THE EFFICACY OF A HOMOEOPATHIC COMPLEX (*IPECACUANHA, THEBAICUM AND PHOSPHORUS*) IN THE TREATMENT OF POSTOPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING HYSTERECTOMY.

GRANT CAVILL TAYLOR

Dissertation submitted in partial compliance with the requirements for the Master's Degree in Technology: Homoeopathy in the Department of Homoeopathy at Technikon Natal.

I, Grant Cavill Taylor, do hereby declare that this dissertation represents my own work in both conception and execution

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Signature of Student Date of Signature

APPROVED FOR FINAL SUBMISSION BY:

_____ 17/02/00

Signature of Supervisor Date of Signature

Supervisor: Dr Ashley H. A. Ross M.Tech. (Hom)(TN) B.Mus. (UCT)

THIS DISSERTATION IS DEDICATED TO MY PARENTS - PAM AND VIN TAYLOR FOR THE ENDLESS LOVE, HELP AND SUPPORT THEY HAVE SHOWN ME OVER THE YEARS, AND FOR THE HOST OF OPPORTUNITIES THEY HAVE MADE AVAILABLE TO ME.

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ABSTRACT

The purpose of this randomised double blind placebo controlled trial was to evaluate the efficacy of a homoeopathic complex in the treatment of postoperative nausea and vomiting (PONV) in women undergoing hysterectomy. It was hypothesised that the homoeopathic medication would reduce the incidence of nausea and vomiting in this experimental type clinical trial.

Sixty-two women, between the ages of 18 and 70, undergoing either abdominal, or vaginal hysterectomy, were used as the study population. The trial group (Group 1) received medication consisting of lactose tablets impregnated with a complex of *Ipecacuanha* 12CH, *Thebaicum* 12CH and *Phosphorus* 12CH in 96% alcohol. The placebo group (Group 2) received identical lactose tablets impregnated with 96% alcohol. The highest incidence of the development of PONV was anticipated during the 4 hour post-recovery period. The use of a complex of remedies was therefore based on the understanding that knowledge of the idiosyncratic post-anaesthetic presentation of individual patients would be impossible. Accurate, individually based prescriptions would be impossible during this period.

Doses of tablets were administered (sublingually) pre- and postoperatively to patients. Objective vomiting assessments were recorded as the number

of occurrences of vomiting or retching over the trial period. Patients' subjective nausea assessments were recorded on an eleven point visual analogue scale (VAS), where 0 represented no nausea, and 10 represented nausea as severe as possible. Assessments were recorded three times over the four hour post-anaesthetic trial period.

Qualitative statistical analysis was conducted on the data recorded as nausea and vomiting assessments from the patients within the experimental and control groups. Comparative analysis within the respective groups revealed a statistically significant improvement in nausea assessments in the experimental group at a 5% level of significance (α = 0.05). This improvement was shown between consultations 1 and 2 (P = 0.018) and between consultations 1 and 3 (P = 0.028). This improvement was however, not noted in the placebo group. No significant improvement was shown to exist in vomiting assessments in either group. No statistically significant difference in the incidences of nausea or vomiting was shown to exist between the two groups.

It can thus be concluded that the homoeopathic complex (*Ipecacuanha, Thebaicum* and *Phosphorus*) is effective at reducing the incidence of nausea in patients undergoing anaesthesia for hysterectomy. No efficacy was shown to exist on the incidence of vomiting.

It was recommended that future trials conducted on this subject include analysis of data from patients excluded from the trial for receiving rescue medication. It was advised that that the trial period be extended to 24 hours for future trials.

It was also suggested that a third randomised homogenous trial group be included in a study of this nature. This group should receive identical placebo tablets, at the same dosage intervals, but the subjects should not be briefed on the trial. This additional group would indicate the extent of the possible "Placebo" enigma present in the control group.

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DEFINITION OF TERMS

Acupressure : A non-invasive supportive technique that utilises pressure applied to well defined points on the body to provide relief from symptoms (Thompson 1999).

Acupuncture : The Chinese practise of piercing specific areas of the body along peripheral nerves and precise "meridian" lines, with fine needles to relieve pain, to induce surgical anaesthesia, and for therapeutic purposes (Dorland's 1995:13).

ASA 1 or 2 : Refers to a grading of preoperative physical status devised by the American Society of Anaesthetists:

Category 1: Healthy patient.

Category 2 : Patient with mild systemic disease - No functional limitations (Dripps et al. 1961 - as cited in Miller 1990).

Hysterectomy : The process of the removal of the uterus either via an incision in the abdominal wall (abdominal hysterectomy), or less commonly through the vagina (vaginal hysterectomy). At the time of the hysterectomy the cervix and or the ovaries and uterine (fallopian) tubes may be removed (Rivlin 1996:241).

Materia Medica : Reference book containing all the necessary information required for proper use of medicines. The books deal with the origin, composition and properties, as well as reference source and the classification of the medicinal agents. Where appropriate the toxicological character of a drug, as well as its reactive propensity as a homoeopathic therapeutic agent is included. Also contained in these books are the pathological, toxicological and clinically established characteristics and indications, the potencies used most frequently the preferred route of administration and dosage, taught at medical schools (Gaier 1991: 337-338).

Nausea : "a subjectively unpleasant sensation associated with awareness of the urge to vomit" (Thompson 1999); or the perception vomiting may be imminent. This sensation may be brief or prolonged - often occurring in waves. This experience may occur in isolation or precede actual vomiting (Andrews 1992). As a subjective sensation nausea should be evaluated by the patient - not the observer (Korttila 1992).

Placebo : An inactive substance used in controlled studies for comparison with presumed active drugs; or prescribed for relief of symptoms to meet a patient's demands (Berkow et al. 1996: 2647)

Potentisation : Dilution of a substance, then shaking (succussing) it violently to increase the substances homoeopathic strength, while decreasing the side effects this substance can manifest (also called "Dynamisation") (Kayne 1997:49)

Rescue medication: Conventional allopathic drugs administered in cases of intractable, severe or life threatening nausea or vomiting within the hospital set-up. *Maxolon* (metoclopramide monohydrochloride) was the rescue medication administered if necessary in this trial.

Retching : Distinguished from vomiting by manifesting as expulsive efforts without the production of stomach contents, usually indicative of an empty stomach (Korttila 1992).

Succussion : "The action of shaking up, or the condition of being shaken up, vigorously of a liquid dilution of a homoeopathic dilution of a homoeopathic medicine in its phial or bottle, where each stroke ends with a jolt, usually by pounding the hand engaged in the shaking action against the other palm" (Gaier 1991:532).

Vomiting : The forceful expulsion of upper gastrointestinal contents via the mouth. It is commonly, but not exclusively, preceded by retching in which no expulsion occurs, but which involves the activation of the same muscle groups (Andrews 1992).

CHAPTER 1

1.1 Introduction

Pain and emesis are the most common and distressing problems encountered after general anaesthesia and surgery (Koivuranta *et al.* 1997). These problems have long been associated with delayed recoveries in these patients (Alkaissi *et al.* 1999). Pain has received substantial attention, with numerous research papers having been written on the subject. Postoperative emetic problems have however received substantially less attention, partially because of its somewhat poorly understood mechanism (Naylor and Inall 1994), and the host of factors contributing to its development (Diemunsch *et al.* 1999). Postoperative nausea and vomiting have been associated with the anaesthetic substances and their methods of administration in anaesthetising patients for surgical procedures (Rabey and Smith 1992).

More recently a host of non-anaesthetic factors have been shown to be contributory to the pathogenesis of PONV. Despite attempts to manage and prevent occurrences of nausea and vomiting postoperatively, the

frequency remains concerningly high (Andrews 1992), with many patients finding these symptoms even more distressing than postoperative pain (Koivuranta *et al.* 1997). Some patients even regard PONV as the worst feature of recovery (Diemunsch *et al.* 1999).

Homoeopathy is a scientific system of medicinal therapy (Gaier 1991:272), whereby individual homoeopathic medicines act as specific stimulants to the diseased organism as opposed to allopathic medicines which act coercively (Jouanny 1993:20).

Successful homoeopathic treatment should stimulate the body's own innate defence mechanisms to re-attain a state of optimal health. "The highest ideal of cure is rapid, gentle and permanent restoration of the health, or removal and annihilation of the disease in it's whole extent in the shortest, most reliable and most harmless way" (Hahnamann 1921:94). Although homoeopathic remedies have been successfully employed in the treatment of nausea, vomiting and PONV for many years, no clinical trials have to date been conducted in this field.

The purpose of this randomised double-blind placebo-controlled study is to evaluate the efficacy of a Homoeopathic complex (*Ipecacuanha, Thebaicum* and *Phosphorus*) in the treatment of postoperative nausea and

vomiting (PONV) in terms of the patients subjective reports of nausea, and clinically observed occurrences of vomiting following anaesthesia in patients undergoing hysterectomy.

1.2 Objectives

1.2.1 First objective

The first objective of this randomised double-blind placebo-controlled study is to determine the efficacy of a Homoeopathic complex (*Ipecacuanha*, *Thebaicum* and *Phosphorus*) in the treatment of postoperative nausea in terms of patients subjective reports of nausea following general anaesthesia in patients undergoing hysterectomy.

1.2.2 Second objective

The second objective of this randomised double-blind placebo-controlled study is to determine the efficacy of a Homoeopathic complex (*Ipecacuanha*, *Thebaicum* and *Phosphorus*) in the treatment of postoperative vomiting in terms of the clinically observed occurrences of vomiting following general anaesthesia in patients undergoing hysterectomy.

CHAPTER 2

REVIEW OF THE RELATED LITERATURE

2.1 Introduction

Postoperative nausea and vomiting (PONV) has been dubbed the 'big little problem' (Kapur 1991) facing practitioners today. Despite the advent of new medicinal agents and the identification of a host of contributory and aggravator factors, the incidence of PONV still prevails as the most common complaint following anaesthesia and surgery (Koivuranta *et al.* 1997). At present many attempts have been made to develop suitable prophylactic anti-emetics to reduce the incidence of PONV. However, while allopathic drugs remain the mainstay of emetic management and prophylaxis (Arfeen *et al.* 1995), many of the currently available antiemetics are associated with undesirable side effects (Tang *et al.* 1998), or are too costly for routine administration (Oliver *et al.* 1997). In the context of the greatly restricted health budget South African

antiemetics are not routinely administered (Power personal communication 1998, Stienstra *et al.* 1997).

2.2 Consequences of PONV

Nausea and vomiting are unpleasant and undesirable sequelae to anaesthesia with effects ranging from simply "annoying" to potentially life threatening.

Physically the intensity of the act of purging may place excessive stress upon certain structures within a patients system. Oesophageal tears, possibly with haemorrhage (Mallory-Weiss syndrome), rupture of the oesophagus (Boerhaave syndrome), gastric herniation, rib fracture, intraocular haemorrhage, excessive suture line tension, muscular strain, increased hematoma formation and fatigue may all result from protracted vomiting (Andrews 1992). Two of the most concerning physical problems occurring in the postoperative period is the aspiration of gastric contents and the triggering of cardiorespiratory reflexes (Arfeen *et al.* 1995, Tang *et al.* 1998), due to the impairment of emetic reflex co-ordination from the anaesthetic agents.

The metabolic consequences of emesis include dehydration, electrolyte imbalances and anorexia. These consequences are usually of secondary importance in cases of PONV since these effects normally occur following protracted vomiting (Andrews 1992), while PONV is not normally so prolonged.

Watcha and White (cited in Thompson 1999:1130) found that for many patients the PONV experience was more disabling than the operation itself. This lead to feelings of embarrassment and degradation and an overall dissatisfaction with the "surgical experience". Furthermore there is a threefold greater incidence of PONV developing post surgically in patients who have previously experienced PONV, or are susceptible to motion sickness (Kenny 1994). This suggests an altered emetic reflex sensitivity following repeated inputs.

In addition PONV may also lead to increased expenses through cost of treatment, and loss of earnings. Carroll *et al.* (1994) showed the average cost of allopathically treating patients who experienced PONV was $14.94, with an additional estimated loss of revenue of $415 per patient in an out-patient surgical centre (cited in Thompson 1999 :1130).

2.3 Pathophysiology

Nausea and vomiting are fundamental instinctive reflexes basic to humans. These protective reflexes occur primarily as a response by the body against the absorption of toxins or in response to certain stimuli. The stimuli which may induce nausea and vomiting can originate anywhere along the gastrointestinal tract, or in addition can be of a visual, olfactory, vestibular or psychogenic nature (Thompson 1999).

The vomiting reflex is a complex one with its mechanism still being a poorly understood one. Emesis is co-ordinated via the vomiting centre (VC) within the medulla in proximity to the fourth ventricle. This VC receives input from many afferent sensory pathways including cranial nerve (CN) VIII (vestibularcochlear nerve), CN X (vagus nerve), the limbic system and the chemoreceptor trigger zone (CRTZ) (Thompson 1999).

