A COMPARATIVE STUDY TO ASSESS THE EFFICACY OF MAGNESIUM SULPHATE ON THE ATTENUATION OF HEMODYNAMIC RESPONSE TO PNEUMOPERITONEUM DURING LAPAROSCOPIC SURGERIES

A STUDY OF 60 CASES

DISSERTATION SUBMITTED FOR THE DEGREE OF

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BRANCH – X (ANAESTHESIOLOGY)

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CHENNAI

TAMILNADU

BONAFIDE CERTIFICATE

This is to certify that this dissertation entitled **"A COMPARATIVE STUDY TO ASSESS THE EFFICACY OF MAGNESIUM SULPHATE ON THE ATTENUATION OF HEMO DYNAMIC RESPONSE TO PNEUMOPERITONEUM DURING LAPAROSCOPIC SURGERIES"** is a bonafide record work done by **Dr.S. DHARANI** under my direct supervision and guidance, submitted to the Tamil Nadu Dr. M.G.R. Medical University in partial fulfilment of University regulation for MD, Branch X –Anaesthesiology.

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DECLARATION

I Dr. S. DHARANI solemnly declare that this dissertation titled **"A COMPARATIVE STUDY TO ASSESS THE EFFICACY OF MAGNESIUM SULPHATEON THE ATTENUATION OF HEMODYNAMIC RESPONSE TO PNEUMOPERITONEUM DURING LAPAROSCOPIC SURGERIES"** has been done by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University or board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai, in partial fulfilment of the rules and regulation for the award of Doctor of Medicine degree Branch –X (Anaesthesiology) to be held in April 2013.

Place : Madurai

Date: **Dr. S. DHARANI.**

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ABSTRACT

BACKGROUNDS:

Magnesium is a well known inhibitor of catecholamine release. This study investigates whether i.v., magnesium sulphate attenuates the hemodynamic response to pneumoperitoneum during laparoscopic surgeries by changing the neurohumoral responses.

METHODS:

In a randomised, double blind control study, 60 patients of both sexes were chosen. 30 patients in the study group received i.v., magnesium sulphate 50 mg/kg, 1 minute before pneumoperitoneum and 30 patients in the control group received normal saline. Perioperative anaesthetic care was standardised in all patients. Intraoperative heart rate and blood pressure was monitored.

RESULTS:

Systolic and diastolic blood pressure and heart rate was significantly higher in the control group when compared to the study group.

CONCLUSION:

Intravenous magnesium sulphate attenuates the arterial pressure increase during laparoscopic surgeries.

INTRODUCTION

“The cleaner and gentler the act of operation, the less pain the patient suffers, the smoother and quicker the convalescence, the more exquisite his healed wound, the happier his memory of the whole incident”

- Lord Moynihar (1920)

The rising popularity of laparoscopic surgery is one of the most spectacular events in modern surgical history, putting an end to the era of ‘ Big surgeons Big incisions ‘

HISTORY

The history of laparoscopic revolution can be traced back to the tenth century A.D. The Arabian physician Abulkasim (936 -1013 AD) is often credited with being the first to use reflected light to inspect an internal organ, the cervix.

Subsequently instruments were developed and the early pioneers introduced trochars and cystoscopes directly into the peritoneal cavity. At the turn of the 20th century, George Kelling of Dresden used a cystoscope to observe the abdominal organs in dogs. He realised pneumoperitoneum was very essential for exposure and therefore used room air for insufflations of the peritoneal cavity. He then coined the term “celioscopy” to describe the technique.

The Swedish physician Hans Christian Jacobaeus in 1910 first used this procedure in man. He also coined the term “laparoscopy”. Earlier procedures were entirely diagnostic.

Goetz and later Veress developed a spring loaded insufflation needle for safe creation of pneumoperitoneum. Air was the first gas to be used for pneumoperitoneum. It was cheap and easily available. Later oxygen was also used. However both these gases support combustion and have a potential for gas embolism because of poor Ostwald’s blood gas solubility coefficient (0.006, 0.013).

In 1970s, nitrous oxide was used by gynaecologists because of its low cost and high turnover. However it supports combustion if mixed with methane from the bowel.

In 1924, Richard Zollikofer promoted the use of carbondioxide. It is relatively inert, readily absorbed by peritoneal membrane (blood/gas solubility 0.48) and is readily exhaled via the lung. It has now become the standard gas for pneumoperitoneum.

Other alternative gases like helium, xenon and argon are inert and expensive and have very low blood gas solubility (0.00018) and therefore high chances of gas embolism.

Raoul Palmer in Paris stressed the importance of monitoring intra-abdominal pressure. It was Kurt Semm of Germany, who developed an automatic insufflations device, that measured intra-abdominal pressure and gas flow. Before that syringes were used to insufflate air into the peritoneal cavity.

LAPAROSCOPIC SURGERIES:

Although in 1985, Erich Muhe of Germany first described his technique of laparoscopic cholecystectomy in humans using a galloscope, it was in 1987 that the complete removal of a diseased gall bladder in a patient was performed by Mouret in Lyon, France.

Diminished pain and cosmetic disfigurement as well as quicker resumption of normal activities has increased its acceptance nowadays. Initially it was done for short gynaecological diagnostic procedures. However as more and more patients are being referred for surgery, now they are conducted in older and high risk patients who were previously considered unfit for laparotomy.

After the widespread use of laparoscopic intraperitoneal approach for appendicectomy and cholecystectomy, it is now being used for a variety of extraperitoneal surgeries, including inguinal hernia surgeries, adrenal and renal surgeries. The extraperitoneal insufflations of carbondioxide has a risk of increased carbondioxide absorption.

Extremes of patient positioning, insufflations of exogenous gases and increased intra-abdominal pressure pose a severe strain on the patient's physiology. The anaesthesiologist should be aware of these changes and the possible complications, so that early detection and prompt treatment may be instituted.

The rapid development in the field of laparoscopic surgeries and the inclusion of high risk patients would not have been possible without a concurrent advance in the anaesthetic drugs and techniques. Advances in laparoscopic surgeries has been associated with parallel development in anaesthetic approaches. The anaesthesiologist must constantly improvise and evolve his approach in the face of a never ending domain of laparoscopic surgery.

PATHOPHYSIOLOGY OF PNEUMOPERITONEUM:

Upto intra abdominal pressure of 15 mm Hg the cardiac output does not change significantly. The mean arterial pressure may rise initially but thereafter normalises or decreases. Heart rate may also rise transiently. Joris et al observed a significant increase in systemic vascular resistance (65%) and pulmonary vascular resistance (90%) and a decrease in cardiac index (20%) while the pulmonary capillary wedge pressure and central venous pressure increased.

Pneumoperitoneum leads to cephalad shift of diaphragm, reduced lung expansion, reduced diaphragmatic excursion causing pattern of restrictive lung disease. There is a fall in functional residual capacity, tidal volume and minute ventilation. Pulmonary vascular resistance increases, uneven distribution of ventilation to non dependent parts of the lung produces ventilation perfusion mismatch, hypoxia and hypercarbia.

Oliguria (urine output < 0.5ml/kg) has been usually seen. As IAP increases, the compression of renal vasculature, the renal parenchyma and the inferior vena cava leads to decreased renal blood flow, cortical and medullary perfusion and renal venous outflow. Apart from renal compression there is a release of neurohormonal factors as renin, aldosterone, endothelin and anti-diuretic

hormone resulting in systemic vasoconstriction and fluid retention. Regional blood flow to all intra-abdominal organs including hepatic, mesenteric, intestinal mucosa, stomach, duodenum, pancreas and spleen is reduced as IAP approaches 15 mm Hg. However the blood flow to the adrenal glands is preserved.

