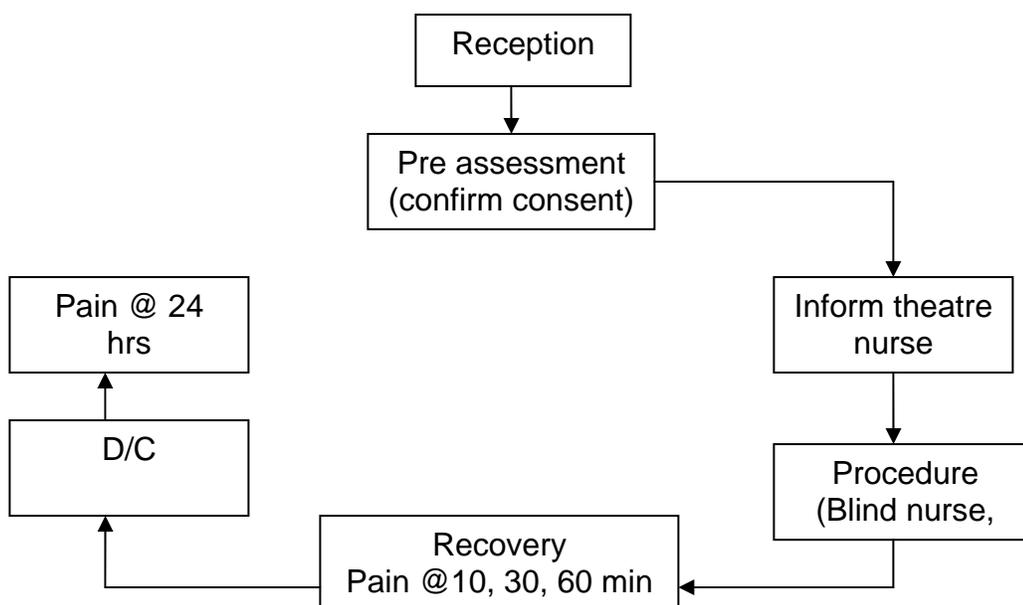
- Confirm which pts are taking part in trial and place bradma onto ` Research list`. Open envelope with their number and turn on appropriate gas. Ensure that this is done in a way where no one else in room is aware of gas being used!
- Ensure that a spare full CO2 cylinder is always available for each session.

**Pharmacy:**

- CO2 is classified as a drug and so pharmacy is supporting this trial
- Helping with the randomisation of patients. Setting up the envelope system. They have the master numbered research list that states what gas was used

**Anne Cleland, RN and Dr Andrew Herbert:**

- Collect and load data into computer and analyse data
- Store all trial data and consent forms in locked drawer in charge nurses office.
- Oversee the trial. Anticipate and fix any glitches!
- Support and coach the team until completion

**Patient/Participant**

## **CO2 Trial Methods:**

Design: A randomised, double blinded controlled trial comparing the effects from either carbon dioxide or air on pain post procedure will be undertaken with consecutive consented patients.

Informed Consent: All eligible patients are provided, by mail, an appointment date and time, letter of explanation about research and a consent form. They arrive with their consent form filled out, at appointment time. Patient is assessed on arrival and eligibility re confirmed. Patients who are excluded as per exclusion criteria or decline participation in trial will receive standard treatment of air.

Exclusion Criteria: Age under 16 or over 90. Inability to understand participant information. Patients with severe chronic obstructive pulmonary disease (COPD). Refusal of participation.

Blinding: Patient, endoscopist and all nurses. The endoscopy assistant in charge of the procedure room for that session who will be responsible for switching the gas. Gas unit will be covered.

Endoscopist: All 4 of department endoscopists will take part in the trial. All have had extensive experience, ranging from 15-25 years. There is expected to be one or two trainee endoscopist, under the supervision of the endoscopists, undertaking the colonoscopies of a minority of the participants. This is normal department practice at MCH, a training hospital.

Sedation/Analgesia: Will be given as per endoscopist discretion. Midazolam 2-5 mg, Fentanyl 25-100 mcg and Hyoscine 10-20mg are commonly administered.

Outcome Measures: The main outcome measure will be pain. Other outcome measures will be length of recovery time, patient demographics, complication rate.

Measurement: Pain: At 10 minutes, 30 minutes and 1 hour after procedure patient will be asked to score their pain on a 10 point Visual Analogue Scale (VAS). At 24 hours later the patient will be phoned and will be asked to verbally score their pain with a 0-10 pain scale. Arrangements will be made prior to discharge for contact phone plan/text/email, to capture pain scale at 24 hours.

## Appendix 5

1. Mauchly's Test of Sphericity:**Table One: Mauchly's Test of Sphericity<sup>b</sup>**

Measure: MEASURE\_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon <sup>a</sup>		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
time	.186	337.547	5	.000	.514	.520	.333

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

b. Design: Intercept + CO2CAirA

Within Subjects Design: time

2. Levenes Test of Equality of Error Variances:**Table Two: Levene's Test of Equality of Error Variances<sup>a</sup>**

	F	df1	df2	Sig.
Pain Score @ 0 min	.003	1	202	.957
Pain Score @ 10 min	60.860	1	202	.000
Pain Score @ 30 min	60.876	1	202	.000
Pain Score @ 60 min	36.826	1	202	.000

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + CO2CAirA

Within Subjects Design: time

3. Boxes Test of Equality of Covariances Matrices:

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

Box's M	181.256
F	17.737
df1	10
df2	189012.440
Sig.	.000

## Appendix 6

Between: Main Effect for Group

**Table Seven:Tests of Between-Subjects Effects**

Measure:MEASURE\_1

Transformed Variable:Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	2164.151	1	2164.151	261.062	.000	.564
CO2CAirA	143.935	1	143.935	17.363	.000	.079
Error	1674.539	202	8.290			

**Table Seven:Tests of Between-Subjects Effects**

Measure:MEASURE\_1

Transformed Variable:Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	2164.151	1	2164.151	261.062	.000	.564
CO2CAirA	143.935	1	143.935	17.363	.000	.079
Error	1674.539	202	8.290			

**Table Eight:Multivariate Tests<sup>b</sup>**

Effect	Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared	
time	Pillai's Trace	.586	94.189 <sup>a</sup>	3.000	200.000	.000	.586
	Wilks' Lambda	.414	94.189 <sup>a</sup>	3.000	200.000	.000	.586
	Hotelling's Trace	1.413	94.189 <sup>a</sup>	3.000	200.000	.000	.586
	Roy's Largest Root	1.413	94.189 <sup>a</sup>	3.000	200.000	.000	.586
time * CO2CAirA	Pillai's Trace	.052	3.644 <sup>a</sup>	3.000	200.000	.014	.052
	Wilks' Lambda	.948	3.644 <sup>a</sup>	3.000	200.000	.014	.052
	Hotelling's Trace	.055	3.644 <sup>a</sup>	3.000	200.000	.014	.052
	Roy's Largest Root	.055	3.644 <sup>a</sup>	3.000	200.000	.014	.052

## Appendix 7

Pain: 5<sup>th</sup> Vital signWhat is pain?