The vestibular nerve relays input from the vestibular labyrinthine system - an essential component in the induction of vomiting from motion stimuli. There is, however, limited evidence to suggest that the vestibular system may be involved in an emetic response to chemical substances. Animal studies have shown that the removal of the vestibular system reduced emetic episodes in response to certain chemical stimuli, but had no

beneficial influence to other chemicals (Andrews 1992). The main receptors involved in triggering emesis from the vestibular labyrinthine system are histamine and acetylcholine.

The vagus nerve conveys sensory input from chemo- and mechanoreceptors in the gastrointestinal tract, the respiratory tract and the cardiovascular system. The mechanoreceptors occur primarily within the muscular wall of the intestine, and are activated by contraction and distension of the gut. Distension of the gastric antrum (e.g. by over-eating) or the proximal small intestine (e.g. by obstruction) may induce nausea and vomiting. The vagus nerve's chemoreceptors occur primarily in the mucosa and respond to alterations in the intraluminal environment (Andrews 1992.). Serotonin is thought to be the main activating substance involved in relaying the sensory information from these chemo- and mechanoreceptors to the brain (Thompson 1999).

The Limbic system is implicated in an anticipatory "type" nausea response. In 1993 Sleisenger showed this response to be a learned one, and has been well researched with respect to its involvement in chemotherapy-induced nausea and vomiting utilising the ferret model (as cited by Thompson 1999:1131). Although this response has not been investigated with respect to PONV, it could logically be expected that

patients with a previous history of PONV would anticipate this response to be repeated. In this instance their anxiety would be the facilitatory trigger for the nausea and vomiting.

In the 1950's the work of Wang and Borison (as cited in Andrews 1992:5s) demonstrated a group of cells of the area postrema were responsible for detecting certain chemical stimuli and activating the vomiting centre resulting in emesis. This area became termed the Chemoreceptor Trigger Zone (CRTZ) for emesis. The area postrema is relatively permeable to polar molecules in the blood or cerebrospinal fluid, since it is one of the circumventricular areas of the brain outside of the cerebrospinal fluid barrier and the blood brain barrier (Andrews 1992). Due to this permeability and it's 'exposed' location it is an area well suited to chemoreception. It is believed that once certain "harmful" stimuli have been detected by the CRTZ it relays its information to the VC, which would initiate a vomiting response (Thompson 1999).

2.3.1 Vomiting reflex

The motor components of the vomiting reflex are mediated by both autonomic and somatic nerves. The integration of these motor components occurs in the brain stem, while the most likely output centre

responsible for co-ordinating the vomiting process into a recognised pattern is the nucleus tractus solitarius (Naylor and Inall 1994).

2.3.1.1 Prodromal phase

The prodromal phase is usually, but not exclusively characterised by nausea. However the mechanism of nausea and its initiation is not well understood physiologically. It is believed to result from a disruption in the pattern of normal gastro-intestinal tract motility, in response to stimuli detected by the higher brain centres (Thompson 1999). Nausea is associated with signs such as hot and cold diaphoresis, cutaneous vasoconstriction, pupillary dilation tachycardia and increased salivation (Andrews 1992, Thompson 1999). However because nausea is a subjective experience, the patients subjective assessment is the only true assessment of nausea (Thompson 1999).

2.3.1.2 Ejection phase

This phase is composed of retching and vomiting. The process is complex initiated with measures to protect the airways and ending in the ejection of the evoking stimulus. Measures to protect the airways begin with deep breathing resulting in closure of the glottis and elevation of the pharynx to close the nasal passages. The diaphragm then contracts strongly

downward, in conjunction with contraction of the abdominal muscles thus increasing intragastric pressure. This results in the forced ejection of gastric contents upward through the oesophagus and mouth (Andrews 1992).

2.4 Incidence

Postoperative nausea and vomiting occurs with a general incidence of 10% to 80% of patients' anaesthetised. This incidence is largely dependent on the patient, type of surgery and anaesthetic involved (Diemunsch *et al.* 1999). This level has remained for decades despite the introduction of promising new therapeutic agents (Arfeen *et al.* 1995).

2.4.1 Anaesthetic factors

There exists a greater incidence of nausea and vomiting following general anaesthesia compared with regional anaesthesia. (Koivuranta *et al.* 1997).

An increased incidence of PONV is also observed following the administration of opioids as premedication, where they have a tendency to stimulate the vomiting centres causing increased nausea and vomiting (Neal 1997:64), while *atropine*- and *hyoscine*-based premedications

appear to decrease emetic effects (Neal 1997:53). There is an apparent lowered incidence of PONV associated with the use of propofol, compared with *thiopentone*, when used as induction agents (Myles *et al.* 1996, Power personal communication, 12.11.1998).

The use of *nitrous oxide* (NO_2) as a maintenance agent may be associated with a raised incidence of PONV. The studies conducted in this area are, however, inconclusive (Rabey and Smith 1992). The maintenance agents *isoflurane, enflurane* and *halothane* tend to have lower incidences of PONV than opioid containing agents, while *fentanyl* is associated with a considerably increased development of PONV (Rabey and Smith 1992).

2.4.2 Patient factors for the development of PONV

Patient age is a risk factor for the development of PONV. Children (<5 years of age) undergoing the same operation are less likely than adults to develop PONV. Ironically, adults over the age of 55 are less likely to experience PONV than younger adults. (Kenny 1994, Thompson 1999).

There exists a two to three times increased incidence of PONV in women, postulated to be hormonal in origin (Helmers *et al.* 1993). This difference

in incidence only becomes apparent after puberty. The severity of the vomiting experienced in female patients is also reported to be greater than that of male patients (Lerman 1992). Severe nausea is, furthermore, far more common in female patients (Koivuranta *et al.* 1997).

Beattie *et al.* (1993) showed a correlation between the stage of the menstrual cycle and the development of PONV to exist. In a study of women undergoing laparoscopic tubal ligation, it was shown that there is an increased risk of PONV developing post-operatively in women who are menstruating (in the first eight days of their menstrual cycles) compared with non-menstruating women.

Andersen *et al.* (1993), showed by a retrospective study, the most frequently occurring complications following the hysterectomy operation were postoperative wound infection, postoperative bleeding, prolapsed pelvic structures, abdominal pain and ileus (inhibited bowel motility), therapeutic complications and "other" surgical complications (including PONV).

A previous history of motion sickness or PONV post-surgically results in a three-fold increase in the likelihood of PONV occurring after subsequent anaesthetisation (Lerman 1992). The likely development of PONV is

similarly increased where there is retarded gastric motility and delayed emptying, generally termed ileus (Lerman 1992).

Naylor and Inall (1994) suggest stimulation of the labyrinthine apparatus (as in moving the patient from one bed to another) is associated with a higher incidence of nausea and vomiting.

Obese patients are believed to be more likely to develop PONV than patients of normal weight. It is hypothesised that fat-soluble anaesthetic agents accumulate in, and take longer to clear from adipose tissue (Kenny 1994). However Koivuranta *et al.* (1997) showed obesity to have only a minor effect on nausea in female patients. A similar occurrence was also reported by Cohen *et al.* (1994) and Haigh *et al.* (1993) (Cited in Koivuranta *et al.* 1997:449).

In a survey of postoperative nausea and vomiting conducted by Koivuranta *et al.* (1997) there was a greater incidence of nausea and vomiting In the ward post surgically compared with the occurrence of nausea and vomiting in the recovery room.

It is generally accepted that there is a higher incidence of PONV among indian patients. The general incidence of PONV observed in black patients

is lowest, while the incidences of PONV among white and coloured patients has an occurrence between these two race groups (Moodley personal communication 1999).

2.4.3 Surgical factors

A comparative survey of the attitudes and perceptions of Swiss anaesthesiologists and surgeons regarding PONV conducted by Wilder-Smith *et al.* (1997) showed gynaecological surgery to have, respectively, the highest incidence of PONV, from the anaesthesiologists perspectives, and the second highest incidence, from surgeons perspectives. The occurrence of PONV in patients undergoing major gynaecological surgery in general is recorded by Helmers *et al.* (1993) to be as high as 60%. The highest incidence of PONV within the broader field of gynaecological surgery, is found following abdominal and vaginal hysterectomy, where an incidence as high as 73% can exist (Diemunsch 1999).

The duration of the anaesthesia appears to have a direct correlation to the development of PONV. In general the longer the anaesthesia, the greater the likelihood of PONV developing. This is believed to be due to a prolonged intestinal ileus, and a longer time required for the body to clear the implicated stimuli (Andrews 1992).

2.5 Current PONV treatment

2.5.1 Allopathic treatment

While allopathic drugs remain the mainstay of treatment for the PONV problem, a comparative survey conducted by Wilder-Smith *et al.* (1997) revealed that there is still a united dissatisfaction amongst surgeons and anaesthesiologists related to the number of negative side effects and cost of these antiemetic drugs. There is thus still the need to look for alternative treatments.

The four different types of receptors involved in the vomiting process include dopaminergic, histaminic (H_1-), cholinergic (muscarinic) and serotonergic (5-HT_3). There are currently no pharmaceutical agents capable of blocking the efferent motor impulse to vomit, which would be an effective agent in all four of the above cases (Thompson 1999).

Phenothiazines' (*prochloraperazine, chlorpromazine and perphenazine*) anti-emetic action occurs via dopamine blockade at the CTZ (Lilley *et al.* 1996:766) Side effects include extrapyramidal effects (acute dystonias, dyskinesia, tardive dyskinesia, akathisia, and Parkinsonism), postural

hypotension, slower recovery and auditory hallucinations (Berkow *et al.* 1996: 1639-1642, Rowbotham 1992).

Benzamides (*metoclopramide and domperidone*) have both peripheral and central anti-emetic properties. Being gastrointestinal prokinetic drugs they act primarily as antidopaminergic agents mainly affecting the chemoreceptor trigger zone (CTZ), but also increasing gastric motility and sphincter tone (Thompson 1999). *Metoclopramide* also has an antagonistic action at the 5-HT_3 receptor sites accentuating its antiemetic efficacy. This efficacy has however received more scepticism recently (Desilva *et al.* 1995). Side effects include extrapyramidal symptoms (especially dyskinesias and dystonia, but also Parkinsonism-like symptoms of cogwheel rigidity, festinant gait and masked facies), excessive sedation, hypotension, tachy- or bradycardia, and restlessness (Berkow *et al.* 1996: 1639-1643., Neal 1997: 52-53,58-61).

Anticholinergics (*hyoscine and atropine*) agents act centrally and peripherally as anticholinergics, by blocking acetylcholine receptors on the vestibular nuclei within the labyrinth (Lilley *et al.* 1996:766). In the past they have been used widely in the practice of anaesthesia. Some data suggests transdermal *hyoscine* may have certain anti-emetic properties

(Rowbotham 1992). For it to be effective however it should be applied several hours prior to surgery (Thompson 1999). Side effects include more severe and protracted drowsiness in patients on induction, and delayed recovery. *Atropine* is not used postoperatively due to its cardiovascular effect of vagal interference resulting in tachycardia (Rowbotham 1992).

Butyrophenones (*droperidol and haloperidol*) induce blockade of dopamine receptors. It is used perioperatively for its sedative and antiemetic properties (Holderness and Strauhan 1991:303-304). Side effects are similar to those associated with phenothiazines including extrapyramidal reactions especially acute dystonias, dysphoria, drowsiness, hypotension and excessive restlessness, and excitement (Rowbotham 1992). There is also the tendency for delayed discharge to result following the administration of *droperidol* , hence the reluctance to administer it in the out-patient setting (Thompson 1999).

Histaminic blockers (*cyclizine*) work at the H_1- receptors and have been shown to be effective as antiemetics. Their efficacy is believed to be related to their antimuscarinic activity affecting vestibular trigger pathways and the VC. Side effects include sedation and dry mouth (Lilley *et al.* 1996:766)

Serotonin [5-hydroxytryptamine (5-HT_3)] antagonists (*ondansetron, granisteron and tropisteron*) are thought to potently and selectively block certain of the 5-HT_3 receptors, found in high concentration in the nucleus tractus solitarus and area postrema, corresponding to the CRTZ area responsible for emesis. Efficacy studies conducted on high "emesis risk" patients undergoing chemotherapy, found *ondansetron* to be an effective anti-emetic agent with few side effects (Thompson 1999). However according to Tang *et al.*(1998) none of the currently available 5-HT_3 receptor antagonists are completely effective in preventing PONV. This, in conjunction with their expense, means they cannot be seen as front-line prophylactics (Desilva *et al.* 1995). Side effects include extrapyramidal effects (as described above) and drowsiness.