Hepatic perfusion has a unique autoregulatory mechanism known as “hepatic arterial buffer response(HABR)”. Richter et al demonstrated a loss of this response at an IAP of 12 – 15 mm Hg. Impairment of microcirculation occurs with pressures as low as 15 mm Hg and within a short interval (60 min.).

Rise in IAP compresses inferior vena cava and increases lumbar spinal pressure by reducing drainage from lumbar plexus, thereby increasing intracranial pressure and intraocular pressure. Raised intra-abdominal pressure results in increased cerebral blood flow. Hypercapnia associated with laparoscopy further produces reflex vasodilatation in the central nervous system attributing to increased intracranial pressure.

PHYSICAL PROPERTIES OF THE COMMON INSUFFLATION GASES

GAS	INERT GAS VALENCY	SOLUBILITY
AIR	-	2.92
N_2	3, 5	2.3
N_2O	-	130
CO_2	-	**171**
He	-	0.97
Ar	-	5.6

CARBON DIOXIDE:

It is the insufflating agent of choice nowadays. It is relatively inert, readily absorbed, non combustible and cheap. It is used from either central pipelines or cylinders. It is highly soluble with a solubility coefficient of 0.48 at 37□C. The rate of absortion of any gas depends on its solubility, absorption area, the pressure gradient across the membrane and the diffusion constant. The rate limiting factor for carbon dioxide absorption is local perfusion. But the surface area and the IAP also play a significant role. CO_2 is readily absorbed from the peritoneum, passes through the portal and systemic circulation and is readily excreted through the lungs.

It is carried in blood in three forms: 90% in the form of bicarbonate, 5 – 10% dissolved in plasma and the rest is combined with protein, mainly haemoglobin.

The increase in $PaCO_2$ was first demonstrated in 1969 in a group of patients undergoing pelvic laparoscopy using CO_2 insufflations, under halothane anaesthesia, using volume limited constant minute volume ventilation. This effect was not seen during the use of other insufflating gases and hence was thought to be due to the absorption of the gas from the peritoneum. During carboperitoneum the CO_2 excretion increased, but the oxygen consumption

remained stable indicating that the increase in CO_2 is not due to hypermetabolism. Although permissive hypercapnia is used as a treatment modality in certain medical conditions, maintaining normocapnia is important during laparoscopic surgeries.

Absorption of carbondioxide during pneumoperitoneum causes minimal hypercarbia and acidosis. Mild hypercarbia ($PaCO_2$ of 45 – 50 mmHg) does not cause significant hemodynamic changes. While severe hypercarbia ($PaCO_2$ of 50 - 60 mmHg) has an impact on the cardiovascular system causing vasoconstriction, tachycardia and even arrhythmias. The increase in IAP is the factor mainly responsible for the increase in catecholamines.

Marathe first demonstrated that despite a significant increase in the $PaCO_2$, the cardiovascular changes occurred only when the levels increased 33 percent above the baseline. This discrepancy suggests that the deleterious hemodynamic changes that occur during pneumoperitoneum are either due to a long duration of CO_2 insufflations or high intra-abdominal pressure.

PHYSIOLOGICAL EFFECTS OF CARBON DIOXIDE:

Carbon dioxide has a major regulatory effect in the control of respiration by both the central and peripheral mechanisms. It readily crosses the blood brain barrier, forms carbonic acid and dissociates into H^+ ions which acts on the chemosensitive area in the ventral medulla. Activation of this area results in stimulation of inspiratory centre and increase in respiratory rate. Hypercarbia can also cause hypoxic pulmonary vasoconstriction and lead to increased pulmonary resistance, which could cause a right ventricular stress in a poorly compensated heart.

The cardiovascular effects of carbon dioxide are balanced between its direct cardiodepressant effects and stimulatory effects. High levels of carbon dioxide will cause release of catecholamines due to sympathetic system activation. This causes an increase in cardiac output, heart rate, stroke volume and contractility. On the other hand, the acidosis caused by hypercarbia has a direct myocardial depressant effect. Cardiac conduction disturbances are also known to occur.

Hypercarbia causes an increase in the cerebral blood flow. For every 1 mmHg increase in $PaCO_2$ the CBF increases by 1.8 ml / 100 g / min. The CBF doubles as the $PaCO_2$ increases from 40 to 80 mmHg. This could be disastrous in patients with intracranial lesions.

CARBOPERITONEUM RELATED COMPLICATIONS:

Hypercarbia is the main reason for carboperitoneum related complications. Hypercarbia causes an increase in the mean pulmonary arterial pressure and pulmonary hypertension. The reflex vasodilatation causes an increased cerebral blood flow and increase the ICP. It has the least effect on hepatic blood flow and renal blood flow.

INTRA ABDOMINAL PRESSURE:

Abdomen is a closed space bounded by the diaphragm, costal margins, the contracting abdominal muscles and containing the intestines. There is a steady pressure within the closed abdominal cavity. The normal intra-abdominal pressure is 0 to 5 mmHg. When the values are more than 12 mmHg, the IAP is said to be high.

Depending on the level of IAP the pathophysiological changes in the body vary during laparoscopic surgeries. The IAP can be classified as low (7 to 11 mmHg) , standard (12 to 15 mmHg) and high (>15 mmHg) during pneumoperitoneum.

PHYSIOLOGICAL EFFECTS OF LOW IAP: (7 – 11 mmHg)

Upto a pressure of 10 mmHg, there are no significant hemodynamic and metabolic changes. But the hepatic blood flow, portal venous circulation and microvascular circulation are all affected even at a pressure of 10 mmHg. Postoperative liver dysfunction and elevation of liver enzymes have been documented when IAP is as low as 10 mmHg. The advantages include lesser incidence of shoulder pain, lower pain scores and lesser postoperative nausea and vomiting in the low pressure group compared to the standard pressure group.

PHYSIOLOGICAL EFFECTS OF STANDARD IAP: (12 – 15 mmHg)

The cardiac output does not decrease significantly at an IAP of 15 mmHg. There is an increase in the afterload and a reduction in stroke volume due to the depression of the myocardium by carbon dioxide. The venous return actually increases due to the compression of the capacitance vessels rather than collapse. But there is a diminished flow velocity in the femoral vein causing stagnation of blood flow and increased risk of venous thromboembolism.

The mean arterial pressure (MAP) increases transiently due to shunting of blood away from the peritoneal cavity, but normalises later. The heart rate also increases transiently as a compensatory response to maintain the cardiac output

but there is no long term change in the heart rate. Sometimes bradycardia and asystole also have been reported. The possible mechanism could be direct stimulation of vagus and increase in parasympathetic discharge.

Pneumoperitoneum at standard IAP affects the pulmonary function also. Due to the upward shift of the diaphragm, there is a decrease in the lung expansion and the capacities of the lung and an increase in the pulmonary vascular resistance. Mismatch between the ventilation and perfusion occurs and leads to increased incidence of hypoxia and hypercarbia.

IAP of 15 mmHg causes compression of the renal vessels and a decrease in urine output. Regional blood flow to all intra-abdominal organs get decreased. Raised intra-abdominal pressure can increase the lumbar spinal pressure and lead to increased intracranial and intraocular pressures.

PHYSIOLOGICAL EFFECTS OF HIGH IAP: (> 15 mmHg)

When the IAP approaches 20 mmHg, there is a compression of the inferior vena cava leading to decreased venous return and a deleterious decrease in the cardiac output. The increased systemic vascular resistance, high intrathoracic pressure all lead to further fall in cardiac output. Keskin A et al has shown that at an IAP of 20 mmHg there is a decrease in the myocardial oxygen extraction, lactate extraction and ATP production. This altered myocardial metabolism

leads to deterioration of the cardiac contractility. The pulmonary capillary wedge pressure, CVP and left sided filling pressure is all increased at an IAP of 15 to 20 mmHg.