'Pain is unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage' IASP (International Association of the Study of Pain, 1996)

'Pain is whatever the experiencing person says it is, existing whenever they say it is.' (McCaffery, 1983)

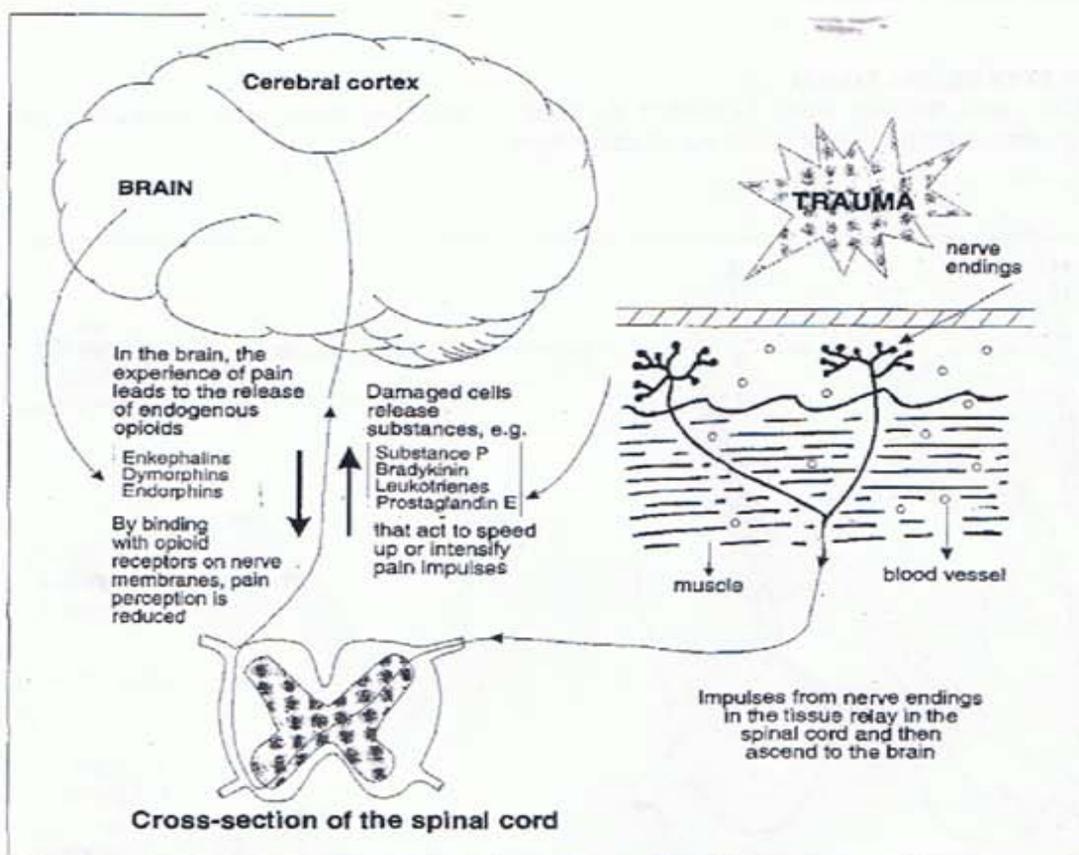
Pain Pathway

Figure 1.6 Response to the 'chemical cascade' caused by tissue damage

## Pain Fibres

### **A delta: First or fast pain**

Pain is instant, sharp and localized. Fibres end in 'thinking' part of brain so we can accurately localize the pain.

Opioids do not block the pain message from A delta fibres. These pain receptors still be working to protect from further tissue damage.

True / False: Withholding analgesia until diagnosis is made is best practice?

### **C Fibres: Second Pain, Slower**

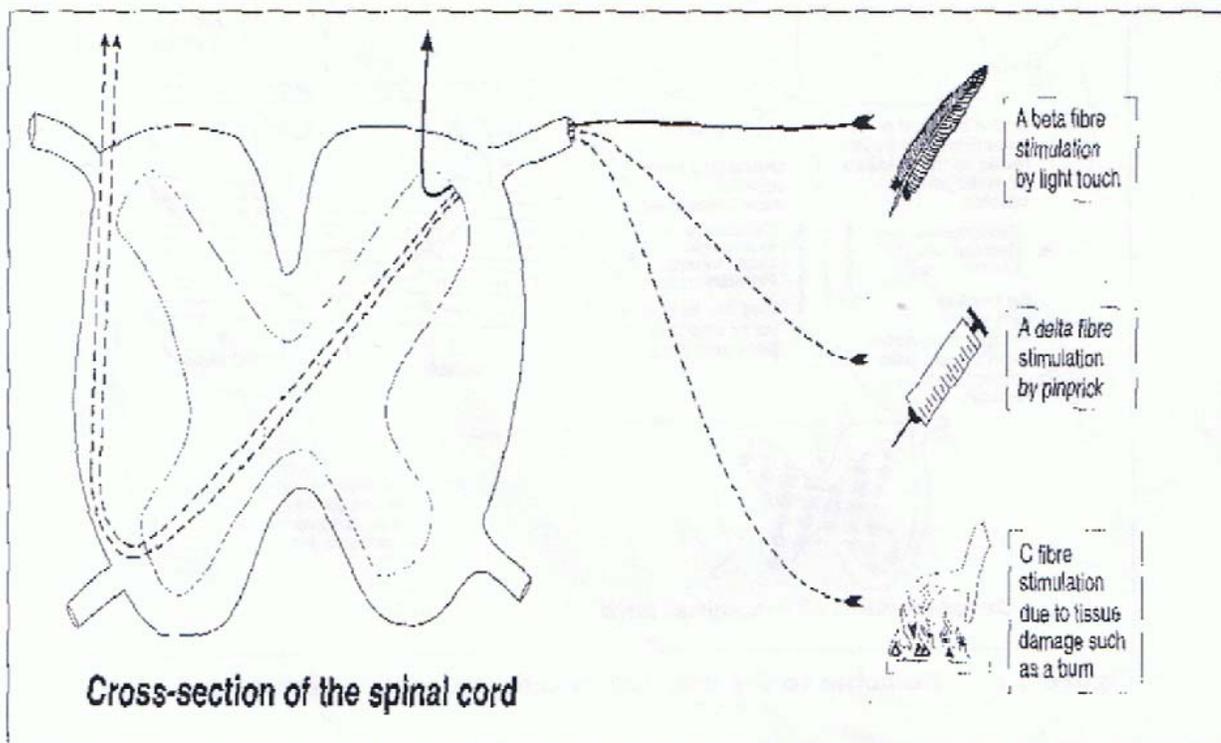
Pain is dull, burning, aching, throbbing over wide area. Terminate over a wide area in the brain. Generalised pain.