2.5.2 Alternative forms of treatment

Bone *et al.* (1990) conducted a comparative trial on the efficacy of Ginger rhizome (*Zingiber officinale*) as an antiemetic agent in women undergoing major gynaecological surgery. Both this trial and a more recent one conducted by Phillips *et al.* (1993) found *Zingiber officinale* to be as effective as *metoclopramide* as an antiemetic agent. Both trials also found that fewer patients on the *Zingiber officinale* treatment required postoperative antiemetics as compared to patients on the placebo, or *metoclopramide* treatments. Arfeen *et al.* (1995) however contested these findings in their double blind randomised controlled trial of ginger for the prevention of postoperative nausea and vomiting. Their findings demonstrated that *Zingiber officinale* powder BP in 0.5 and 1.0g doses did not reduce the incidence of PONV. Their findings suggested that incidences of PONV tended to increase as the dosage of ginger increased from 0 to 1.0g, this trend was however not statistically significant. While some of the chemical structures of the compounds present in the *Zingiber* rhizome have been identified, the active ingredient and it's mechanism of action is not understood (Phillips *et al.* 1993).

In the 1980's Dundee and his co-workers (as cited in Wetchler 1992) noted that acupuncture of the Pericardium 6 (P6 - Neiguan) acupuncture

point significantly reduced the incidence of perioperative nausea and vomiting in patients undergoing minor gynaecological procedures. Several more recent studies demonstrated the efficacy of acupuncture (both manual and electrical) and acupressure on nausea and vomiting after gynaecological surgery (as cited in Alkaissi *et al.* 1999:270). The P6 (Neiguan) point is situated 2 Chinese inches (two thumb widths at the interphalangeal joint) from the distal wrist crease, between the tendons of the flexor carpi radialis and palmaris longus (Rowbotham 1992). A recent study by Alkaissi *et al.* (1999) on the "true" and placebo effects of acupressure in the prevention of postoperative nausea and vomiting after outpatient gynaecology surgery showed a reduced incidence of vomiting and decreased need for antiemetics using acupressure of the P6 point.
The mechanism of action of acupuncture and acupressure on nausea and vomiting has not been established (Alkaissi *et al.* 1999).

Behavioural and supportive techniques form an important part of the management of PONV. These interventions include relief from anxiety, distraction, relaxation, and guided imagery techniques and therapeutic touch (Thompson 1999). Methods which should, according to Thompson (1999), be undertaken to reduce patient anxiety include adequate patient education on the various procedures pre- and post-surgery; providing

support and reassurance to the patient; and what they should do should they experience symptoms of PONV.

2.6 Homoeopathy

2.6.1 Historical background

Homoeopathy is by no means based on recent concepts. Hippocrates stated as long ago as the fifth century B.C that there were two methods of treating disease. The one method followed a treatment by opposites, where a medicine was used to counteract or oppose the signs and symptoms of disease. The other method was based on treatment by similars, a process of stimulating healing within the organism by introducing a substance which would mimic the signs and symptoms of that disease presented. In the treatment by similars the remedy was used to stimulate the bodies own healing powers, thus strengthening the body (Gibson 1991:84).

2.6.2 The founder of Homoeopathy

Samuel Hahnemann, a German medical doctor formulated, for the first time in the history of medicine, the complete laws and principles governing

health and disease, and proved these laws with actual clinical experience (Vithoulkas 1980:5).

Dr Hahnemann made his initial discoveries into this "new" form of medicine around 1790 while experimenting with Cinchona officionalis (Peruvian bark) - the substance from which quinine is derived. While using the substance on himself he was surprised to discover he begun to develop the signs and symptoms of intermittent fever (today better known as malaria). Knowing that Cinchona was an effective treatment for malaria, he noted a strange correlation between the substance and the disease it was being used to remedy. Hahnemann begun experimenting with other substances used at that time, and in so doing begun to draw up drug pictures of many remedies. At the same time he begun to formulate certain principles for the administration of these drugs (Blackie 1978:16-23).

Homoeopathy is a therapeutic method based upon the law of similars ("like cures like").This law is founded upon the observation that all medicines capable of producing symptoms in healthy individuals can cure these selfsame symptoms if present at the time of illness (Eizayaga, 1991:59). It is believed homoeopathic treatment works on the principle of stimulating the body's innate defence mechanisms towards optimal

function, thus facilitating the return to a curative effect (Gaier 1991:134-36 & 432-441.). Homoeopathic remedies have received much attention in recent years owing to their efficacy, their safety, cost effectiveness and ease of access as a form of treatment (Rees and Willey 1993:304).

2.6.3 The concept of the minimum dose

In an attempt to find the ideal dose of a medicine Hahnemann experimented with diluting his remedies. He discovered by doing this that these diluted remedies had curative benefits, but they did not produce any side effects. He worked on a one in one hundred (Centisimal [C or CH]) scale of dilution.

2.6.4 The concept of potency

Hahnemann noted in his experimentation with substances that medicines prepared by means of serial dilution and succussion had more powerful therapeutic benefits than the original crude substance. He also noted that remedies prepared without succussion did not display this increased therapeutic power. Hahnemann therefore named the dilution and succussion of his medicines dynamisation or potentization (Gibson 1991:74).

2.6.5 Homoeopathic simillimum treatment

In Homoeopathy the law governing the prescription of a given medicine occurs when the specific symptom-complex that a patient presents with, is comparative to the symptom-complex that a medicine is capable of producing in a healthy person. The most effective remedy which can be prescribed would be that remedy whose symptomatology presents the clearest and closest resemblance to the symptom-complex of the sick person. Thus "let likes be treated by likes"(Boyd 1989:2).

Homoeopathic prescriptions are based on the individualising symptoms of the patient presenting at the time of the consultation (Clover 1991: 60-70).

2.6.6 Combination remedies

Combinations of as many as ten remedies may be administered to a patient at the same time. A combination of medicines such as this is termed a "complex". The choice of medicines in a complex is designed to match the totality of symptoms of an illness (Cook 1989: 73). The principal reason for employing a complex medicine would be where there are adverse circumstances involved in the case and it is impossible to ascertain which medicine would be the most appropriate for that case. The

complex thus increases the chance of a correct prescription being administered (Kayne 1997:106).

Due to the nature and structure of this study, and the acute state which is induced on a system following anaesthesia, *a priori* knowledge of the idiosyncrasies of individual patient presentations would be impossible. For this reason it was decided to employ a combination of remedies on all patients regardless of idiosyncrasy. Although this form of prescription is somewhat "untraditional" it is nonetheless effective (Ullman 1995 -internet extraction *www.homeopathic.com/research/scienti.htm*).

The selection of remedies for a complex to treat PONV must therefore be based upon established toxicology and any general indications contained within the Materia Medica. This method of prescribing is known as pathological prescribing and pays attention to the physical complaint (Clover 1991:71). The complex, which was employed in this study, consisted of the following remedies with their relevant Materia Medica indications.

Ipecacuanha: The principal feature of *Ipecacuanha* is its persistent nausea and vomiting. Nausea that is not relieved by vomiting, and is aggravated by stooping. There is much restlessness. Patient has much salivation.

Foamy profuse discharges (Vermeulen 1997:897). *Ipecacuanha* syrup is, ironically, used allopathically as an emetic agent (Holderness and Straughan 1989:449). Since there exists a corresponding action between the toxicology of a substance and its therapeutic action (Jouanny 1993:15) this substance can be used homoeopathically in dilution.

Thebaicum: Patients are drowsy and generally sluggish. There is paralysis and inactivity of organs especially digestive organs and the bowels (ileus). Convulsive episodes of retching and vomiting. Nausea and inclination to vomit when moving (Vermeulen 1997:1241) These are all commonly seen symptoms following general anaesthetics, and especially following abdominal and gynaecological surgery, where ileus frequently occurs (Smith 1984:60). *Thebaicum* therefore covers PONV *per se* as well as its commonly noted antecedents of ileus and post-operative movement.

Phosphorus: Nausea and headache with vertigo. Post operative vomiting and constant nausea. *Phosphorus* is used to treat haemorrhages, and small wounds which bleed profusely (Vermeulen 1997:1281). '*Phosphorus*...given...before the operation will prevent the sickness which commonly follow...' (Rawat 1996:496.) *Phosphorus* therefore has direct correspondence to both postoperative nausea and vomiting and the noted tendency to postoperative haemorrhage.

2.6.7 Potency selection

Each of these remedies will be employed in a 12CH in the complex. This potency was selected because the 12CH potency (having a deconcentration of $1x10^{-24}$) is the first dilution in which mathematically no molecules of the base substance is understood to exist (Avagadro's constant = 6.023×10^{23}). No purely pharmacological effect could therefore be considered accountable for any results which occurred. It is generally accepted in clinical prescriptions that the greater the degree of similarity between the anticipated symptoms of a condition and the drugs proving symptom complex, the higher the potency (30CH and greater) selected (Jouanny 1993:91). The employment of 12CH potencies (middle range potencies 9CH-15CH) has thus also been based on the relatively low degree of similitude which exists between the pathology of PONV and the clinical picture seen in the pathogenesis of the various remedy provings. Medium potencies are also most effective in influencing tissue and organ function to return to a normal state of physiology (Gaier 1991:433).

2.7 Conclusion

From the above information it can be seen there still exists a high prevalence of nausea and vomiting postoperatively. There thus exists the necessity for further investigations to be conducted into the field of postoperative nausea and vomiting. It is the researcher's intention to conduct a double blind placebo controlled trial to investigate whether or not a homoeopathic complex (*Ipecacuanha, Thebaicum and Phosphorus)* can effectively provide an alternative means of decreasing the incidence of PONV following hysterectomy.

CHAPTER 3

MATERIALS AND METHODS

3.1 Study design

Randomisation was conducted by a neutral member in the study Dr Ashley Ross (Department of Homoeopathy, Technikon Natal).The randomisation process was carried out as follows: eighty two pieces of paper, numbered 01 - 82, were mixed up and placed in an envelope. The numbers appearing on the first forty one pieces of paper drawn out of the envelope were assigned to the verum (treatment) group. The remaining numbers not allocated to the placebo group were assigned to the placebo group. The bottles of medication and placebo were then assigned numbers according to this randomised table.

Patients fulfilling the selection criteria and having given informed consent to participate in the trial were assigned a number from 01 to 82 in order of admission on to the trial. This method gave each element within a population an equal chance of being included in a sample. The number a patient was allocated was recorded on the patient's data. The code

relating to the medication was thus blinded to the patients and to the experimenter, with the key to the code only being revealed at the end of the study.

3.2 Ethics

Prior to conducting the clinical trial the researcher applied for ethical approval from the University of Natal Medical School (see Appendix A). Following such approval the Medical Superintendent of Addington hospital was requested to permit the trial to take place within the hospital. Once the Medical Superintendent granted permission, the trial began (see Appendix B).

3.3 Subjects

A minimum of sixty female patients was included in this study. All the patients were obtained from the Obstetrics and Gynaecology department at Addington hospital. All women presenting for abdominal or vaginal hysterectomies were briefed by the researcher on the trial and given an "Information to Patients" form (see Appendix C). Once they understood this information, they were given the opportunity to ask questions. Thereafter they were requested to join the study. Patients who

volunteered to participate in this clinical trial were assessed according to the selection criteria governing admissibility into the trial. Those patients who met the selection criteria were accepted in to the study. These subjects then signed an "Informed Consent" form (see Appendix D). The patient was then assigned a number (from 01 - 82) corresponding to the assignation of a bottle of tablets (as described in 3.2 above).

3.3.1 Inclusion criteria

- Patients scheduled for abdominal or vaginal hysterectomies, aged between 18 and 75 were eligible for this study.

3.3.2 Exclusion criteria

Patients were excluded from the study if they:

- were lactating;
- had ingested opioids, alcohol, antiemetics or had experienced incidences of vomiting within a 24 hours period prior to surgery;
- had an ASA status greater than 2;
- received rescue antiemetic treatment at any time throughout the trial period; or
- if they were transferred to another ward while in the trial period.

Prior to any treatment, a preoperative history assessment was conducted on each patient (see appendix E).

3.4 Treatment

The tablets used for this study were prepared by Pharma Natura a registered homoeopharmaceutical company. Medicines were prepared in accordance with standards set out in the German pharmacopoeia. Eighty-two bottles of medicine were provided. Forty-one bottles contained 12 lactose tablets impregnated at a 1% (volume / volume) with the complex (*Ipecacuanha* 12CH, *Thebaicum* 12CH and *Phosphorus* 12CH) in 96% ethanol. The remaining forty one bottles contained 12 indistinguishable lactose tablets impregnated at a 1% (volume / volume) with 96% ethanol. Thus equal numbers of experimental and control samples were provided.

In this trial a dose comprised three tablets. The patients were administered one dose from their assigned bottle of tablets (Dose A) within 60 minutes of being transferred to theatre on the scheduled day of their surgery. A second dose, (Dose B), was administered upon return to the ward. The third dose of tablets (Dose C), was given 90 minutes

(11/2 hours) after Dose B. The final dose (Dose D) was administered 180 minutes (3 hours) after Dose B.

These tablets were administered sublingually where they were allowed to dissolve freely under the tongue. The tablets were not swallowed and were thus not entering the stomach, so could not increase the risk of emesis.

The trial was run for a period of 4 hours postoperatively, a time period relatively bearable for the patients, and too short for the more serious effects of PONV sequellae to become life threatening, should they have arisen.