High IAP leads to an increase in the peak airway pressures and the plateau pressures. As in the standard IAP, a reduction in functional residual capacity causes ventilation perfusion mismatch and leads to hypoxia. Ventilation with PEEP (positive end expiratory pressure) improves the gas exchange and oxygenation. But the presence of PEEP could increase the intrathoracic pressure and cause further fall in cardiac output. Therefore PEEP should be applied with caution. A modern ventilation technique uses the ‘ alveolar recruitment strategy’ which consists of manual ventilation to an airway pressure of 40 mmHg for 10 breaths per minute , followed by the usual mechanical ventilation with mild PEEP of 5 cm H_2O.

At an IAP of > 20 mmHg there is a significant decrease in portal venous blood flow and liver dysfunction. Renal hypoperfusion is also significant and leads to acute tubular necrosis and anuria. There is a rise in serum potassium levels but it does not reach levels that would be clinically harmful. Some prophylactic measures have been suggested to prevent acute tubular necrosis. They include a renal dose of dopamine infusion (1 – 3 mcg/kg/min) and warm insufflations of

carbon dioxide. Blunting of the pressor responses using β – blockers, α_2 - agonists, lignocaine or other drugs could decrease the renal ischaemia.

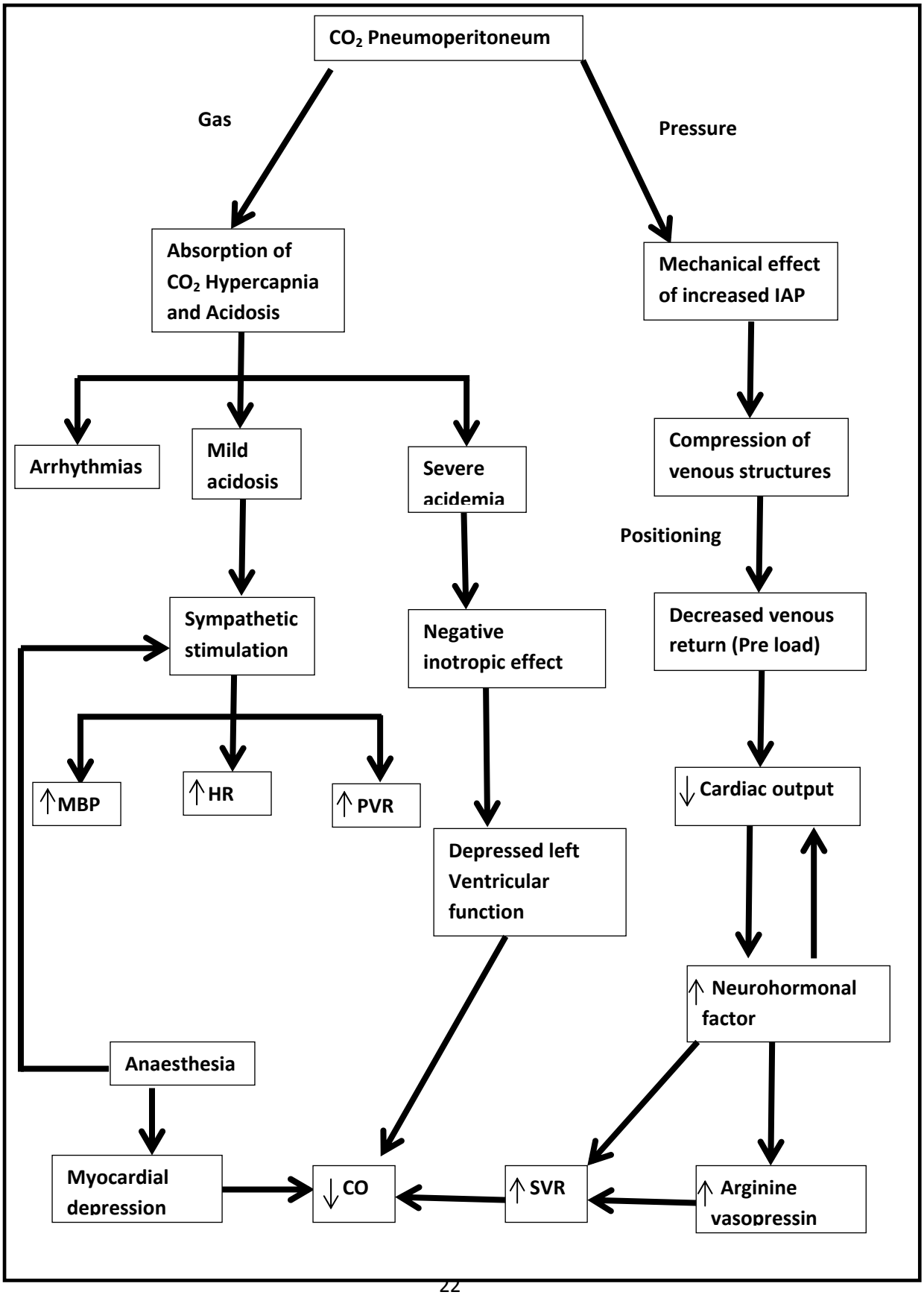
Though the high IAP could result in a better surgical exposure, better access to the abdominal organs and a safe surgical approach, the adverse hemodynamic consequences, pulmonary and hepatorenal dysfunction and higher incidence of PONV may lead to increased postoperative morbidity.

GASLESS LAPAROSCOPY:

In case of elderly patients with cardiorespiratory compromise another method of creating working space in the abdomen is used. In this , the abdominal integument is lifted (laparolift or laparotensor) without using any gas. The anterior abdominal wall is elevated to 10 – 15 cm using a mechanical retractor. Since the intra-abdominal pressure is not elevated there is no absorption of carbon dioxide and this technique causes negligible effects on the cardiovascular, respiratory and renal systems.

Some surgeons use a 4 mmHg of pneumoperitoneum in addition to the lifting of the abdominal wall. However due to the increased technical difficulty, increased operating time and lack of benefit with regard to postoperative nausea and vomiting it did not gain much popularity.

HEMODYNAMIC EFFECTS OF PNEUMOPERITONEUM:



The extent of cardiovascular changes depend on the intra-abdominal pressure, patient position, carbondioxide absorption, ventilator strategy and surgical technique and nature and duration of the procedure. The patient's intravascular volume, pre-existing cardiopulmonary status, depth of anaesthesia, anaesthetic agent used, neurohormonal factors and perhaps patient medication all influence the cardiovascular responses to the creation of pneumoperitoneum and laparoscopy. The combined effect of all these factors manifest in a given patient. The intraperitoneal pressure and the type of gas used have the predominant effect in the cardiovascular changes with the other factors modulating these effects. It is difficult to differentiate between the hemodynamic changes caused by the nature of the gas and the increased IAP.

Ishizaki et al proposed that the maximum safe limit of intra-abdominal pressure that had minimal hemodynamic effects was 12 mmHg. Some changes caused by increased IAP include increased systemic vascular resistance and decreased cardiac output. Other manifestations include decreased intra-abdominal microcirculation, cardiac arrhythmias and increased catecholamine and vasopressin release.

Since hemodynamically significant alterations were seen only when the $PaCO_2$ increased to more than 33 percent from baseline, incidentally it was thought that the insufflating gas had negligible systemic effects. This hypothesis was proved

by Kaminski et al in a canine model where similar hemodynamic changes were observed during both carbon dioxide and helium insufflations. However Saunders et al performed a study in a pig model where they compared carbon dioxide with nitrogen insufflations. They concluded that the hemodynamic changes were entirely due to carbon dioxide absorption and the resultant acid – base changes.