Opioids effective with C fibre pain

## Non Pain Fibres

### **A beta fibres: Touch**

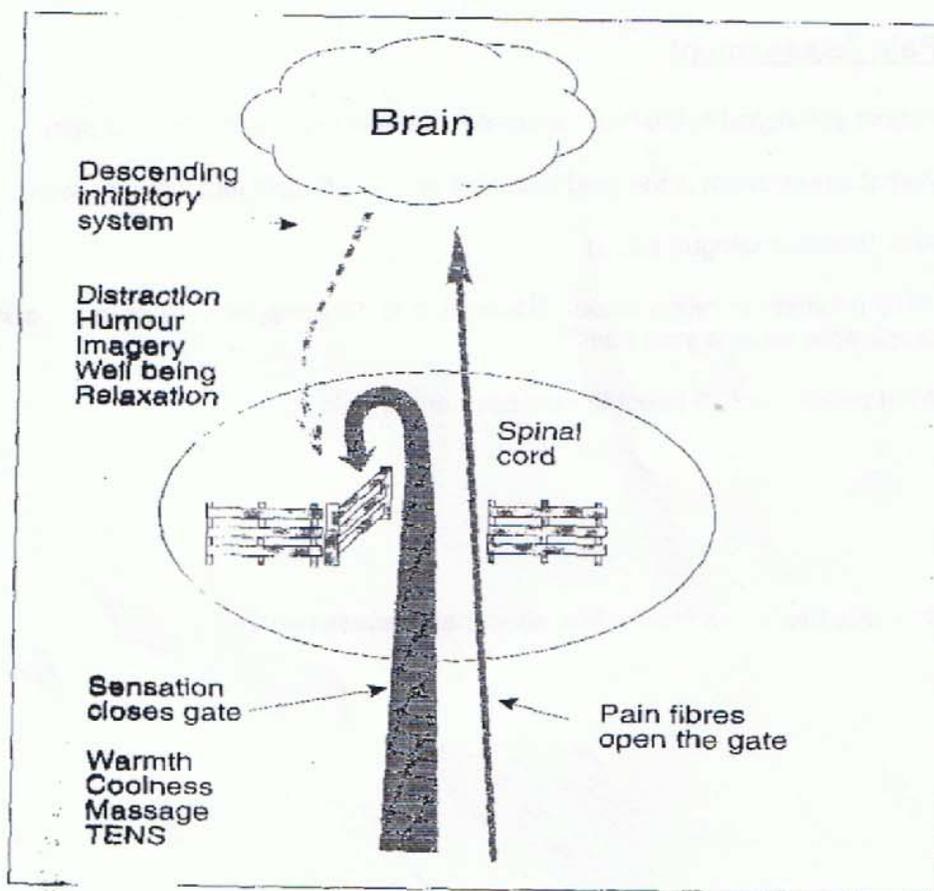
Concentrated on skin. Activated by touch and sensation and normally don't generate pain. . Most rapid conducting fibre



## Gate Control Theory

**Multidimensional nature of pain...Expansion of the many aspects of the pain message.**

- Tissue damage results in a volley of nerve fibres (A delta and C) go to spinal cord. If inhibitory impulse do not descend from the brain to close the 'gate', these impulses continue to ascend to the brain where the pain is perceived.
- Anxiety, excitement, anticipation, lack of control may open the gate and increase the perception of the pain
- Distraction, suggestion, relaxation, imagery can close the 'gate' and prevent the sensory transmission of pain
- 'Rubbing a hurt' transmits A beta fibres (touch not pain) and may clog up the gate and as they are faster fibres these touch fibres may get thru and in effect block the pain fibres.
- Chemical cascade in tissue damage opens the gate. E.g. as in inflammation: bradykinin, prostaglandins Our body can produce its own opioid like substance to modulate the pain message. E.g. endorphins



## Visceral Pain

- Viscera organs within the body are mainly innervated by the slower, diffuse C fibres characterized by generalized and referred pain.
- Visceral sensations are an every day occurrence; varies from feeling of fullness, urge to defecate as well as the sensation of pain.
- Visceral nociceptors (pain receptors) do not usually pick up stimuli from normal everyday transport of material, air or peristaltic movement of the colon. They are thought to be high threshold receptors which picks up receptors in the noxious range.
- 3 types of visceral pain: (think about the colon)
  - Ischemia.
  - Tension.(distention and forceful contraction)
  - Inflammatory.

*Visceral Hypersensitivity ( e.g IBS, IBD, oesophagus )*

"In response to a triggering event such as inflammation, environmental stress, psychological stress, or trauma, the gut becomes sensitized to luminal distension, resulting in visceral hypersensitivity"

## Pain Assessment

Patient self report is the most accurate measurement of the level of pain.