There are no known side effects to the medicine and thus there were no risks associated with the homoeopathic medicine. In the event of severe or protracted PONV, "rescue" anti-emetics were administered, resulting in this subject being excluded from the trial group (refer to 3.4.2).

It was accepted that the allopathic medication regimen given to patients preoperatively and during the anaesthetic and their movements (transfer) postoperatively, was within standardised parameters, since all the

subjects were receiving treatment in the same hospital, and were undergoing the same operative procedures.

3.5 Measurements

Measurements for nausea and vomiting were recorded 3 times -30 minutes, 90 minutes (11/2 hours) and 240 minutes (4 hours) after Dose B was administered. Each postoperative assessment was recorded on a "Postoperative History" form (see Appendix F).

Patients subjective perceptions of nausea were recorded on an 11-point Visual Analogue Scale (VAS) of 0 (no nausea) to 10 (nausea as bad as possible) (Steenstra *et al.* 1997).

The incidence of vomiting or retching was recorded as the number of episodes which occurred over the 4 hour trial period. Vomiting at the time of extubation was not considered as postoperative vomiting for the purpose of this study.

3.6 Data analysis.

3.6.1 Sample size of study.

The sample size of the study was 31 patients per group. Group 1 consisted of 31 patients making up the experimental group. Group 2 consisted of the remaining 31 patients making up the placebo group. Parametric methods such as the t-test were used to analyse continuous variables, while categorical variables were analysed using non-parametric methods. These methods included the Mann-Whitney test and Wilcoxon's signed rank test.

3.6.2 Statistical methods

The two main categorical variables of interest in this study were nausea and vomiting. Therefore two clinical experiments were conducted, one on the patients subjective assessment of nausea, and one on the number of emetic episodes. Three readings were taken for each of these two categorical variables. Readings were taken at 30 minutes, 90 minutes (11/2 hours) and 240 minutes (4 hours) after Dose B was administered (first dose upon return to the ward postoperatively).

In addition to the above two clinical experiments, supplementary information collected from the two groups was analysed. This supplementary information consisted of nine variables - seven of which were categorical , while two were continuous variables.

Continuous variables were analysed using parametric methods of data analysis, while the categorical variables were analysed using non-parametric methods of data analysis.

3.6.3 Statistical analysis

3.6.3.1 Procedure 1.1:

Comparison between Group 1(treatment) and Group 2 (placebo)

The two sample unpaired t-test was used to compare Group 1 and 2 with respect to each continuous variable.

(i) **Hypothesis testing**

The null hypothesis H_0, states that there is no significant difference between Group 1 and 2 with respect to the variable of comparison at the $\alpha = 0.05$ level of significance. The alternative hypothesis H_1, states that there is a significant difference at the same level of significance.

H_0: $\mu 1 = \mu 2$

H_1: $\mu 1$ and $\mu 2$ are significantly different from each other.

***(ii)* Decision rule:**

At $\alpha = 0.05$ level of significance, the null hypothesis is rejected if $P < \alpha$ where P is the observed significance level or probability value. Otherwise the null hypothesis is accepted at the same level of significance.

Reject H_0 if $P < \alpha$

Accept H_0 if $P \geq \alpha$

P is the observed significance level or probability value

(Fisher and Belle 1993).

3.6.3.2 Procedure 1.2:

Comparison between Group 1 and 2 with respect to categorical variables

The Mann - Whitney U - test was used to compare Group 1 and 2 with respect to each categorical variable.

(i) Hypothesis testing

The null hypothesis H_0, states that there is no significant difference between Groups 1 and 2 with respect to the variables of comparison at the $\alpha = 0.05$ level of significance. The alternative hypothesis H_1, states that there is a significant difference at the same level of significance.

H_0: $\mu 1 = \mu 2$

H_1: $\mu 1$ and $\mu 2$ were significantly different from each other.

(ii) Decision rule

At $\alpha = 0.05$ level of significance, the null hypothesis is rejected if $P < \alpha$ where P is the observed significance level or probability value. Otherwise the null hypothesis is accepted at the same level of significance.

Reject H_0 if $P < \alpha$

Accept H_0 if $P \geq \alpha$

P is the observed significance, level or probability value

(Fisher and Belle 1993).

3.6.3.3 Procedure 2.1

Comparison between related samples within Group 1 with respect to continuous variables

The two - sample paired t-test was used to compare results from related samples. In each test the null hypothesis states that there is no significant improvement between the 2 related samples being compared, at the α level of significance. The alternative hypothesis stated that there is a significant improvement.

H_0: There was no significant improvement

H_1: There was a significant improvement

***(ii)* Decision rule**

At $\alpha = 0.05$ level of significance, the null hypothesis is rejected if $P < \alpha$ where P is the observed significance level or probability value. Otherwise the null hypothesis is accepted at the same level of significance.

Reject H_0 if $P < \alpha$

Accept H_0 if $P \geq \alpha$

P is the observed significance level or probability value

(Fisher and Belle 1993).

3.6.3.4 Procedure 2.2

Comparison between related samples within Group 1 with respect to categotical variables

Wilcoxon's signed rank test is used to compare results from related samples. In each test, the null hypothesis states that there is no significant improvement between the 2 related samples being compared, at the α level of significance. The alternative hypothesis stated that there is a significant improvement.

H_0: There was no significant improvement

H_1: There was a significant improvement

(ii) **Decision rule**

At $\alpha = 0.05$ level of significance, the null hypothesis is rejected if $P < \alpha$ where P is the observed significance level or probability value. Otherwise the null hypothesis is accepted at the same level of significance.

Reject H_0 if $P < \alpha$

Accept H_0 if $P \geq \alpha$

P is the observed significance level or probability value

(Fisher and Belle 1993).

3.6.3.5 Procedure 3.1

Comparison between related samples within Group 2 with respect to continuous variables

Procedure 2.1 was repeated within Group 2 using the same decision rule.

3.6.3.6 Procedure 3.2

Comparison between related samples within Group 2 with respect to categorical variables

Procedure 2.2 was repeated within Group 2 using the same decision rule.

3.6.3.7 Procedure 4

Averages variances and standard deviation for continuous variables

Averages were needed for the construction of barcharts. Averages and variances were used for power analysis.

3.6.3.8 Procedure 5

Comparison using barcharts

Visual summaries of the analytical findings are given by means of barcharts. Average readings were used to construct the barcharts represented.

3.6.3.9 Statistical package:

The statistical package Statistical Package for Social Sciences (SPSS) version 9 was used for data entry and analysis

CHAPTER 4

RESULTS

4.1 Introduction

This chapter covers the results obtained from statistical analysis of the data collected from the two groups used in this trial.

4.2 Criteria for the admissibility of the data

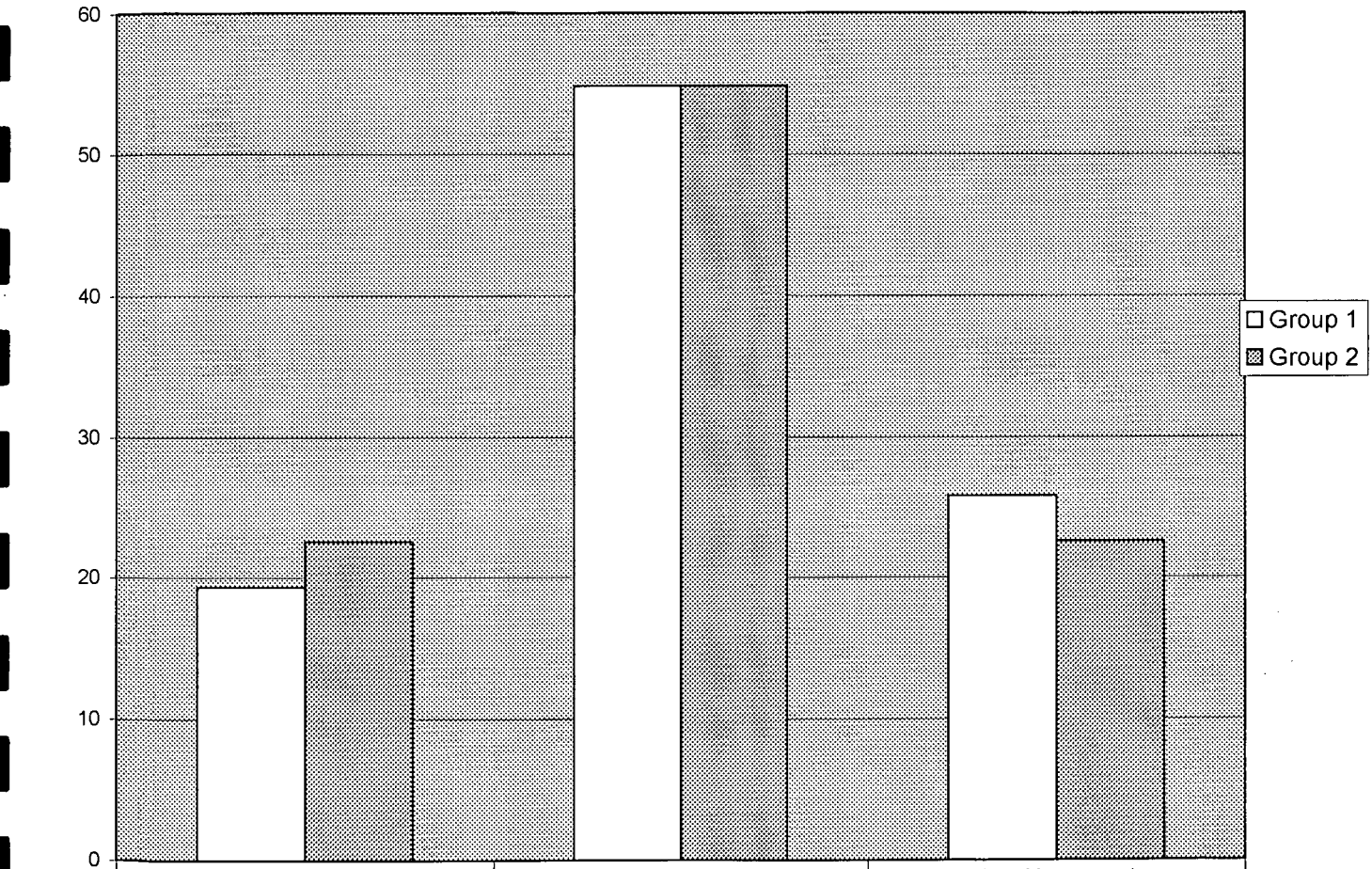
Only the data collected from this trial was accepted for use in the results chapter. The only data use in the analysis was collected in the manner described in chapter 3.

Anaesthetisation was performed by anaesthetists working in the surgical theatre at Addington hospital. All hysterectomies were performed by Obstetrics and Gynaecology registrars, consultants or surgeons.

4.3. - Barcharts 4.1 representing comparative frequencies of supplemental information (categorical variables) in Groups 1 (Treatment) and 2 (Placebo).