CHANGES IN CARDIOVASCULAR SYSTEM:

The filling pressure of the heart, pulmonary artery occlusion pressure and central venous pressure which are marginally reduced by induction of anaesthesia, increase when carbondioxide insufflation starts. But the increased filling pressure is not associated with an increase in left ventricular end systolic or diastolic area. Lebovitz et al suggested that the systemic vascular resistance increase markedly during initial phases of insufflations and then restores to previous values partially, 10 – 15 minutes later. Rafferty et al suggested that the increase in mean arterial pressure represents an increase in afterload and is associated with an increase in left ventricular wall stress.

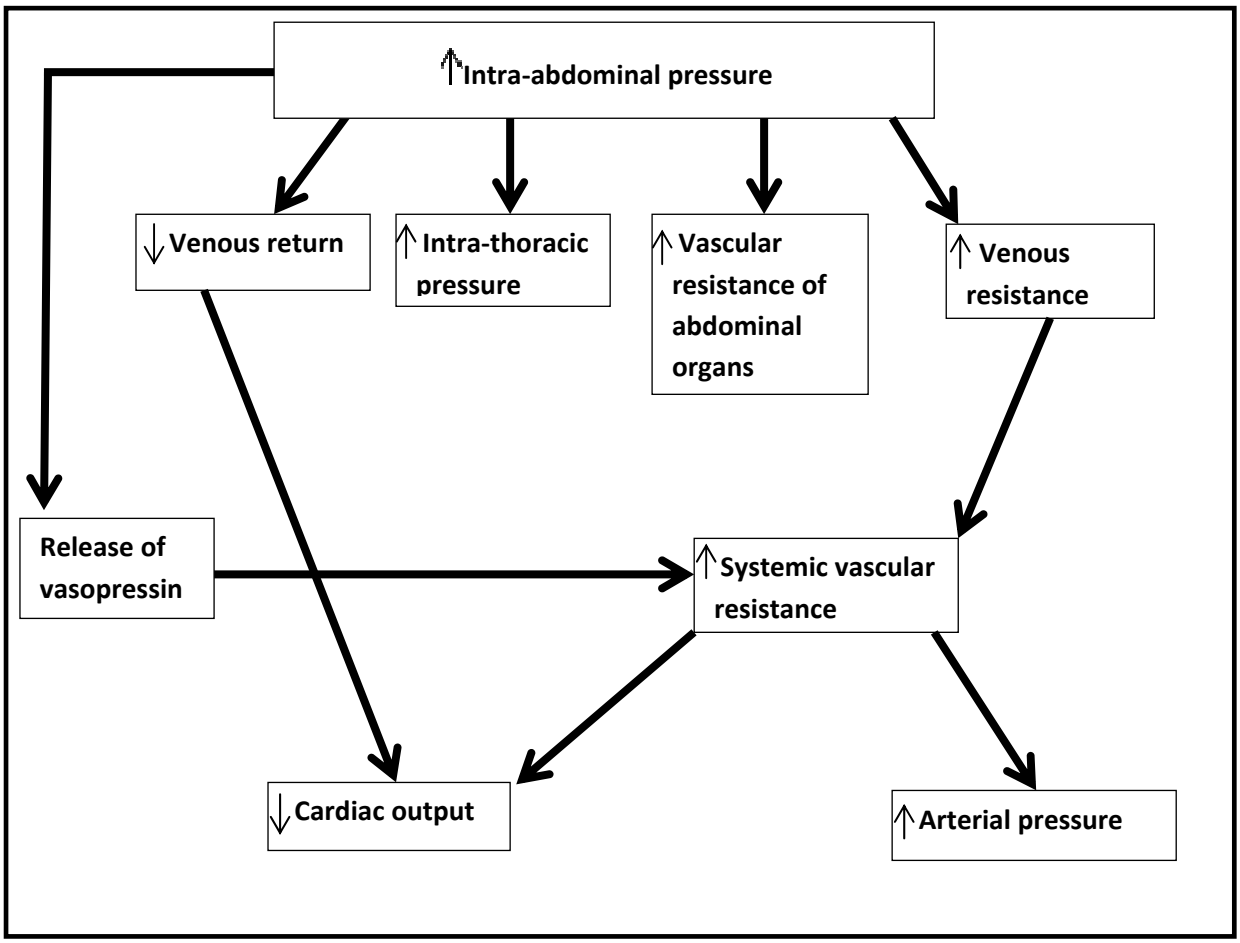
The effect on cardiac output differs. Zuckerman et al has shown a 30 % reduction of CI, while others have shown no significant change. Dorsay et al found no difference in cardiac output during pneumoperitoneum. Anderson et al and Myre et al, using invasive hemodynamic and transesophageal

measurements also showed that the cardiac index did not change during pneumoperitoneum.

Both invasive and non invasive methods have been used to demonstrate the cardiovascular changes to pneumoperitoneum. Techniques like transthoracic bio-impedence, esophageal Doppler probe, transesophageal echocardiography and pulmonary artery catheter have been used and studied for this purpose. Majority of the methods report similar trends.

Joris et al reported these hemodynamic changes to be phasic in nature. The initial fall in cardiac output and increase in systemic vascular resistance is later followed by an increase in the cardiac output and a fall in SVR ten minutes after insufflations of carbon dioxide.

CAUSES OF HEMODYNAMIC CHANGES:



Several factors have been proposed for the changes during laparoscopy. A lighter level of anaesthesia could cause an increase in afterload. But if nociception is the cause, the hemodynamic changes should occur at the time of trochar insertion rather than creation of pneumoperitoneum. The sympathetic nervous system stimulation caused by CO_2 absorption could be a cause. But the increase in systolic pressure occurs before the elevation of $EtCO_2$ and returns to normal despite sustained increase in $EtCO_2$. So the causal role of carbon

dioxide becomes unlikely. The intra-peritoneal pressure effects and position changes are usually superimposed. They are insufficient or absent in patients with normal left ventricular function.

Catecholamine and other humoral factors have been shown to increase after the onset of pneumoperitoneum. There is a marked elevation of plasma vasopressin concentration in patients undergoing laparoscopic surgeries. It may be triggered by neurogenic stimuli from peritoneal distension or chemical stimulation from carbondioxide. It can be speculated that these potential causal factors dissipate during sustained pneumoperitoneum.

PATIENTS WITH CARDIAC DISEASE:

Fumihiro et al studied the effects of laparoscopy in patients with already impaired cardiac function. They reported that the pattern of hemodynamic changes were similar to those of non cardiac patients. These patients showed a similar increase in CVP and PCWP and no significant change in heart rate, mean arterial pressure and cardiac output. But the increase in CVP and PCWP might not be well tolerated in these patients. Iwase et al reported a significant impairment of renal function and pulmonary edema in patients with cardiac disease. Uchikoshi et al commented that when pneumoperitoneum was used for long time in cardiac patients, it could precipitate cardiac failure.

PATIENT POSITIONING:

During laparoscopic surgeries the patient is positioned to produce gravitational displacement of the abdominal viscera and for better visualisation of surgical site. The overall effect depends on the degree of tilt, whether the change in position is before or after pneumoperitoneum and suppression of reflexes by anaesthetic and cardiovascular drugs. Compensatory cardiovascular reflexes like the barorecepter reflex maintain the cardiovascular stability by responding to increased hydrostatic pressure with vasodilatation and bradycardia. Although these reflexes are attenuated during anaesthesia, effects induced by these position changes remain insignificant.

The reverse trendelenberg or head up position causes a decrease in venous return and a 11% decrease in cardiac output. The decrease in cardiac output depends on the degree of tilt. Steeper the tilt, more is the fall in cardiac output. The CVP and PCWP are also influenced by patient position. But it is usually favourable for respiration.

The trendelenberg or head down position results in decreased total lung volume and compliance and favours development of atelectasis. This can be minimised by judicious administration of PEEP. These changes are more pronounced in obese, elderly debilitated patients and use of lithotomy position. It causes an increase in venous return and cardiac output and an increase in intracranial and

intraocular pressure. Brachial plexus injury, aspiration and endobronchial intubation are other problems of this position.