Verbal assessment is the gold standard of pain assessment when possible.

VAS (Visual analogue scale)

NRS (Numerical rating scale) : "Using a 0 to 10 scale with 10 as the worst pain imaginable, what is your pain?"

What patient factors affect the assessment of pain?

What are the Nurse factors that affect pain assessment?



NHI No \_\_\_\_\_

**PRE-PROCEDURE CHECKLIST FOR INPATIENTS****(WARD NURSE COMPLETE):****INPATIENT CHECKLIST:**

Yes No

- Patient read procedure information sheet  
  Has NOT FOR RESUSCITATION order  
  I.V. canula inserted  
  Withheld codeine, iron tablets, PR medication  
  Hospital gown on and ready for transfer in own bed  
  Current notes/drug and observation charts, old notes and x-rays  
  Iodine skin test if having PEG  
  **PRE-PROCEDURE ASSESSMENT complete** (previous page)

RN Name: \_\_\_\_\_

Signed: \_\_\_\_\_

Date: \_\_\_\_\_

**PRE-PROCEDURE ASSESSMENT****(GASTRO NURSE COMPLETE):****ASSESSMENT DATA***(Please tick or fill in where applicable):*

VENTILATION: Respiration:  Regular  Shallow  Laboured  
 Comments \_\_\_\_\_

CIRCULATION/  
PERFUSION: Heart Rhythm:  Regular  Irregular  
 Skin:  Dry  Moist  Normal  Jaundiced  Pale  Cyanotic  
 Comments \_\_\_\_\_

COGNITION/  
COMMUNICATION: Behaviour:  Alert  Drowsy  Orientated  Disorientated  
 Co-operative  Unco-operative  Calm  Anxious

PAIN/DISCOMFORT:  Yes  No Location \_\_\_\_\_ Pain Score (0-10) \_\_\_\_\_

Comments (eg duration, description, exacerbated by alleviating factors)  
 \_\_\_\_\_  
 \_\_\_\_\_

GI NUTRITION:  Dysphagia  Nausea  Vomiting  Weight Loss/Gain  
 PR Bleeding  Altered bowel habit  
 Comments \_\_\_\_\_

ABDOMEN:  Distended  Not distended

Glasses  Contact Lens

Hearing Aid:  Left  Right

Comments \_\_\_\_\_

Natural teeth  Partial plate

Dentures:  Top  Bottom

Comments \_\_\_\_\_

**TRANSPORT ARRANGEMENTS:**

Relative/Friend picking up  Ambulance  Taxi  Other

Contact details \_\_\_\_\_

- Assessment discussed and agreed with patient  
 Discharge discussed and agreed with patient  
 Procedure information leaflet discussed with patient  
 Operation/consent form signed

IV Cannulation site \_\_\_\_\_

Cath size \_\_\_\_\_

By whom \_\_\_\_\_ Signed \_\_\_\_\_







## Appendix 9



BOC Limited  
 988 Great South Road  
 PENROSE AUCKLAND  
 Tel: + 64 9 525 5600

## MATERIAL SAFETY DATA SHEET # 0101

Product Name **CARBON DIOXIDE, MEDICAL (BOC LIMITED - NZ)**

### 1. IDENTIFICATION OF THE MATERIAL AND SUPPLIER

**Supplier Name** BOC LIMITED (NEW ZEALAND)  
**Address** 988 Great South Road, Penrose Auckland, NEW ZEALAND  
**Telephone** +64 9 525 5600  
**Emergency** 0800 111 333 (NZ only)

**Synonyms** MEDICAL CARBON DIOXIDE, PRODUCT CODE: 197.

**Uses** MEDICAL APPLICATIONS.

### 2. HAZARDS IDENTIFICATION

NOT CLASSIFIED AS HAZARDOUS ACCORDING TO CRITERIA IN THE HS (MIN DEG OF HAZ) REGS 2001  
 CLASSIFIED AS A DANGEROUS GOOD ACCORDING TO NZS 5433

### 3. COMPOSITION / INFORMATION ON INGREDIENTS

Ingredient	Formula	Conc.	CAS No.
CARBON DIOXIDE	CO <sub>2</sub>	>99%	124-38-9

### 4. FIRST AID MEASURES

**Eye** Hold eyelids apart and flush continuously with water. Continue until advised to stop by the Poisons Information Centre, a doctor, or for at least 15 minutes. Keep patient calm.

**Inhalation** Remove from area of exposure immediately. If assisting a victim avoid becoming a casualty, wear an Air-line respirator or Self Contained Breathing Apparatus (SCBA). Be aware of possible explosive atmospheres. If victim is not breathing apply artificial respiration and seek urgent medical attention. Give oxygen if available. Keep warm and rested.

**Skin** Not applicable.

**Ingestion** Ingestion is considered unlikely. However, if ingestion occurs, drink large volumes of water. Seek medical attention. For advice, contact a Poisons Information Centre on 0800 764 766 (0800 POISON) or +643 479 7248 (New Zealand) or a doctor.

**Advice To Doctor** Treat symptomatically.

**First Aid Facilities** Eye wash facilities and safety shower are recommended.

### 5. FIRE FIGHTING MEASURES

**Flammability** Non flammable.

Colour  
 Rating  
**AMBER**



BOC Limited  
988 Great South Road  
PENROSE AUCKLAND  
Tel: + 64 9 525 5600

## MATERIAL SAFETY DATA SHEET # 0101

Product Name **CARBON DIOXIDE, MEDICAL (BOC LIMITED - NZ)**

### 5. FIRE FIGHTING MEASURES cont.

- Fire and Explosion** Non flammable. Temperatures in a fire may cause cylinders to rupture. Call fire brigade. Cool cylinders exposed to fire by applying water from a protected location. Do not approach cylinders suspected of being hot.
- Extinguishing** Non flammable. Use water fog to cool containers from protected area.
- Hazchem Code** 2RE

### 6. ACCIDENTAL RELEASE MEASURES

- Spillage** GAS CYLINDERS: If the cylinder is leaking, eliminate all potential ignition sources and evacuate area of personnel. Inform manufacturer/supplier of leak. Wear appropriate PPE and carefully move it to a well ventilated remote area, then allow to discharge. Do not attempt to repair leaking valve or cylinder fusible plugs.