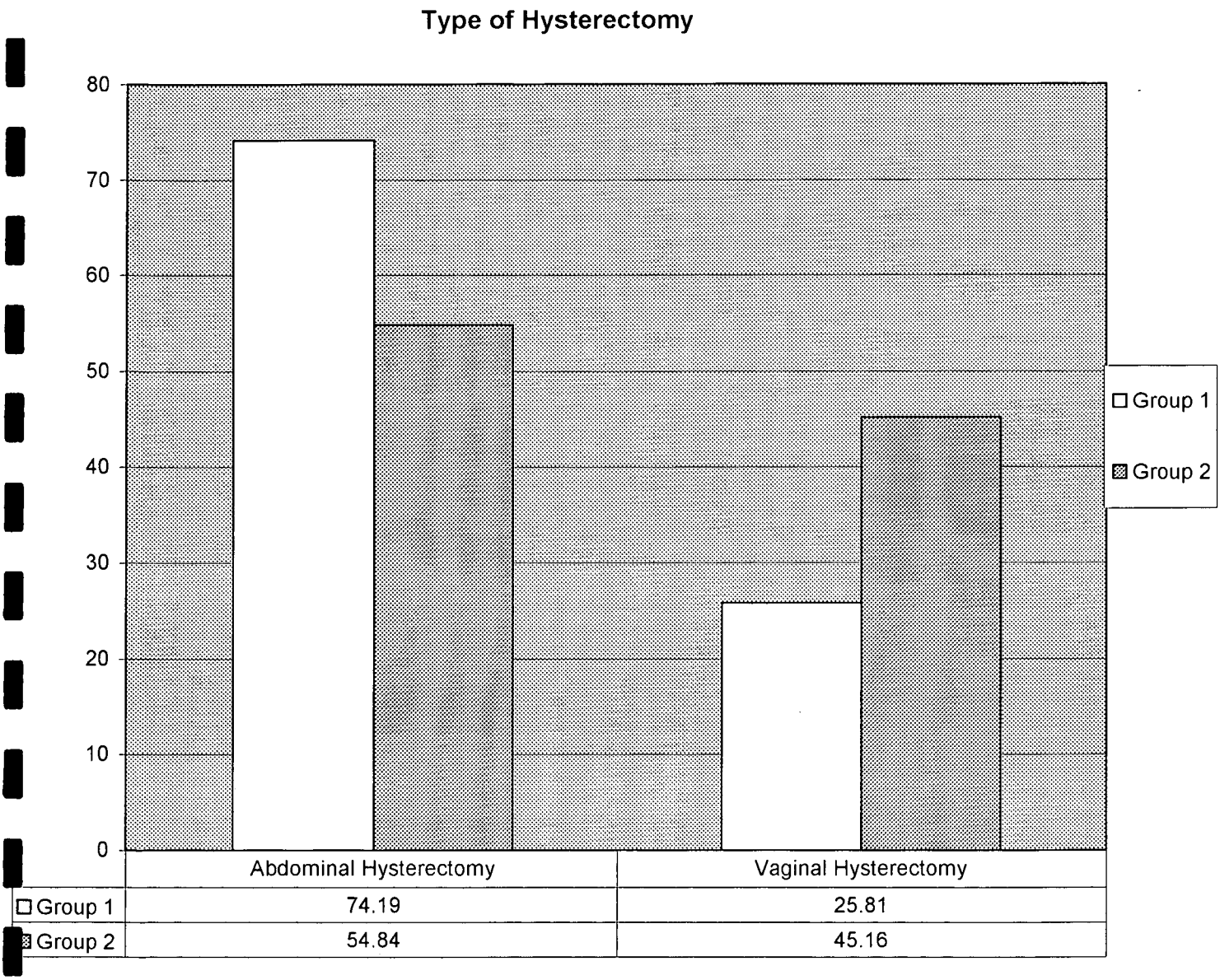
4.1.1 MENSTRUAL STATUS

Menstrual Status



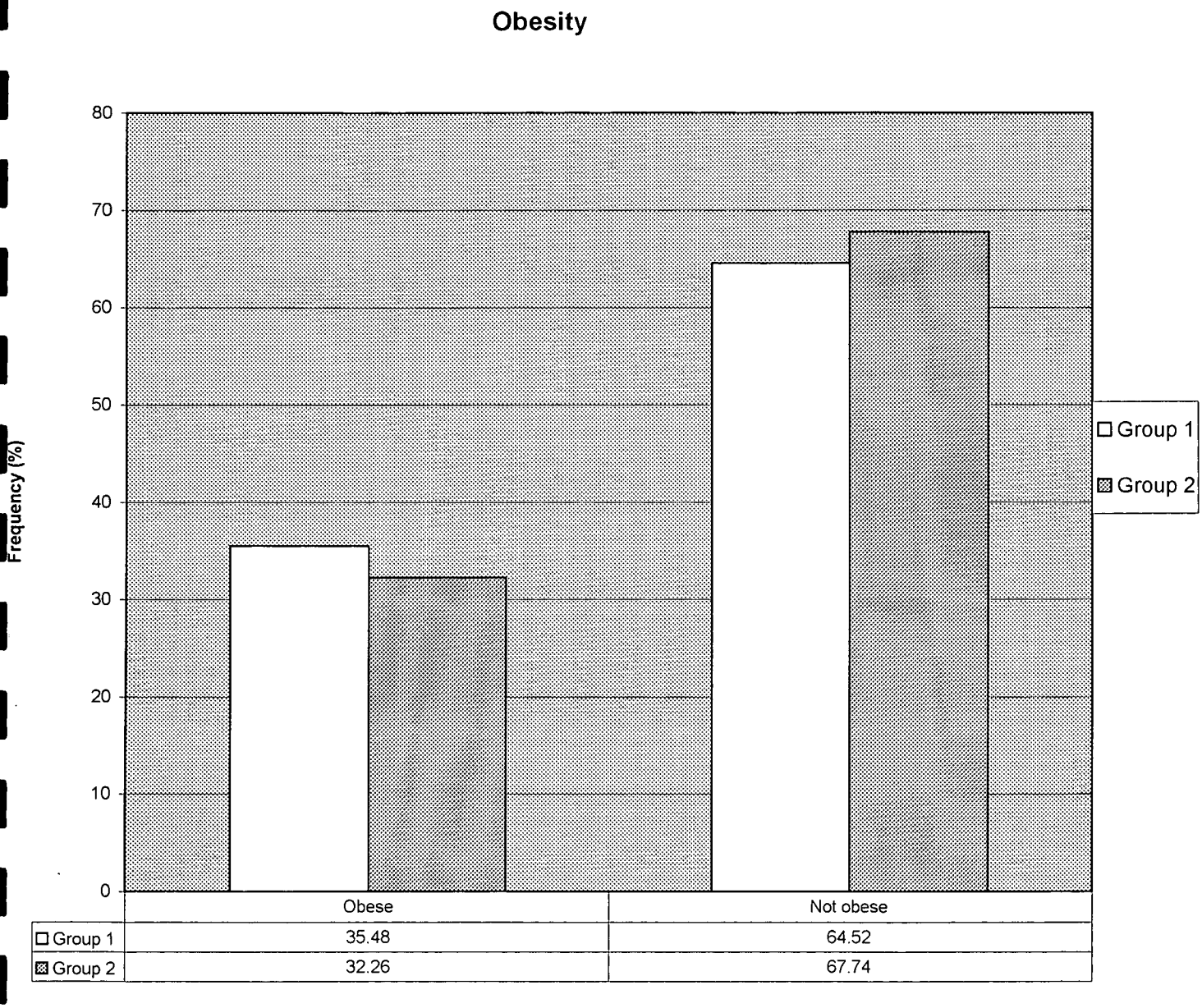
	Menstruating	Not Menstruating	Post Menopausal
Group 1	19.35	54.84	25.81
Group 2	22.58	54.84	22.58

4.1.2 TYPE OF HYSTERECTOMY

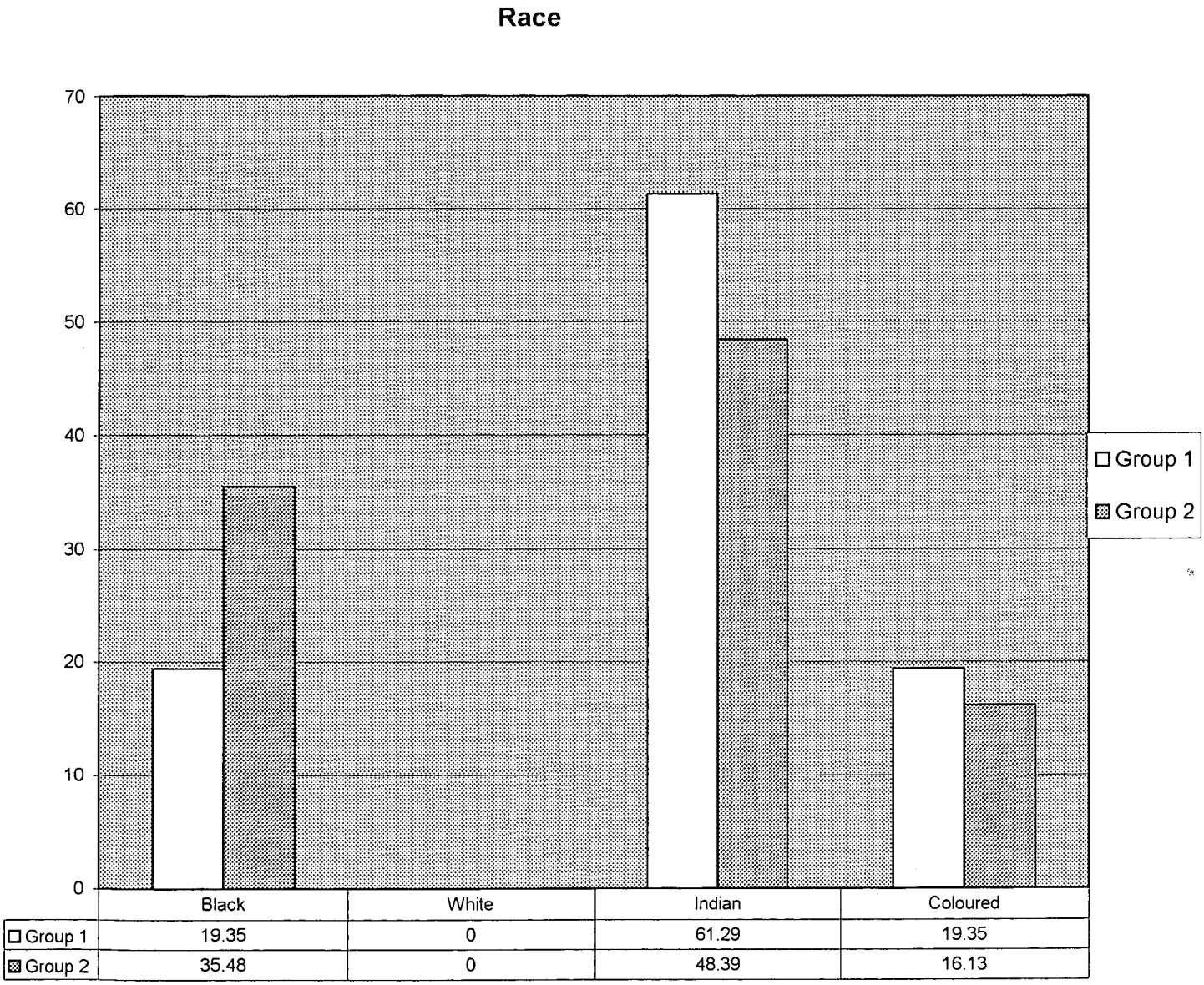


	Abdominal Hysterectomy	Vaginal Hysterectomy
Group 1	74.19	25.81
Group 2	54.84	45.16

4.1.3 OBESITY

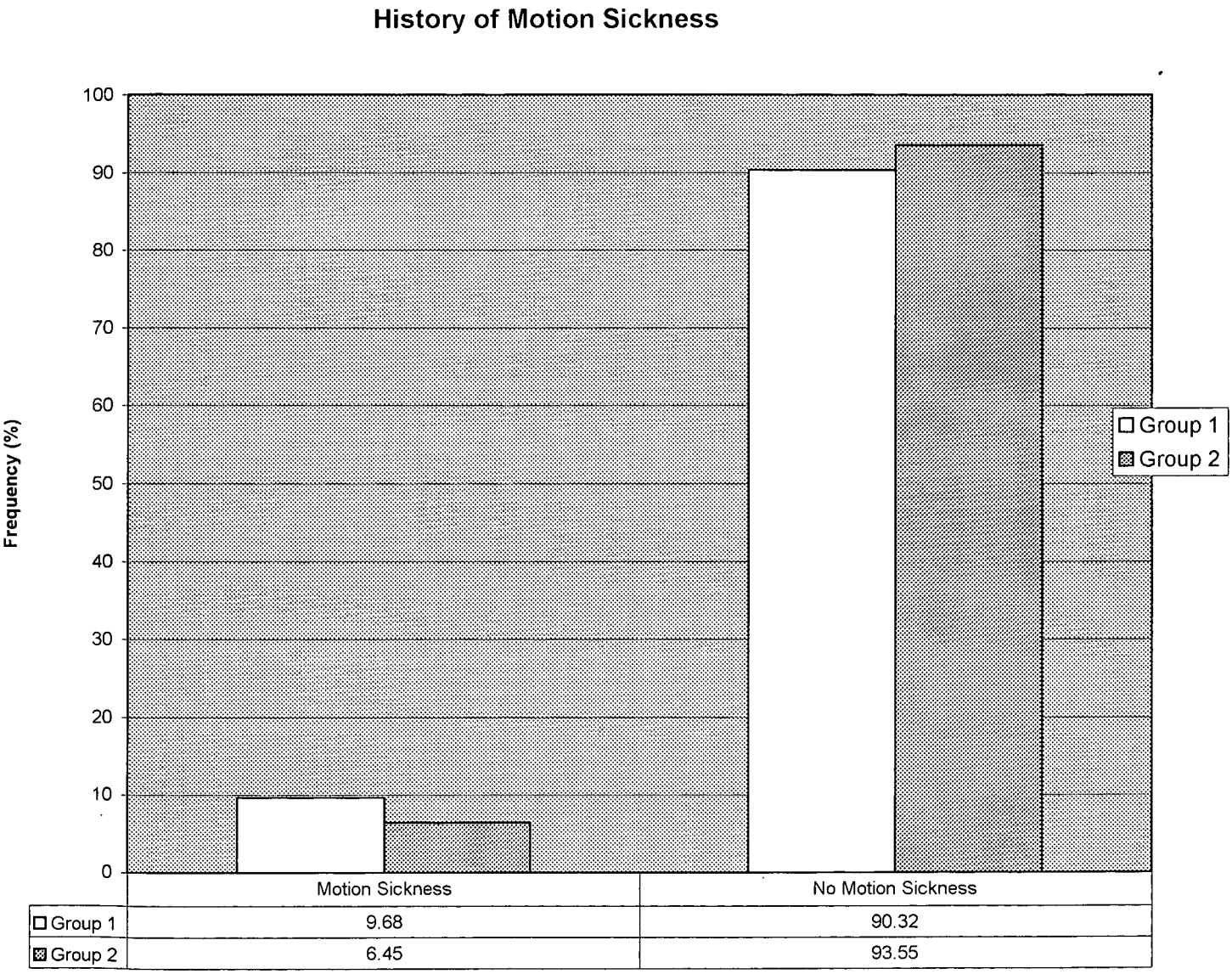

Obesity
Frequency (%)
80
70
60
50
40
30
20
10
0
Group 1
Group 2
Obese
Not obese
Group 1 35.48 64.52
Group 2 32.26 67.74