Zuckerman et al showed that the position changes had no effect on the measured hemodynamic parameters. All hemodynamic parameters return to baseline over time because the effect of pneumperitoneum and position are short lived.

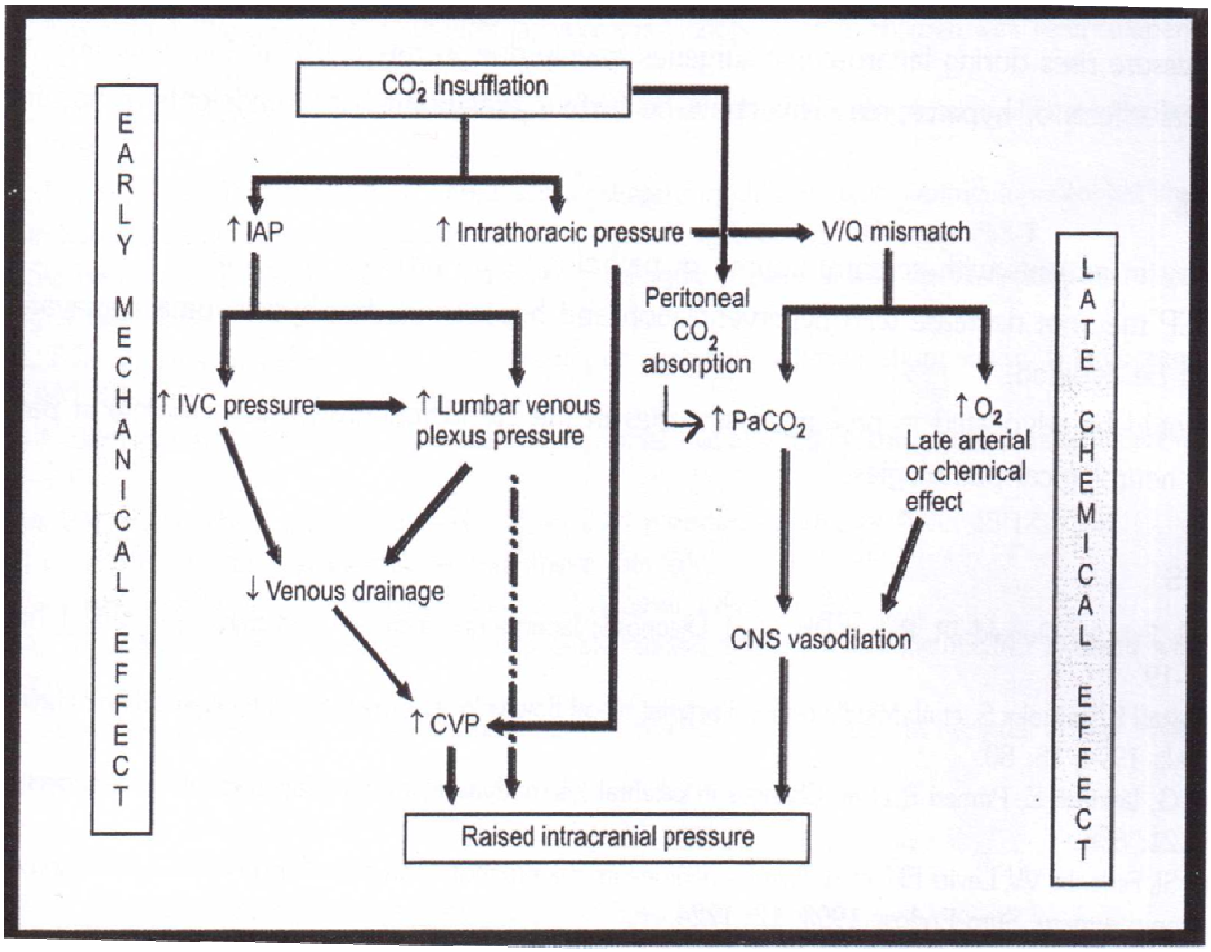
VENTILATORY EFFECTS OF PNEUMOPERITONEUM:

The significant respiratory changes include limitation of diaphragmatic and abdominal wall movement, atelectasis, dead space ventilation, decreased lung volumes and increased shunt fraction and peak inspiratory pressure. Functional residual capacity (FRC) that is already decreased due to general anaesthesia, decreases further by 20 to 25 percent 5 minutes after pneumoperitoneum. The compliance decrease by 30 to 50 percent and the resistance increases by as much as 79 percent five minutes after pneumoperitoneum. These observations were suggested by Cereda M, et al. Some studies suggest that a 10□ to 20□ head up or head down position does not cause any significant alteration in shunt fraction or lung volumes.

Flowers JL et al suggest that as early as 15 minutes after pneumoperitoneum these changes return to normal. These changes are well tolerated in healthy patients without any respiratory disease. In patients with baseline decrease in lung volumes and capacities, such as ASA III to IV, obese patients, there could be dramatic changes in pulmonary compliance, causing the lungs to shift to a flat non-compliant portion of the pressure – volume curve. The duration of pneumoperitoneum is insignificant unless complications such as bronchospasm or subcutaneous emphysema occur.

Using gasless laparoscopy, i.e., abdominal wall lift using fan retractor was suggested as an alternative in respiratory compromised patients. Though it significantly improves the effect on peak airway pressure and resistance, the elastance of respiratory system remains elevated. It is probably due to impairment of movement of the anterior abdominal wall and the diaphragm.

NEUROPHYSIOLOGICAL EFFECTS OF PNEUMOPERITONEUM:



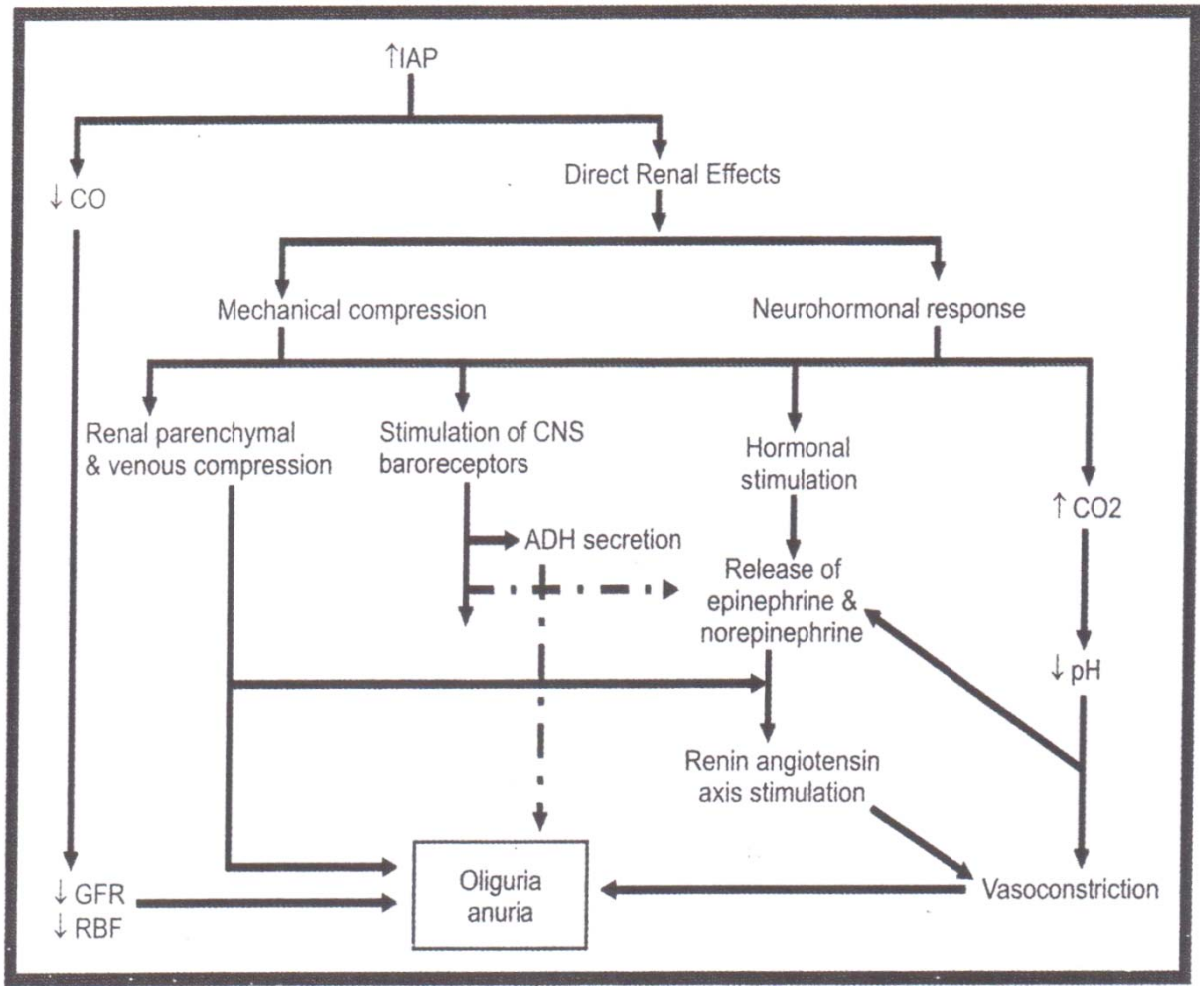
The effects of pneumoperitoneum on the central nervous system can be divided into two – an early mechanical effect and a late chemical effect.