### 7. HANDLING AND STORAGE

- Handling** Use safe work practices to avoid eye or skin contact and inhalation. Observe good personal hygiene. Prohibit eating, drinking and smoking in contaminated areas. Wash hands before eating.
- Storage** Do not store near sources of ignition or incompatible materials. Cylinders should be stored below 45 C in a secure area and upright to prevented cylinders from falling. Cylinders should also be stored in a dry, well ventilated area constructed of non-combustible material with firm level floor (preferably concrete), away from areas of heavy traffic and emergency exits.

### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

- Ventilation** Use with adequate natural ventilation. Open windows and doors where possible. In poorly ventilated areas, mechanical extraction ventilation is recommended. Maintain vapour levels below the recommended exposure standard.
- Exposure Standards** CARBON DIOXIDE (124-38-9)  
ES-TWA : 5000 ppm (9000 mg/m3)  
ES-STEL : 30000 ppm (54000 mg/m3)  
WES-TWA : 5000 ppm (9000 mg/m3)
- PPE** Wear safety glasses and leather gloves. Where an inhalation risk exists, wear Self Contained Breathing Apparatus (SCBA) or an Air-line respirator.



Colour  
Rating  
**AMBER**



BOC Limited  
988 Great South Road  
PENROSE AUCKLAND  
Tel: + 64 9 525 5600

## MATERIAL SAFETY DATA SHEET # 0101

Product Name **CARBON DIOXIDE, MEDICAL (BOC LIMITED - NZ)**

### 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: COLOURLESS GAS  
Odour: ODOURLESS  
pH: NOT AVAILABLE  
Vapour Pressure: 6000 kPa @ 25 C  
Vapour Density: 1.53 (Air = 1)  
Boiling Point: NOT AVAILABLE  
Melting Point: NOT AVAILABLE  
Evaporation Rate: NOT AVAILABLE  
Solubility (water): 0.759 cm<sup>3</sup>/cm<sup>3</sup>  
Specific Gravity: NOT AVAILABLE  
% Volatiles: NOT AVAILABLE  
Flammability: NON FLAMMABLE  
Flash Point: NOT RELEVANT  
Upper Explosion Limit: NOT RELEVANT  
Lower Explosion Limit: NOT RELEVANT  
Autoignition Temperature: NOT AVAILABLE  
Density: 1.84 g/L @ 20 C

### 10. STABILITY AND REACTIVITY

**Reactivity** Moist carbon dioxide is corrosive, hence acid resistant materials are required (stainless steel). Certain properties of some plastics and rubbers may be affected by gas or liquid, ie. embrittlement, leaching of plasticisers, etc.

**Decomposition Products** May evolve toxic gases if heated to decomposition.

### 11. TOXICOLOGICAL INFORMATION

**Health Hazard Summary** Asphyxiant gas - non irritant. When released into air the concentration of carbon dioxide is diluted. Carbon dioxide concentrations of 3-5 % in air cause increased respiration and headache. Concentrations of 8-15% cause headache, nausea and vomiting which may lead to unconsciousness if not moved to open air and given oxygen. Inhalation of a mixture containing no oxygen may result in unconsciousness from the first breath and death will follow in a few minutes. Adverse health affects to long term exposure to carbon dioxide have not been reported. However in environments such as submarines where exposure to levels of 0.5 - 1.0% may occur, specialist medical opinion should be sought on the effects of long term exposure.

**Eye** Non irritant gas.

**Inhalation** Non irritant - Asphyxiant.

**Skin** Non irritating.

**Ingestion** Due to product form, ingestion is considered highly unlikely.

### 12. ECOLOGICAL INFORMATION

**Environment** Carbon dioxide is a natural component of the earth's atmosphere (0.027 - 0.035 % v/v). However, increases in the atmospheric carbon dioxide levels have been linked with global warming, and hence emission of carbon dioxide into the atmosphere should be mimimised as far as possible.

Colour  
Rating  
**AMBER**

## Appendix 10



**Massey University**  
COLLEGE OF HUMANITIES AND SOCIAL SCIENCES

SCHOOL OF HEALTH SCIENCES  
Private Bag 11 222  
Palmerston North  
New Zealand  
T 64 6 356 9099  
F 64 6 350 5668  
[www.massey.ac.nz](http://www.massey.ac.nz)

31 January 2008

To Whom It May Concern:

I have reviewed the application for the study entitled 'Carbon Dioxide Insufflation During Colonoscopy Minimizes Post Colonoscopy Pain? A Randomized Controlled Trial' submitted by Anne Cleland for methodological soundness. I find the study to be clearly conceptualized and the methods appropriate for the questions posed. The design is sufficient to control for internal threats to validity, the sample size sufficient for the level of analysis proposed and the procedures and measures clear.

Sincerely,

Steven J. La Grow  
Professor  
School of Health and Social Services

## Appendix 11



MIDCENTRAL HEALTH

Doc. Code: **I-2-R30**Policy for Research  
Appendix 2MIDCENTRAL HEALTH APPROVAL FORM FOR  
RESEARCH ACTIVITY

To be completed by the Principal Researcher and Group Manager. The Group Manager is to forward a copy of the form to the MidCentral Health Clinical Board, via CO&SI. All relevant supporting documentation is to be included.