4.1.4 RACE



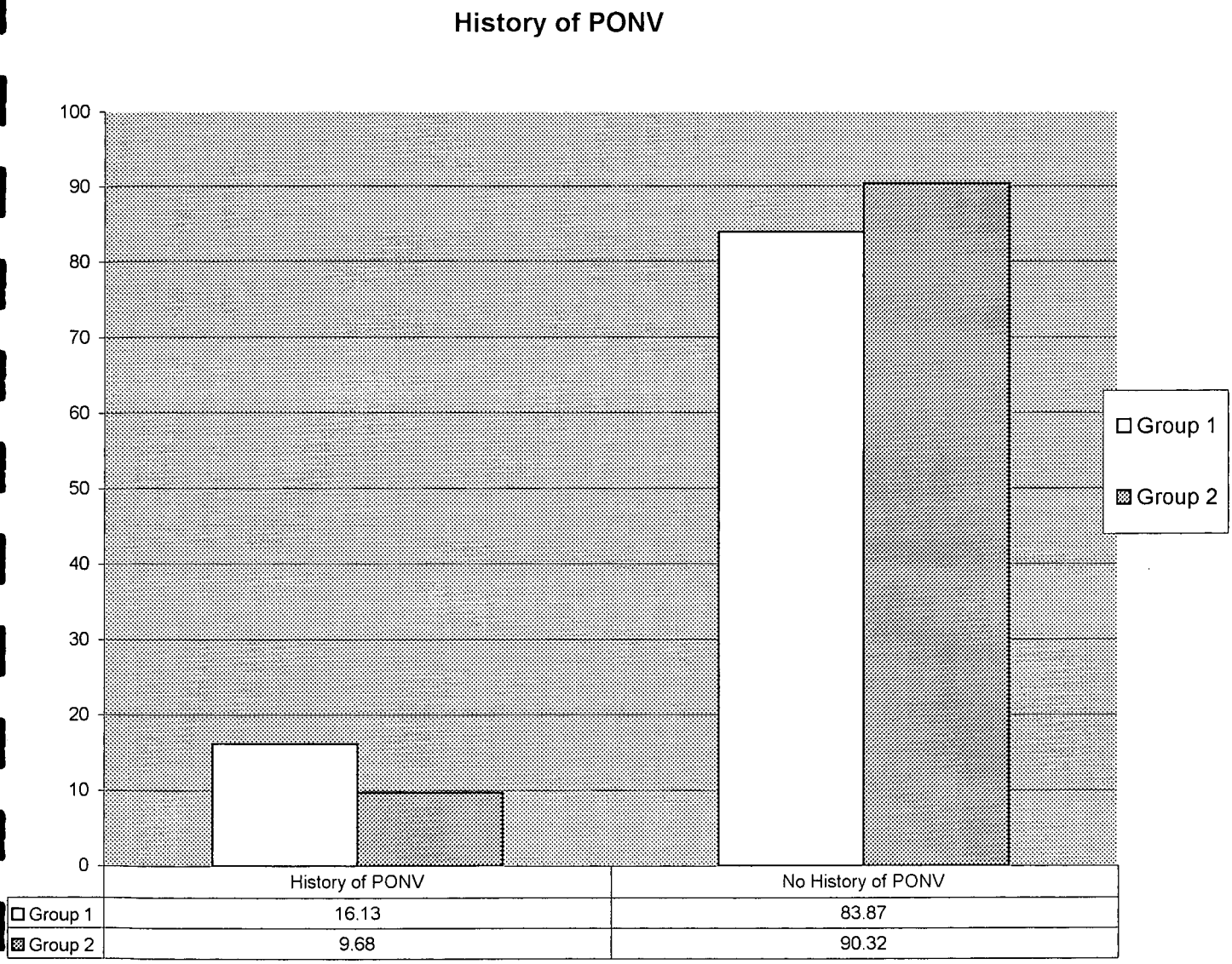
	Black	White	Indian	Coloured
Group 1	19.35	0	61.29	19.35
Group 2	35.48	0	48.39	16.13

4.1.5 HISTORY OF MOTION SICKNESS



	Motion Sickness	No Motion Sickness
Group 1	9.68	90.32
Group 2	6.45	93.55

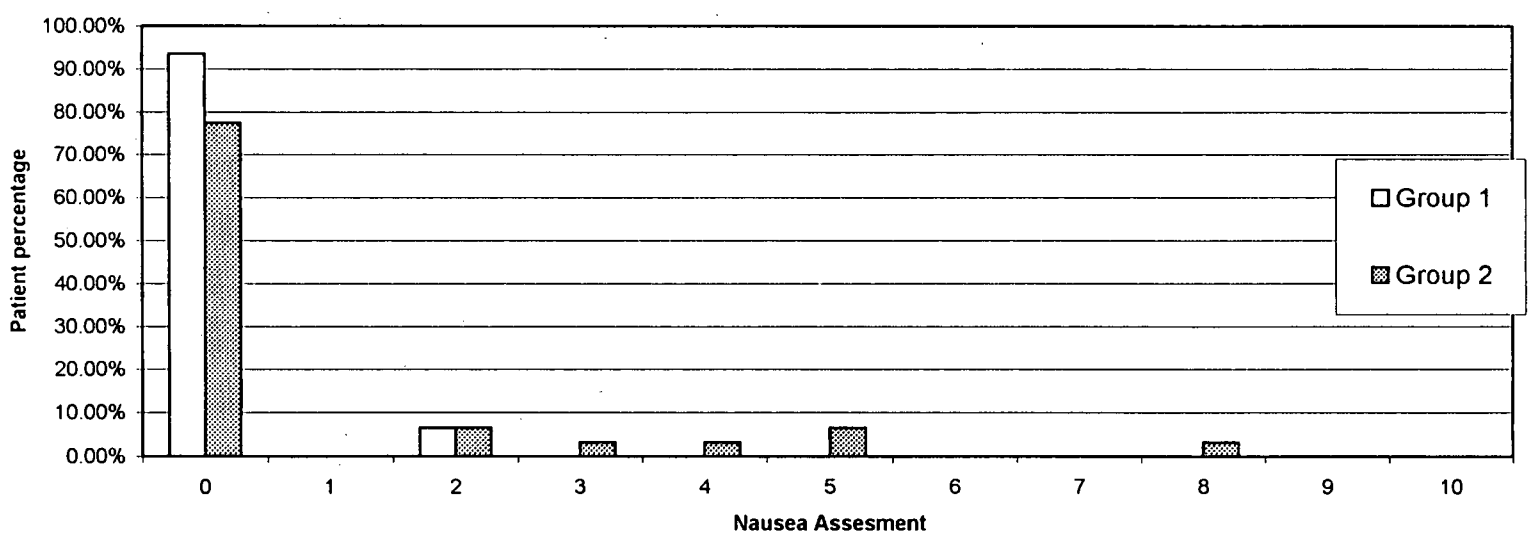
4.1.6 HISTORY OF PONV

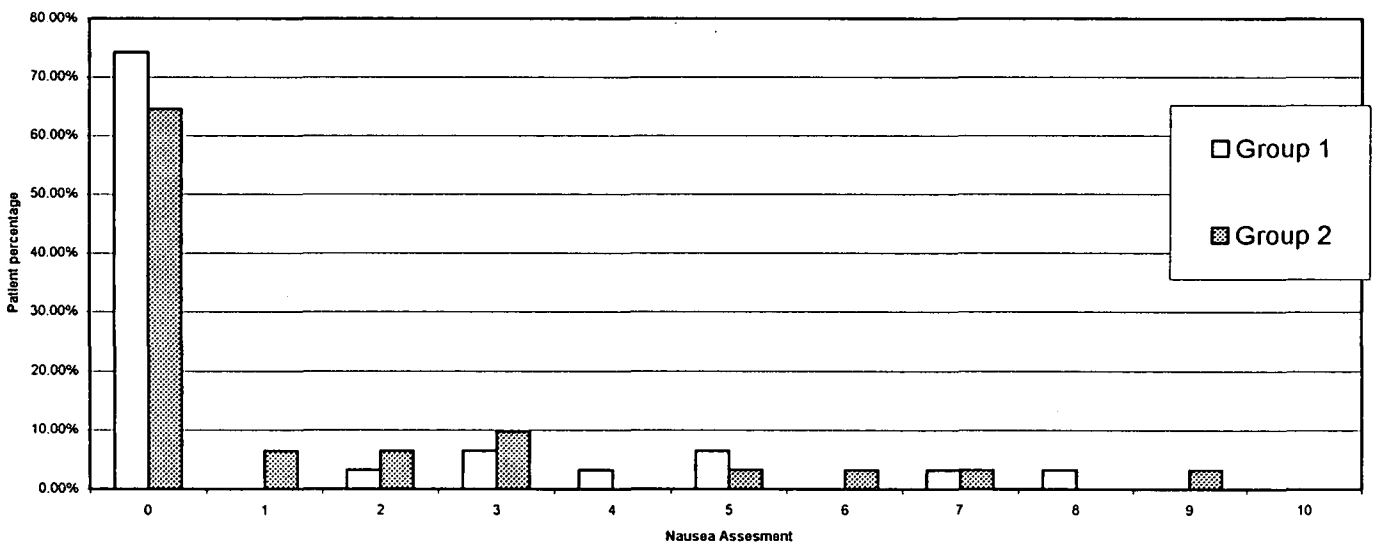


	History of PONV	No History of PONV
Group 1	16.13	83.87
Group 2	9.68	90.32

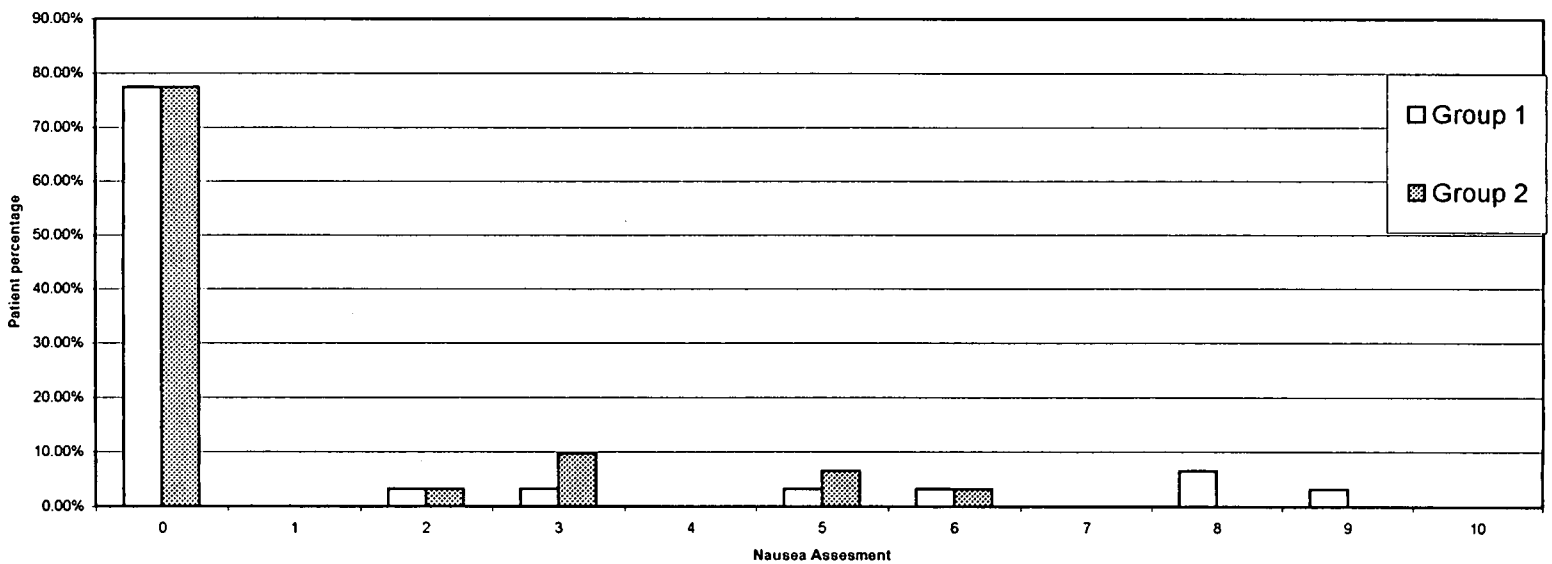
4.4 Barcharts 4.2 representing comparisons between Group1 (Treatment) and Group 2 (Placebo) of patient perception of severity of nausea.