EARLY MECHANICAL EFFECT: The increased IAP compresses the inferior vena cava and impairs venous drainage from the lumbar plexus, thus increasing the CSF pressure in the spinal column. Also the increased intra-thoracic pressure causes an increased cardiac filling pressure and CVP in the superior

vena cava, which leads to an increased intra-cranial pressure. This rise in ICP is based on the Monroe – Kellie hypothesis.

LATE CHEMICAL EFFECT : It is seen about 10 to 15 minutes after pneumoperitoneum. it is due to the reflex vasodilatation of the cerebral vessels causing an increase in cerebral blood flow. Hypoxia and hypercapnia caused due to ventilation perfusion mismatch in addition to the hypercapnia caused by the pneumoperitoneum are implicated for the late increase in ICP.

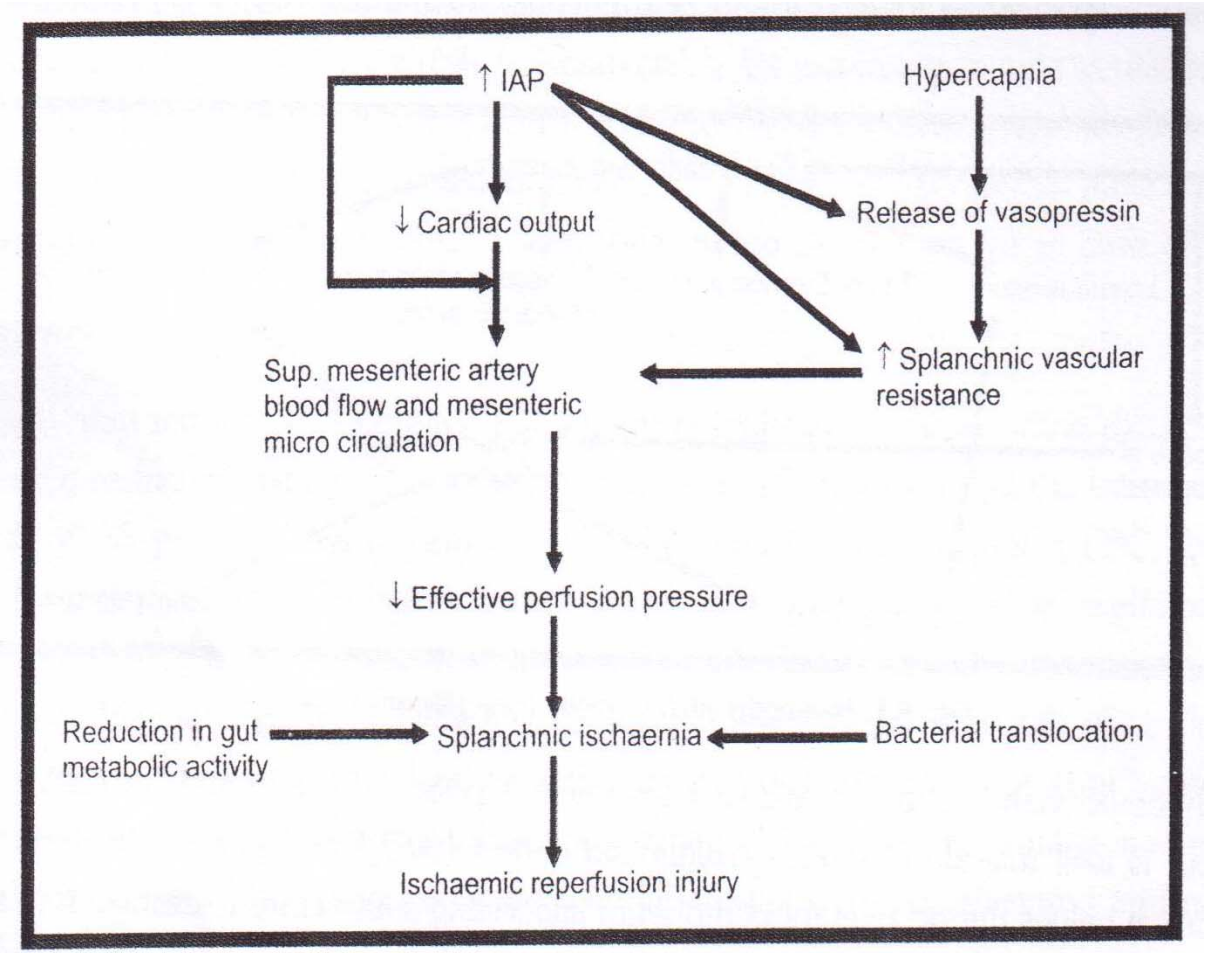
RENAL EFFECTS OF PNEUMOPERITONEUM :



Thorington and Schmidt demonstrated through animal studies that an IAP of 15 to 30 mmHg could lead to oliguria and an IAP of > 30 mmHg could lead to anuria. The deterioration of renal function is more at IAP > 15 mmHg. The mechanism of renal dysfunction may be due to the decreased cardiac output, the direct effect of the compression by the pneumoperitoneum or the catecholamine release causing vasoconstriction. The renal venous pressure is also increased.

Diminished renal blood flow triggers the renin – angiotensin – aldosterone axis. Renal protective measures such as dopamine infusions and warm carbon dioxide have been proved to be effective. The recently introduced gasless laparoscopy has been more favourable for renal function. High urine output has been demonstrated in this technique.

EFFECT ON INTRA-ABDOMINAL ORGANS:



High IAP reduces the mesenteric blood flow, intestinal microcirculation and the mucosal pH. Stuttman et al and Burton et al have reported incidents of fatal intestinal ischaemia following laparoscopic surgeries. Blood flow to all abdominal organs is reduced by the high IAP, except the adrenal glands.