Research Practice Title: <u>Carbon Dioxide Insufflation During Colonoscopy</u>	
Principal Researcher: <u>Anne Cleland RN</u> <i>minimises Post Colonoscopy Pain</i>	
Designation: <u>Registered Nurse</u>	Service Area: <u>Gastroenterology</u>
Research Practice Experience: <u>Completed Health Research Design and Method - Master's paper 2007</u>	
Other Researchers Involved: <u>Dr Andrew Herbert</u>	
Brief Description of Research Practice Purpose and Methodology: <u>A randomised double blinded controlled trial with 240 consecutive consented patients referred for elective colonoscopy. The goal is to establish that carbon dioxide instead of air, insufflated during colonoscopy reduces post colonoscopy pain.</u>	
<b>Section A: Initial Registration and Approval of Research Practice</b>	
Documented evidence:	<input checked="" type="checkbox"/> Research purpose and parameters
<input checked="" type="checkbox"/> Consultation with all MCH involved parties	<input type="checkbox"/> Risk and indemnity cover
<input checked="" type="checkbox"/> Resources required e.g. staff, equipment, other service involvement	<input type="checkbox"/> Approved research budget
Group Manager signature to proceed: <u>[Signature]</u>	Date: <u>30/1/08</u>
Professional approval gained, where applicable (e.g. Professor of Nursing)	
<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable	
Designation: <u>Director of Nursing</u>	Signature: <u>[Signature]</u> Date: <u>30/1/2008</u>
External approval gained, where applicable (e.g. Central Regional Ethics Committee, Educational Institution)	
<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable	
State where from: <u>Central Regional Ethics Committee</u>	
Documented evidence (where applicable):	
<input type="checkbox"/> National application form for ethical review of a research project (NAF-2005-v1)	
<input type="checkbox"/> 'Participants who are unable to give informed consent to participate' form (NAF-Part 7)	
<input type="checkbox"/> Locality assessment form	<input type="checkbox"/> 'Use of human tissue' form (NAF-Part 5)
<input type="checkbox"/> 'Genetic research' form (NAF-Part 6)	
<b>Section B: Final Group Manager Approval to Proceed</b>	
<input type="checkbox"/> Final contractual agreement completed	
Proposed start/end dates of research: _____	
Group Manager signature: <u>[Signature]</u>	
Service Line: <u>Medical Services</u>	Date: <u>23-05-08</u>
<i>This submission has been considered to meet ethical and professional requirements, and clearly demonstrate potential clinical, professional and/or strategic benefit to the organisation.</i>	
<b>Clinical Board Acknowledgement of Registration</b>	
Signed: <u>[Signature]</u>	Designation: <u>MEDICAL DIRECTOR</u> Date: <u>26/5/08</u>
Completed form to be forwarded to CO&SI for lodging on MCH Research Register	

## Appendix 12

### Registered Drug Form (*refer question B19*)

<b>INFORMATION REQUIRED FOR TRIALS INVOLVING ADMINISTRATION OF DRUGS CURRENTLY REGISTERED IN NEW ZEALAND.</b>
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Trade name of drug:	Carbon dioxide
Chemical name of drug	Carbon dioxide
Pharmacological class:	Medical Gas
Brief details of any special features:  (E.g., long half life, receptor selectivity)	Rapidly absorbed by the colon lumen, enters the venous system and excreted through the lungs
Recommended dose range:	Colon insufflation at 2-4 Litres a minute
Form of administration in the study:	Delivered via the colonoscope into the colon
Known or possible interactions with non-trial drugs the participants may be taking:	No known drug interaction
Side effects and adverse reactions:	Possible CO <sub>2</sub> retention and subsequent acidosis with CO <sub>2</sub> retainers and severe chronic obstructive airway disease (COPD)

## References

## Appendix 13

NAF-2005-v1 page 17

**FORM A**  
**DECLARATION OF ELIGIBILITY OF A CLINICAL TRIAL FOR CONSIDERATION OF**  
**COVERAGE UNDER ACCIDENT COMPENSATION LEGISLATION**

**Instructions:** This form is to be completed and the statutory declaration signed by the applicant. It should be forwarded to the appropriate Ethics Committee together with the documents seeking ethical approval for the proposed study.

The information provided must be sufficiently detailed to enable the Ethics Committee to be satisfied that the proposed research is not conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the research is carried out.

The provision of this information will enable the ethics committee to be satisfied that participants in the clinical trial will be considered for coverage under accident compensation legislation, for injury caused as a result of their participation in the research.

**DETAILS OF PROPOSED RESEARCH STUDY**

- Title of research project:  
Carbon Dioxide Insufflation in Colonoscopy Reduces Post Colonoscopy Pain
- Name of Research Director/Investigator:  
Anne Cleland
- Is the Investigator a Registered Health Professional  Yes  No  
*tick or circle as appropriate*
- Location/s of proposed study:  
Gastroenterology, MidCentral Health
- State number of participants:  
240
- Organisations providing support (\$ or "in kind") for the direct and indirect costs of the research.  
Please provide names of organisations and the type of support provided.

MidCentral Health

- Relationship of proposed research to the pharmaceutical industry or other company involved in health research. Please describe the involvement of industry in your proposed research, and provide details of support to be received from them.

Olympus NZ's relationship is limited to its role as manufacturer, supplier and technical advisor of the CO2 insufflator being used. Doc Gas is the company which is the supplier of all CO2 to MidCentral Health, This is their only relationship with the above research.

**STATUTORY DECLARATION:**

I Anne Cleland (name, of town/city) Palmerston Nth solemnly and sincerely declare that as director of the proposed research, the proposed study is not conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is carried out.

And I make this solemn declaration conscientiously believing the same to be true and by virtue of the Oaths and Declarations Act 1957.

Anne Cleland  
Name (please print)

[Signature]  
Signature

30/1/08  
this day of

before me

L.D. van de Waardt  
Name (please print)

[Signature]  
Signature



A Justice of the Peace, or  
 A Solicitor of the High Court  
 or other person authorised to take a statutory declaration.

**Warning:** Please note that it is an offence under part VI subsection 111 the Crimes Act 1961 to make a false statutory declaration.

**Note:** Applicants conducting a research study which is conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is carried out should complete Form B.

## Appendix 14



## Central Regional Ethics Committee

Ministry of Health  
Level 2, 1-3 The Terrace  
PO Box 5013  
Wellington  
Phone (04) 496 2405  
Fax (04) 496 2191

28 March 2008

Ms Anne Cleland  
574 Aranui Road  
RD 5  
Palmerston North

Dear Anne

**Does Carbon Dioxide Insufflation During Colonoscopy Minimize Post Colonoscopy Pain? A randomized controlled Trial.**

Ms Anne Cleland, Dr Andrew Herbert  
MidCentral DHB  
CEN/08/01/005

The above study has been given ethical approval by the **Central Regional Ethics Committee**. A list of members of this committee is attached.

#### Approved Documents

Protocol No. Submission 31 January 2008

- Information sheet Version 2, dated March 2008
- Consent Form Version 2, dated March 2008

#### Certification

The Committee is satisfied that this study is not being conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is being carried out.