4.2.1 NAUSEA ASSESSMENT 1





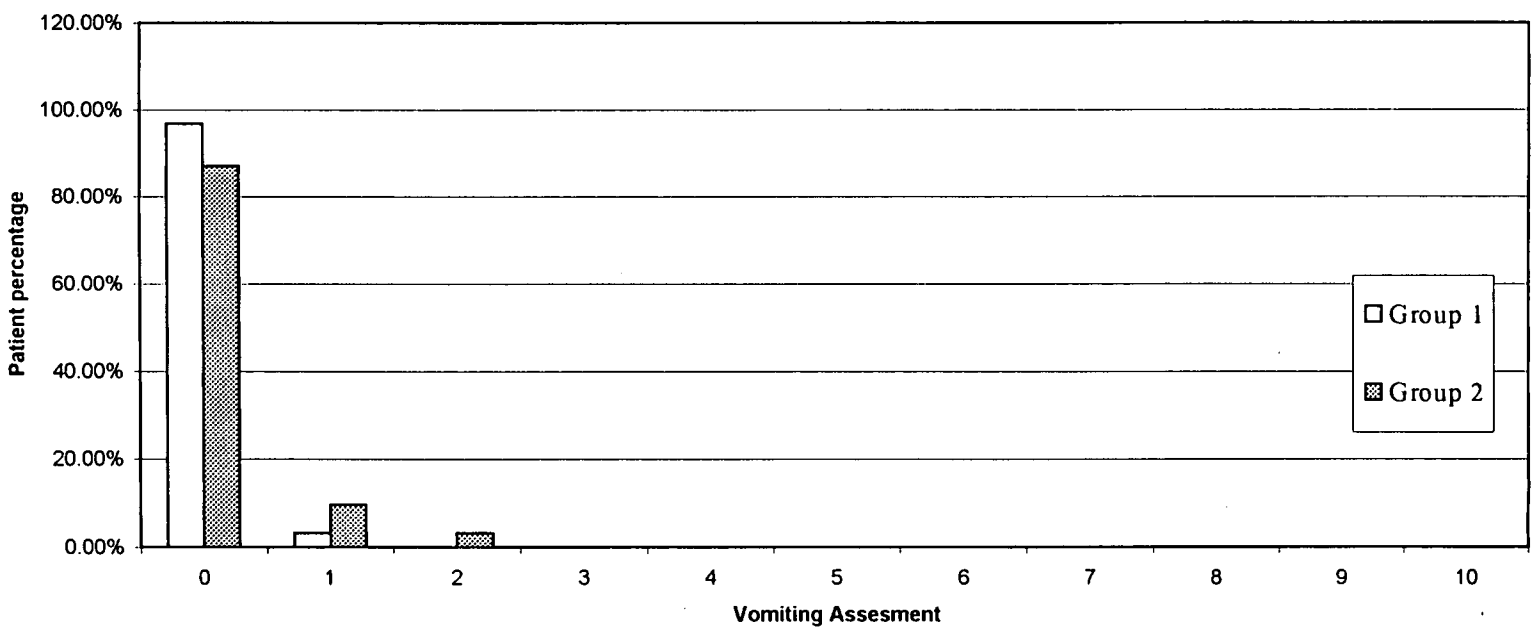
4.2.2 NAUSEA ASSESSMENT 2

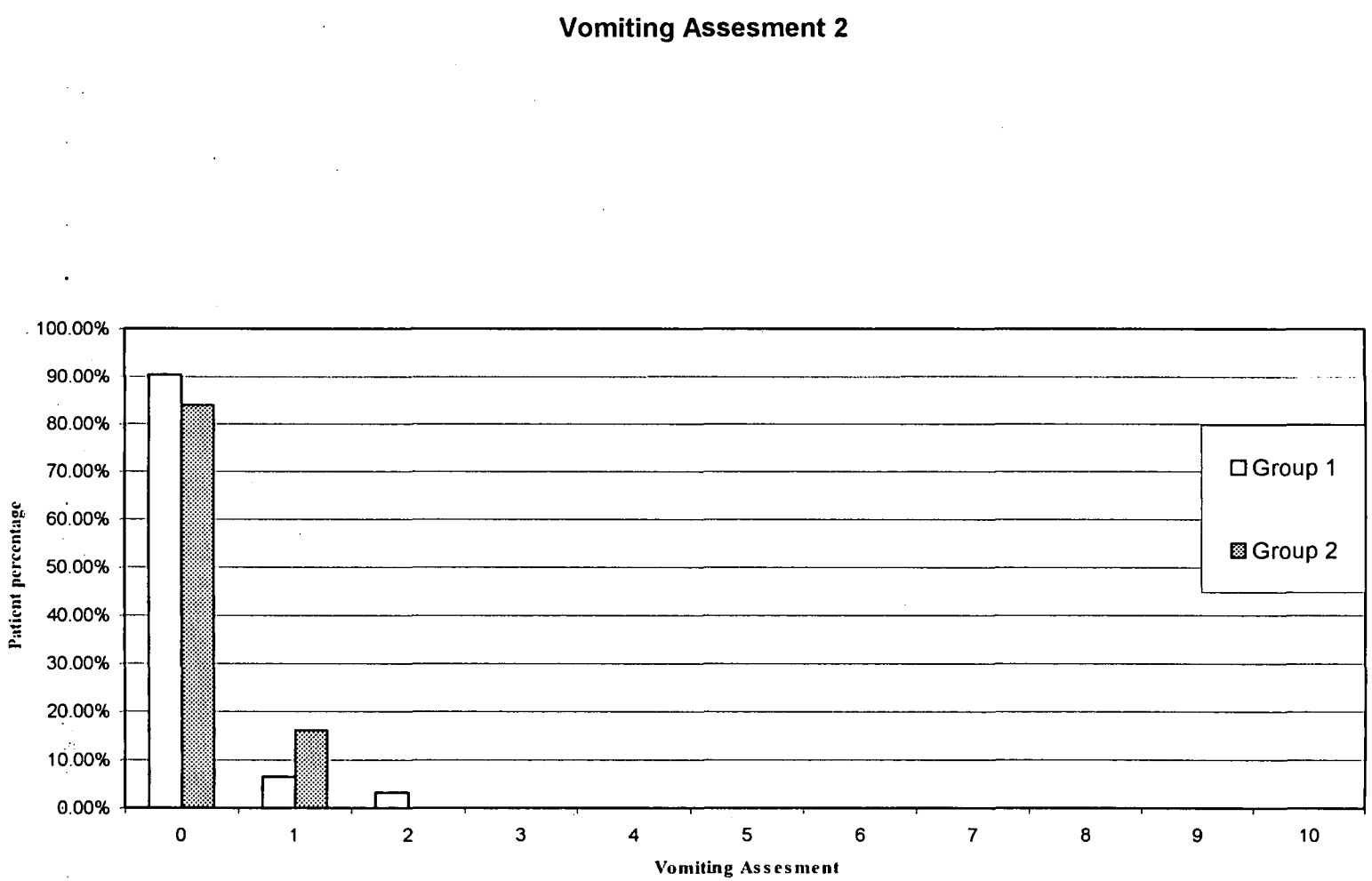


4.2.3 NAUSEA ASSESSMENT 3

4.5 Barcharts 4.3 representing comparisons between Group1 (Treatment) and Group 2 (Placebo) of incidences of vomiting.

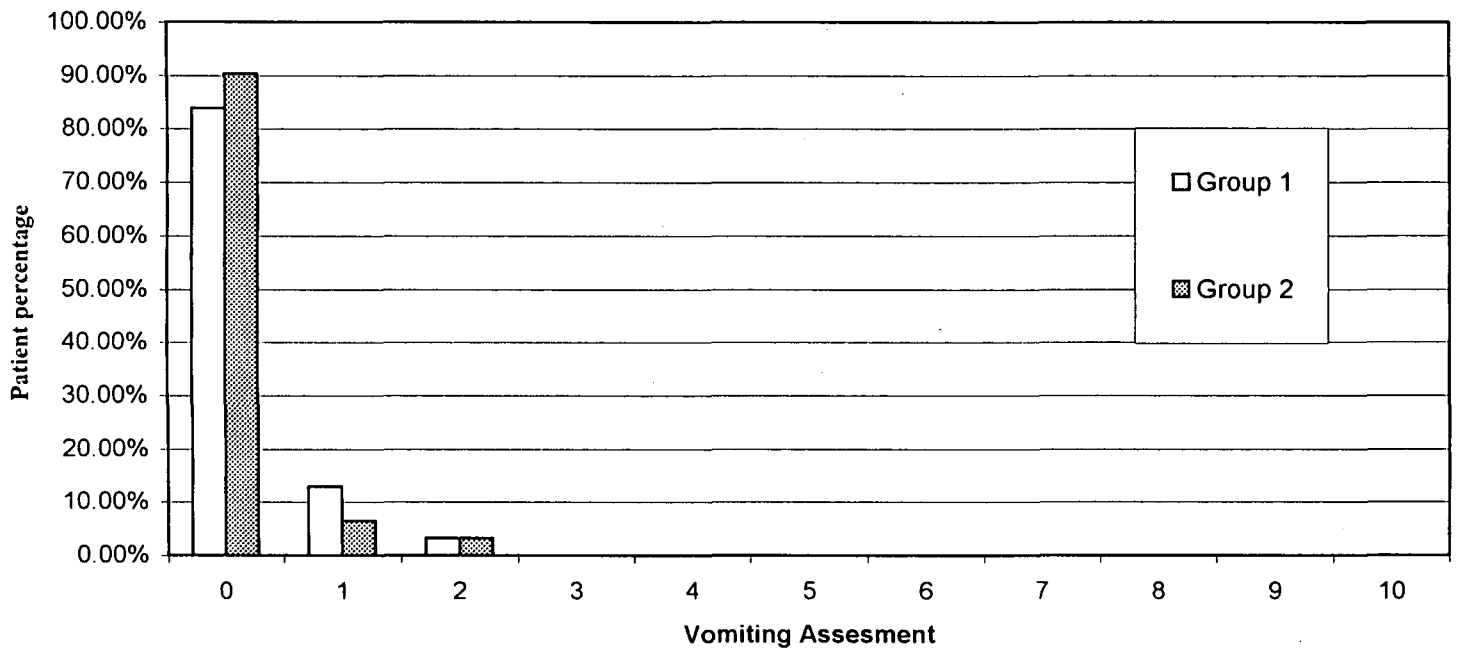
4.3.1 VOMITING ASSESSMENT 1





4.3.2 VOMITING ASSESSMENT 2

Vomiting Assesment 3



4.3.3 VOMITING ASSESSMENT 3

4.6 Comparisons between Group1 (Treatment) and 2 (Placebo) with respect to patient age and duration of anaesthetic - using the Two-Sample Unpaired t-test

4.6.1 Independent Samples Test

Levene's test for equality of variences was used to compare the variences of the two groups. The variences of the two groups were found to be equal with respect to "Age in years" and "Duration of Anaesthetic in minutes" (P=0.731 and P= 0.243 respectively), at the α = 0.05 level of significance.

4.6.2 Independent Samples Test

The means of the 2 groups were compared using the two-sample Unpaired t-test. The test revealed that the two groups have equal means with respect to "Age in years", and "Duration of Anaesthetic in minutes" (P= 0.534 and P= 0.640 respectively) at the α = 0.05 level of significance.

95% confidence intervals for the differences between the two groups means were also obtained as [-3.1435 , 6.1113] and [-13.0268 , 21.0268] respectively. Note that both confidence intervals contain zero.

4.7 Comparison between Groups 1 (Treatment) and 2 (Placebo) with respect to supplemental categorical variables - using the Mann-Whitney U-test

The Mann-Whitney U-test showed that the two groups had equal means or averages with the following variables:

Menstrual status (P= 0.114); Abdominal hysterectomy (P= 0.114); Vaginal hysterectomy (P= 0.114); Obesity (P= 0.790); Race (P= 0.240); History of motion sickness (P= 0.644) and History of PONV (P= 0.452) at the α = 5% level of confidence.

4.8 Comparison between related samples within Group 1 (Treatment) with respect to categorical variables (nausea and vomiting)- using the Wilcoxon Signed ranks test

Wilcoxon's signed-rank tests were used within Group 1 to investigate whether there were any significant improvements between the successive treatments. At the α = 0.05 level of significance, the tests revealed that there were significant

improvements between consultations 1 and 2 and between consultations 1 and 3 with respect to nausea (P= 0.018 and P= 0.028 respectively).

In the following cases however there was no statistically significant improvement shown: consultations 2 and 3 for nausea (P= 0.726) and consultations 1 and 2; 1 and 3; and, 2 and 3 (P= 0.180, P= 0.096, and P= 0.527).