COMPLICATIONS OF LAPAROSCOPIC SURGERIES:

- Abdominal pain due to the irritant effect of carbon dioxide.
- Shoulder pain due to the formation of carbonic acid.
- CARBONDIOXIDE GAS EMBOLISM – It is rare but potentially fatal. Gas may enter circulation if a needle or trochar accidentally punctures a blood vessel. Early recognition and treatment improves outcome. If a gas embolism is suspected, the surgeon should be alerted, insufflations stopped, 100% oxygen used for ventilation, if possible the patient is put in left lateral tilt with head down position (Durant's position).
- PULMONARY ASPIRATION – Increased intra-abdominal pressure increases the competence of the gastro esophageal sphincter and thus the risk of regurgitation. Despite intubation with a cuffed tube, pulmonary aspiration is still possible.
- PNEUMOTHORAX, SUBCUTANEOUS EMPHYSEMA AND PNEUMOMEDIASTINUM – It is due to the opening of the embryonic channels to the mediastinum, pleural cavity and pericardium. Subcutaneous emphysema is not uncommon after laparoscopic surgery for hernias, reflux esophagitis and obesity. Hypoxia and a rise in $EtCO_2$ are the usual presentations.

- THROMBOEMBOLISM – Due to the slowing of blood flow in the peripheral vascular system thrombosis can occur in the lower limbs. DVT may lead to pulmonary embolism.
- CARDIOVASCULAR – Bradyarrhythmia is very common during laparoscopy. Arrhythmias, ventricular and supraventricular are also not infrequent. It can lead to hypotension and cardiovascular collapse.
- POSTOPERATIVE NAUSEA AND VOMITING – PONV is very common following laparoscopic surgeries. It is a highly distressing complication. Ondansetron, a highly potent and selective 5-HT_3 antagonist has been proven to be very effective.
- PROMOTION OF PORT SITE TUMOUR GROWTH – The mechanism by which this occurs is not clearly known. The theories suggested are – degree of tumour manipulation ; stage and aggressiveness of the tumour ; high IAP and gas turbulence producing a spray effect.

  Carboperitoneum has been implicated to cause port site metastasis by the inflammatory mediators released by the peritoneum.
- ENDOBRONCHIAL INTUBATION – Increased intra abdominal pressure pushes the diaphragm upwards and causes cephalad movement of carina, leading to endobronchial intubation. It is identified intraoperatively by decrease in saturation and increase in plateau airway pressure.

STRESS RESPONSE AND LAPAROSCOPY:

The onset of surgery is associated with a rapid increase in the anterior and posterior pituitary hormones – β endorphin, ACTH, growth hormone, prolactin, arginine and vasopressin together with release of adrenaline and noradrenaline. It is followed by increase in circulating cortisol, aldosterone and renin. With the increase in the catabolic hormones there is a decrease of anabolic hormones like insulin and testosterone.

The unique feature of catabolic hormonal response is the absence of the normal negative feedback mechanisms. For example, the increased cortisol caused by ACTH, fails to inhibit further secretion of trophic hormones.

Various studies have compared the stress markers of laparoscopy and laparotomy, mostly in cholecystectomy. The results showed no significant difference in the response, although few have shown a reduced response in favour of laparoscopy.

Some studied the impact of anaesthesia on endocrine and immunological changes by investigating IL-6 and TNF-α levels. They confirmed that laparoscopic surgeries are associated with lesser immunoendocrine response and the type of anaesthesia does not influence it.

ANAESTHESIA FOR LAPAROSCOPY:

PREOPERATIVE EVALUATION AND PREMEDICATION:

Preoperative evaluation is essentially the same as for other surgical patients. Particular emphasis to be made on the cardiovascular and respiratory system. Patient's cardiac status should be assessed and quantified prior to surgery. In COPD patients pulmonary function tests are advised. In both groups the positive effects of laparoscopy must be balanced against the intraoperative risks.

DVT prophylaxis should be initiated prior to surgery. Due to the risk of regurgitation antacids, H_2 blockers and prokinetic agents are recommended.

ANAESTHETIC TECHNIQUE :

General anaesthesia with endotracheal intubation and controlled ventilation is the choice of anaesthesia. It allows adequate muscle relaxation, a quiet operative field and protection against aspiration. Minute volume has to be increased during carboperitoneum to maintain an $EtCO_2$ at about 35 mmHg.

VOLATILE ANAESTHETICS :

The choice of volatile anaesthetic should be based on the fact that it should counteract the increase in systemic vascular resistance caused by laparoscopy and not potentiate arrhythmias in the presence of hypercarbia. Since nowadays

most laparoscopic surgeries are performed as day care procedures, the recovery profile and PONV should also be considered. Anaesthetics that directly depress the myocardium should be avoided and agents with vasodilating properties such as isoflurane can be used.

INTRAVENOUS ANAESTHETICS:

Thiopentone, propofol, etomidate and midazolam can be used for the induction of anaesthesia. The considerations in choosing the agent are its myocardial depressant effect, action on peripheral vascular system, recovery profile and PONV. Benzodiazepines have modest hemodynamic effects and etomidate is a good choice in cardiac patients.

TOTAL INTRAVENOUS ANAESTHESIA:

Propofol with any short acting analgesic such as alfentanil, fentanyl and sufentanil are used for good recovery characteristics and surgical conditions. Because of a short context sensitive half-life, propofol gives good recovery characteristics.

MUSCLE RELAXANTS:

The use of muscle relaxation and controlled ventilation has decreased the respiratory complications like high airway pressures and pneumothorax. Peterson et al revealed that almost one third of the deaths due to laparoscopic surgeries were due to use of general anaesthesia without intubation. The laryngeal mask airway could be used to improve safety in a patient breathing spontaneously.

BENEFITS OF LAPAROSCOPY :

- Faster recovery
- Heightened feeling of well being
- Reduced hospital stay and postoperative fasting
- Lesser surgical trauma
- Lesser incidence of postoperative pain
- Lesser pulmonary dysfunction

Various pharmacological agents have been used to prevent the hemodynamic response during laparoscopic surgeries. Nitroglycerine was used to correct the reduction in cardiac output associated with increased pulmonary arterial occlusion pressure and systemic vascular resistance. β blockers have been used

to blunt the response to noxious stimuli. α_2 agonists are known to inhibit the catecholamine and vasopressin rise associated with pneumoperitoneum.

Considering all the above factors, this study was created with the aim of investigating whether i.v., magnesium sulphate, a well known inhibitor of catecholamines and vasopressin mediated vasoconstriction, can be used effectively to blunt the responses to pneumoperitoneum during laparoscopy.

AIM AND OBJECTIVE OF THE STUDY:

PRIMARY OBJECTIVE:

To assess the efficacy of magnesium sulphate on the attenuation of hemodynamic response to pneumoperitoneum during laparoscopic surgeries.

SECONDARY OBJECTIVE:

- To determine any adverse effects in the intra operative and postoperative period.
- To determine the sedation in each group.

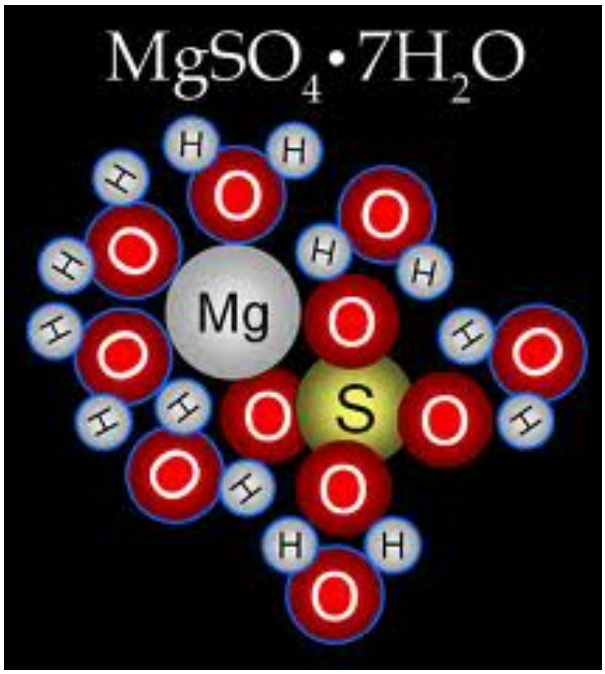
PHARMACOLOGY OF MAGNESIUM SULPHATE:

INTRODUCTION:

Magnesium is the second abundant intracellular cation. It is important for the function of several enzyme systems of the body. It plays a vital role in neurochemical transmission and membrane excitability. Its deficiency is associated with various structural and functional derangements.