#### Accreditation

The Committee involved in the approval of this study is accredited by the Health Research Council and is constituted and operates in accordance with the Operational Standard for Ethics Committees, April 2006.

#### Final Report (for studies less than 1 year)

The study is approved until **28 March 2009**. A final report is required at the end of the study. The report form is available on <http://www.newhealth.govt.nz/ethicscommittees> and should be forwarded along with a summary of the results. If the study will not be completed as advised, please forward a progress report and an application for extension of ethical approval one month before the above date.

#### Requirements for SAE Reporting

The Principal Investigator will inform the Committee as soon as possible of the following:

- Any related study in another country that has stopped due to serious or unexpected adverse events
- withdrawal from the market for any reason
- all serious adverse events occurring during the study in New Zealand which result in the investigator breaking the blinding code at the time of the SAE or which result in hospitalisation or death.
- all serious adverse events occurring during the study worldwide which are considered related to the study medicine. Where there is a data safety monitoring board in place, serious adverse events occurring outside New Zealand may be reported quarterly.

All SAE reports must be signed by the Principal Investigator and include a comment on whether he/she considers there are any ethical issues relating to this study continuing due to this adverse event. It is assumed by signing the report, the Principal Investigator has undertaken to ensure that all New Zealand investigators are made aware of the event.

**Amendments**

All amendments to the study must be advised to the Committee prior to their implementation, except in the case where immediate implementation is required for reasons of safety. In such cases the Committee must be notified as soon as possible of the change.

As part of the conditions of approving a proposal, committees may require an independent review or audit of approved research or innovative practice at any time.

**Please quote the above ethics committee reference number in all correspondence.**

The Principal Investigator is responsible for advising any other study sites of approvals and all other correspondence with the Ethics Committee.

**It should be noted that Ethics Committee approval does not imply any resource commitment or administrative facilitation by any healthcare provider within whose facility the research is to be carried out. Where applicable, authority for this must be obtained separately from the appropriate manager within the organisation.**

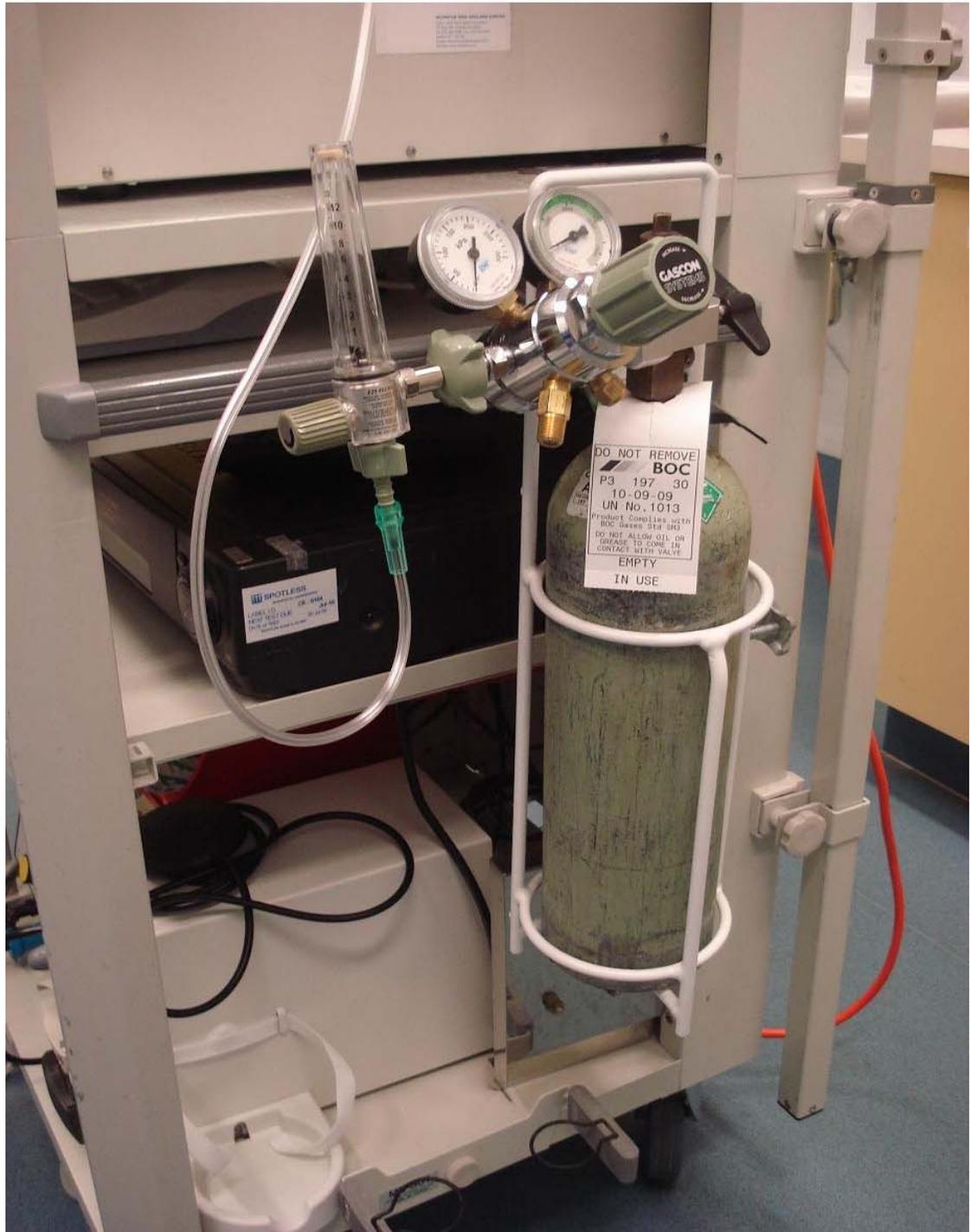
Yours sincerely



**Jiska van Bruggen**  
**Central Regional Ethics Committee Administrator**

Email: [jiska\\_van\\_bruggen@moh.govt.nz](mailto:jiska_van_bruggen@moh.govt.nz)