4.9 Comparison between related samples within Group 2 with respect to categorical variables (nausea and vomiting) - using the Wilcoxon Signed Ranks Test

Wilcoxon's signed-rank tests were used within Group 2 to investigate whether there were any significant improvements between the successive treatments. At the α = 0.05 level of significance, the tests revealed that there were no significant improvements between consultations 1 and 2; 1 and 3; or 2 and 3 with respect to nausea (P= 0.476 and P= 0.0893 and P= 0.100 respectively).

In addition there were no statistically significant improvements shown between consultations 1 and 2; 1 and 3; or 2 and 3 for vomiting (P= 1.000, P= 0.783 and P= 0.655 respectively)

4.10 Comparison between Groups 1 and 2 with respect to the categorical variables Nausea and Vomiting - using the Mann-Whitney U-Test

The Mann-Whitney test showed that the two groups had equal means or averages with respect to the following variables:

nausea consultation 1 (P= 0.058)

nausea consultation 2 (P= 0.546)

nausea consultation 3 (P= 0.832)

vomiting consultation 1 (P= 0.161)

vomiting consultation 2 (P= 0.490)

vomiting consultation 3 (P= 0.468)

Thus no significant difference exists between Groups 1 and 2 with respect to the occurrence of nausea and vomiting at the α = 5% = 0.05 level of significance.

CHAPTER 5

DISCUSSION

The two groups in this study were statistically similar with respect to the supplementary information collected for both categorical and continuous variables. Many of these subsidiary factors had been isolated in previous studies as causing or attributing to incidences of PONV. Since the two groups were similar in these areas none of these factors could account for any statistical differences shown.

This trial demonstrated a statistically significant improvement in the incidence of postoperative nausea within Group 1 (Experimental). This improvement was demonstrated between the first and second consultation postoperatively, as well as between the first and third consultation postoperatively. No improvement was however shown in Group 2 (Placebo) for the same period.

Retrospective analysis of the data also revealed that six patients were excluded from the trial for receiving rescue medication. Five of these patients were from

Group 2 (Placebo). The nausea and vomiting assessments for these patients were unfortunately excluded from the final statistical analysis representing a significant weakness in the study methodology and a potential area of imbalance in the final results.

The results of this study did not however, show a statistically significant difference between the two groups with respect to the incidence of postoperative vomiting following administration of each groups respective treatment.

This trial also failed to demonstrate that there was a statistically significant difference between Groups1 and 2 with respect to the patients perceptions of nausea during the 4 hour trial period.

A significant shortfall in the methodology of the trial was the discontinuation of assessments and exclusion of data from patients who received rescue medication. Furthermore, no weighting was included in the statistical evaluation within a group for patients who were excluded on this criterion.

The overall incidence of PONV was not found to be as high as the level reported by many of the authors cited in the text above. Diemunsch *et al.*(1999) reported an incidence as high as 73% following abdominal and vaginal hysterectomy. The incidence of PONV in this study was found to be lower (Mean Incidence for the three consultations was 27,03% nausea and 12,9% vomiting in the placebo group). This does not however suggest the afore mentioned authors statistics are incorrect. To date no studies have been conducted on the incidences of PONV within the same parameters and hospital this trial was conducted under. The nursing sisters and staff in the ward where the trial was conducted independently observed that the general incidence of PONV among all the patients in the trial was substantially lower than those patients, undergoing the same procedure, but not included in the trial. This observations could be attributed to one or both of the following two factors.

The first factor that could have attributed to these observations was the relief from anxiety and patient education offered by the researcher preoperatively.

(Explanation of procedures for the trial and the surgery was given to all patients involved in the study.)

The second element which could have attributed to these observed differences in incidence, (especially when viewed in conjunction with the lack of substantial difference demonstrated between the outcomes of the two groups), is an additional enigma - the "Placebo Enigma". This once again emphasises the placebo effect in clinical trials: "To the scientist, a major problem posed by placebos is that they influence patient outcomes after any treatment, including surgery" (Pearce 1995). Love et al. (1989) was of the opinion that some patients reported more favourable results in an attempt to "please the therapist".

Due to financial restrictions and for the purposes of accuracy it was not possible to continue patient assessments for a longer time period. It would however have been ideal to extend this observation and assessment time to 24 or 48 hours postoperatively.

Due to the accommodation of this trial into an overextended government hospital it was not possible to ensure the initial dose of tablets (Dose A) and the first dose postoperatively (Dose B) was administered exactly consistently for all patients. Delays in the transfer of patients to theatre preoperatively; delays in the preoperative waiting room and delays in the transfer of patients back to the ward postoperatively resulted in these doses not always being given exactly at the tipulated times. The doses administered in the ward were however administered exactly as defined in Chapter 3.

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

Considering all of the results from this trial it can be concluded that the homoeopathic complex (*Ipecacuanha, Thebaicum and Phosphorus*) was shown to be significantly effective at reducing subjects assessments of nausea in consecutive consultations following hysterectomy. This phenomenon was not demonstrated in the placebo group. There was however no statistically significant difference in the incidence of postoperative nausea and vomiting between the two groups in this study.

This study failed to conclusively demonstrate a statistically significant difference in the efficacy of a Homoeopathic complex (*Ipecacuanha, Thebaicum and Phosphorus*) in the treatment of PONV in women undergoing hysterectomy as compared to the placebo group.

In future trials all assessments should be continued on all patients for the duration of the trial. Information gathered for patients who receive rescue

medication could thus be included in the final statistical analysis. Alternatively any patient who is excluded from the study groups for receiving rescue medication during the trial should have some form of weighted statistical scoring against their respective group so that this valuable information is not lost.

A possible way of overcoming the "Placebo" enigma (discussed above), would be to have three trial groups. Group 1 and 2 could, for example, be the same as above while Group 3 could be a group which receives indistinguishable placebo tablets. The subjects in this group should however not get briefed on the trial pre-operatively, but receive assessments in the same manner as Groups1 and 2.

Future trials should have data assessed for a longer time period than the period stipulated in this trial. A period of up to 48 hours postoperatively could be included in the assessment time.

Since no controlled trials were found where a comparison was conducted on the incidences of PONV within different race groups, a trial such as this one should be conducted on one race only, to maintain consistency in this regard.

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APPENDIX A

FROM : POSTGRAD ADMIN PHONE NO. : 031 2604416 JUN. 23 1999 08:28AM P1

UNIVERSITY OF NATAL
Durban

Faculty of Medicine
Postgraduate Office
Private Bag 7 Congella 4013 South Africa
Telephone +27 (0)31 260 4416
Facsimile +27 (0)31 260 4410
e-mail: walker@med.und.ac.za

Mr GC Taylor
Technikon Natal Homeopathic Day Clinic
Ritson Road
Berea 4001

Fax: 22 3002

22 June 1999

Dear Grant

PROTOCOL: AN EVALUATION OF THE EFFICACY OF A HOMEOPATHIC COMPLEX IN THE TREATMENT OF POSTOPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING A HYSTERECTOMY. GC TAYLOR. TECHNIKON/O & G. REF E030/99

Thank you for the revised version of the E9 page – information given to subjects. This is now correct and full ethical approval is given as of this day.

I wish you every success with your study.

Yours sincerely

Anita Walker
Postgraduate Administration
Aw/ethics/taylorgc.7

APPENDIX B

PROVINCE OF KWAZULU-NATAL
HEALTH SERVICES

ISIFUNDAZWE SAKWAZULU-NATALI
EZEMPILO

PROVINSIE KWAZULU-NATAL
GESONDHEIDSDIENSTE

PRIVATE BAG X 3051
PIETERMARITZBURG
3200

330 LONGMARKET STREET
PIETERMARITZBURG
3201

TELEPHONE
UCINGO
TELEFOON : (0331) 952285

FAX:
ISIKHWAMA SEPOSI : (0331) 423882

Enquiries: Dr. Stewart
Date: 30 June 1999
Ref:

CHIEF MEDICAL SUPERINTENDENT
ADDINTON HOSPITAL
P.O. BOX 977
DURBAN

ATTENTION: DR. J. HURST

RESEARCH PROJECT TO BE PERFORMED IN DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY: ADDINGTON HOSPITAL

Your letter AD 66/1 dated 22nd June 1999 concerning the above matter has reference.

Authority is granted for the research project subject to the conditions indicated in your letter.

Yours sincerely

EMENT SUPPORT

01 JUL 1999

APPENDIX C

INFORMATION GIVEN TO SUBJECTS

We are doing a study on a form of medicine called Homoeopathy, and how it can help prevent patients who are having this operation from feeling nauseous or from getting sick and vomiting as much as usually occurs. When you agree to participate in this study you could be given either pills of the medicine we are studying, or pills with no new medicine in them. Whether you get the new medicine or the other pills depends on chance. This "chance" possibility is done so we can compare the groups of those who got the different kinds of medicine. From this we will see if the new medicine helps to prevent this nausea and vomiting from developing, or if it has no helpful effects.
If you refuse to be in this study, you will receive the normal treatment for this operation.

Ulwazi olunikeziwe abantu mayelana nodaba oludingidwayo

Senza isifundo ngohlobo lomuthi okuthiwa iHomeopathy, nokuthi ungasiza kanjani ekuvimbeni iziguli ukuthi zingabi nesifo sokudiyazela nokuphalaza noma ukubuyisa njengoba kujwayelekile ukwenzeke. Uma uvuma ukuba ubambe iqhaza kulesisifundo unganikezwa amaphilisi alomuthi esifunda ngawo, noma amaphilisi angenawo umuthi omusha. Ngeke wazi ukuthi umuphi umuthi onikwa wona, kungaba umuthi umusha noma omaphilisi. Ukuzama kwakho inhlanhla kwenzelwa khona sizoqhathanisa amaqoqo abanthu labo abathole inhlobo ehlukile yomuthi. Ngalokhu singabona uma umuthi omusha usiza ekuvimbeni ukudiyazela nokuphalaza, noma lomuthi awunalo usizo.
Uma ubamba iqhaza kulesisifundo nasekuhlolweni ukuthi umuthi usebenza kanjani, nolwazi osinike lona lungasebenzi kahle, uzonikezwa imithi ekhona esetshenziselwa ukugula kokudiyazela nokuphalaza.
Uma ungathandi ukuba kulesisifundo uzothola usizo olujwayelekile.

APPENDIX D

INFORMED CONSENT FORM
(to be completed in duplicate by patient /subject*) *Delete whichever is not applicable.

TITLE OF RESEARCH PROJECT:
An evaluation of the efficacy of a Homoeopathic complex in the treatment of postoperative nausea and vomiting in patients undergoing a hysterectomy.

NAME OF SUPERVISORS
Professor J.Moodley and Dr A.Ross.

NAME OF RESEARCH STUDENT
Grant C. Taylor

DATE:_____

PLEASE CIRCLE THE APPROPRIATE ANSWER

1. Have you read the research information sheet? YES / NO
2. Have you had opportunity to ask questions regarding this study? YES / NO
3. Have you received satisfactory answers to your questions? YES / NO
4. Have you had an opportunity to discuss this study? YES / NO
5. Have you received enough information about this study? YES / NO

6. Who have you spoken to?_____
7. Do you understand the implications of your involvement in this study? YES / NO
8. Do you understand that you are free to withdraw from this study? YES / NO
   a) at any time
   b) without having to give a reason for withdrawing, and
   c) without affecting your future health care.

9. Do you agree to voluntarily participate in this study? YES / NO

PATIENT /SUBJECT* Name_____ Signature_____
(in block letters)
WITNESS Name _____ Signature_____
(in block letters)
RESEARCH STUDENT Name GRANT C. TAYLOR Signature_____

APPENDIX E

PREOPERATIVE HISTORY FORM

PATIENTS NAME:

DATE OF SURGERY (DD\MM\YY):
CODE OF MEDICINE:

AGE:____ WEIGHT(Kg):____ HEIGHT(cm):_____

RACE:_____

POST MENOPAUSAL: YES \NO

HISTORY OF PONV: YES \NO

HISTORY OF MOTION SICKNESS: YES \NO

American Society of Anaesthetists(ASA) preoperative Status (circle appropriate category)

ASA 1

ASA 2

MENSTRUAL STATUS (tick relevant category)

Menstruating:_____

Not menstruating:_____

TYPE OF SURGERY (tick relevant category)

ABDOMINAL HYSTERECTOMY:_____

VAGINAL HYSTERECTOMY:_____

APPENDIX F

POSTOPERATIVE ASSESSMENT INFORMATION

Patient Name: _____

Date: _____ **Medicine Code:** _____

Duration of Anaesthesia (min): _____

Postoperative analgesia **Yes / No**

If Yes - Name: _____

Postoperative antiemetics **Yes / No**

CLINICAL SIGNS OF VOMITING: **Yes / No**

If Yes - Number of episodes of vomiting: _____

PATIENT RESPONSE SECTION

Patient perception of nausea (mark with an X at the appropriate place)

0 _____ 1 _____ 2 _____ 3 _____ 4 _____ 5 _____ 6 _____ 7 _____ 8 _____ 9 _____ 10

(NO Nausea) (Nausea as severe as possible)