Appendix 15





## Appendix 16

CO2 ( C ) /Air ( A ) \* Pain Score @ 0 min Crosstabulation

			Pain Score @ 0 min										Total	
			0	1	2	3	4	5	6	7	8	9		10
CO2 ( C ) /Air ( A )	A	Count	24	3	4	1	10	10	13	7	10	12	3	97
		<b>No index entries found.</b> Expected Count	27.4	1.9	4.7	.9	8.5	13.2	11.8	6.2	11.8	8.0	2.4	97.0
		% within CO2 ( C ) /Air ( A )	24.7%	3.1%	4.1%	1.0%	10.3%	10.3%	13.4%	7.2%	10.3%	12.4%	3.1%	100.0%
		% within Pain Score @ 0 min	41.4%	75.0%	40.0%	50.0%	55.6%	35.7%	52.0%	53.8%	40.0%	70.6%	60.0%	47.3%
		% of Total	11.7%	1.5%	2.0%	.5%	4.9%	4.9%	6.3%	3.4%	4.9%	5.9%	1.5%	47.3%
C		Count	34	1	6	1	8	18	12	6	15	5	2	108
		Expected Count	30.6	2.1	5.3	1.1	9.5	14.8	13.2	6.8	13.2	9.0	2.6	108.0
		% within CO2 ( C ) /Air ( A )	31.5%	.9%	5.6%	.9%	7.4%	16.7%	11.1%	5.6%	13.9%	4.6%	1.9%	100.0%
		% within Pain Score @ 0 min	58.6%	25.0%	60.0%	50.0%	44.4%	64.3%	48.0%	46.2%	60.0%	29.4%	40.0%	52.7%
		% of Total	16.6%	.5%	2.9%	.5%	3.9%	8.8%	5.9%	2.9%	7.3%	2.4%	1.0%	52.7%

## CO2 ( C ) /Air ( A ) \* Pain Score @ 10 min Crosstabulation

			Pain Score @ 10 min									Total	
			0	1	2	3	4	5	6	7	8		9
CO2 ( C ) /Air (A)	A	Count	57	6	7	5	6	8	4	2	0	2	97
		Expected Count	70.0	4.7	6.2	3.8	3.8	4.3	1.9	.9	.5	.9	97.0
		% within CO2 ( C ) /Air (A)	58.8%	6.2%	7.2%	5.2%	6.2%	8.2%	4.1%	2.1%	.0%	2.1%	100.0%
		% within Pain Score @ 10 min	38.5%	60.0%	53.8%	62.5%	75.0%	88.9%	100.0%	100.0%	.0%	100.0%	47.3%
		% of Total	27.8%	2.9%	3.4%	2.4%	2.9%	3.9%	2.0%	1.0%	.0%	1.0%	47.3%
C		Count	91	4	6	3	2	1	0	0	1	0	108
		Expected Count	78.0	5.3	6.8	4.2	4.2	4.7	2.1	1.1	.5	1.1	108.0
		% within CO2 ( C ) /Air (A)	84.3%	3.7%	5.6%	2.8%	1.9%	.9%	.0%	.0%	.9%	.0%	100.0%
		% within Pain Score @ 10 min	61.5%	40.0%	46.2%	37.5%	25.0%	11.1%	.0%	.0%	100.0%	.0%	52.7%
		% of Total	44.4%	2.0%	2.9%	1.5%	1.0%	.5%	.0%	.0%	.5%	.0%	52.7%

CO2 ( C ) /Air ( A ) \* Pain Score @ 30 min Crosstabulation

		Pain Score @ 30 min								Total	
		0	1	2	3	4	5	6	8		10
CO2 ( C ) /Air ( A ) A	Count	59	8	12	4	4	6	1	1	1	96
	Expected Count	73.9	6.1	6.6	2.4	2.4	2.8	.9	.5	.5	96.0
	% within CO2 ( C ) /Air ( A )	61.5%	8.3%	12.5%	4.2%	4.2%	6.3%	1.0%	1.0%	1.0%	100.0%
	% within Pain Score @ 30 min	37.6%	61.5%	85.7%	80.0%	80.0%	100.0%	50.0%	100.0%	100.0%	47.1%
	% of Total	28.9%	3.9%	5.9%	2.0%	2.0%	2.9%	.5%	.5%	.5%	47.1%
C	Count	98	5	2	1	1	0	1	0	0	108
	Expected Count	83.1	6.9	7.4	2.6	2.6	3.2	1.1	.5	.5	108.0
	% within CO2 ( C ) /Air ( A )	90.7%	4.6%	1.9%	.9%	.9%	.0%	.9%	.0%	.0%	100.0%
	% within Pain Score @ 30 min	62.4%	38.5%	14.3%	20.0%	20.0%	.0%	50.0%	.0%	.0%	52.9%
	% of Total	48.0%	2.5%	1.0%	.5%	.5%	.0%	.5%	.0%	.0%	52.9%

CO2 ( C ) /Air ( A ) \* Pain Score @ 60 min Crosstabulation

		Pain Score @ 60 min							Total	
		0	1	2	3	4	5	6		7
CO2 ( C ) /Air ( A ) A	Count	68	9	6	7	3	2	1	0	96
	Expected Count	79.5	6.1	3.3	3.3	1.4	1.4	.5	.5	96.0
	% within CO2 ( C ) /Air ( A )	70.8%	9.4%	6.3%	7.3%	3.1%	2.1%	1.0%	.0%	100.0%
	% within Pain Score @ 60 min	40.2%	69.2%	85.7%	100.0%	100.0%	66.7%	100.0%	.0%	47.1%
	% of Total	33.3%	4.4%	2.9%	3.4%	1.5%	1.0%	.5%	.0%	47.1%
C	Count	101	4	1	0	0	1	0	1	108
	Expected Count	89.5	6.9	3.7	3.7	1.6	1.6	.5	.5	108.0
	% within CO2 ( C ) /Air ( A )	93.5%	3.7%	.9%	.0%	.0%	.9%	.0%	.9%	100.0%
	% within Pain Score @ 60 min	59.8%	30.8%	14.3%	.0%	.0%	33.3%	.0%	100.0%	52.9%
	% of Total	49.5%	2.0%	.5%	.0%	.0%	.5%	.0%	.5%	52.9%