Magnesium sulphate is an inorganic salt containing magnesium, sulphur and oxygen with the formula $MgSO_4$. It is often encountered as the heptahydrate compound, commonly called as Epsom salt. Epsom salts are used as bath salts. Oral magnesium sulphate is commonly used as saline laxative or osmotic purgative. Magnesium sulphate is the main preparation of intravenous magnesium.

DRUG DESCRIPTION:



Magnesium sulphate injection USP (50 %), for I.M and I.V use contains 500 mg of magnesium sulphate in each ml, which contain 4.06 mEq of magnesium and sulphate and water for injection. The pH (5.5 - 7.0) is adjusted with sulfuric acid and/or sodium hydroxide. The osmolarity is 4060 mOsm per litre. The solution contains no bacteriostatic agent or other preservatives. It is indicated for a single dose injection. Any unused portion has to be discarded. The molecular formula is $MgSO_4 \cdot 7H_2O$ and the molecular weight is 246.47.

INDICATIONS:

- Replacement therapy for hypomagnesemia.
- As the first line anti-arrhythmic for torsades de pointes and quinidine induced arrhythmias.
- As a bronchodilator after beta-agonists and anticholinergics have been tried.

- To treat eclampsia in pregnant women.
- As a tocolytic to delay premature labour.
- Antenatal intravenous magnesium sulphate has been shown to reduce cerebral palsy and gross motor dysfunction in preterm babies by 30%.
- To prevent magnesium deficiency in patients receiving total parenteral nutrition.

OTHER USES:

- Stress attenuation during laryngoscopy and intubation.
- Intra operative hemodynamic stability.
- For management of box jellyfish poisoning due to its vasodilatory and skeletal muscle relaxation properties.
- For management of paroxysmal atrial tachycardia, when all other measures have failed and there is no myocardial damage. The usual dose is 3 to 4 g.
- For reduction of cerebral edema, a dose of 2.5 g can be given intravenously.

DOSAGE AND ADMINISTRATION:

- INTRAVENOUS: 1 to 4 g of a 10 to 20% solution can be given intravenously, but with caution.
- INTRAVENOUS INFUSION: 4 g in 250 ml of 5% dextrose at a rate not more than 3 ml per minute.

- INTRAMUSCULAR: 1 to 5 g daily in divided doses, for severe hypomagnesemia in adults and older children. Serum magnesium levels should be monitored frequently and used as a guide to therapy.
- USUAL DOSE RANGE: 1 to 40 g daily.
- ELECTROLYTE REPLENISHMENT: 1 to 2 g of a 50% solution, four times a day, until the serum levels have normalised.
- PAEDIATRIC DOSE: 20 to 40 mg per kg of a 20% solution, repeated if necessary.
- FOR ECLAMPSIA: initially 1 to 2 g of a 25% or 50% solution is given I.M. subsequently 1 g is given every 30 minutes until relief is obtained.

SIDE EFFECTS:

- Flushing.
- Sweating.
- Sharply lowered blood pressure.
- Hypothermia.
- Stupor.
- Depressed reflexes.
- Flaccid paralysis.
- Respiratory depression.

OVER DOSAGE:

The therapeutic range for treating convulsions is 2.5 to 5 mEq/L.

Hypermagnesemia will lead to the following features at various plasma concentrations:

- 7.0-10.0 mEq/L - loss of patellar reflex
- 10.0-13.0 mEq/L - respiratory depression
- 15.0-25.0 mEq/L - altered atrioventricular conduction and (further) complete heart block
- >25.0 mEq/L - cardiac arrest

TREATMENT OF OVERDOSAGE:

1. Intravenous calcium - 10 to 20 ml of a 5% solution of calcium chloride is given to counteract the effects of hypermagnesemia.
2. Subcutaneous physostigmine 0.5 to 1 mg may be useful.
3. Artificial respiration is often needed – assisted ventilation via endotracheal intubation or intermittent positive pressure ventilation.

WARNINGS:

- Since the drug is almost exclusively excreted in the kidneys, caution is advised in case of renal dysfunction.
- In case of renal insufficiency, no more than 20 grams should be given within a 48 hour period.
- The main concern of parenteral magnesium is hypermagnesemia. It manifests as flushing, sweating, hypotension, stupor and cardiovascular collapse. Respiratory depression is the immediate danger to life.
- Any calcium preparation, such as calcium gluconate must be ready at any time, as an intravenous antidote.

PRECAUTIONS:

1. When used in conjuction with other respiratory depressants such as narcotics, barbiturates and benzodiazepines, their dose should be reduced to prevent the additive effect.
2. Its teratogenic effects in the fetus have yet to be studied. Hence it is to be given to a pregnant patient only if absolutely indicated.
3. Monitoring of patellar reflex and respiratory rate. The drug causes a depression in patellar reflex at a serum level of 7 mEq/L and respiratory depression at 10 mEq/L.

4. The 50% solution should be diluted to a concentration of 20% or less before parenteral administration. Commonly used solutions are 5% dextrose and 0.9% sodium chloride.

CONTRAINDICATIONS:

1. Complete heart block.
2. Renal dysfunction.
3. Hypermagnesemia.

CLINICAL PHARMACOLOGY:

Magnesium prevents convulsions by decreasing the level of acetylcholine released from the neuromuscular junction.

Normal plasma magnesium concentration is 1.5 to 2.5 mEq/L.

As the level rises to 4 mEq/L the deep tendon reflexes decrease and are lost at a level of 10 mEq/L. Cardiac and respiratory depression may also occur at this level. A plasma magnesium of 12 mEq/L may be fatal.

Magnesium acts peripherally to produce vasodilatation. At low dose it causes flushing and sweating and at higher doses it could lead to hypotension. Calcium acts as an antagonist to both the central and peripheral actions of magnesium.

PHARMACOKINETICS:

Following intravenous infusion, the onset is immediate and the duration is 30 minutes. Following intramuscular injection the onset is delayed by one hour, and the duration of action is 3 to 4 hours.

The drug is solely excreted by the kidneys and the rate of excretion is directly proportional to the glomerular filtration rate.

DRUG INTERACTIONS:

1. CNS depressants – additive effect with barbiturates, narcotics and benzodiazepines.
2. Neuromuscular blockers – excessive neuromuscular blockade and prolongation of action can occur.
3. Cardiac glycosides – magnesium should be administered with extreme caution in digitalised patients because serious conduction abnormalities can occur.

AVAILABILITY:

- 2 ml single dose vial.
- 10 ml single dose vial.
- 50 ml single dose vial.

It could be stored at a room temperature of 15 to 30 degrees. Since it contains no preservatives, the unused portion has to be discarded.

REVIEW OF LITERATURE

Several studies have been conducted to study the hemodynamic changes and the catecholamine response during laparoscopic surgeries. The efficacy of magnesium sulphate in attenuation of the neuroendocrine response has also been studied.

1. British Journal of Anaesthesia 103 (4): 484–9 (2009)

D. Jee, D. Lee, S. Yun and C. Lee.

"Magnesium sulphate attenuates arterial pressure increase during laparoscopic cholecystectomy."

In this study, 35 ASA I patients undergoing elective cholecystectomy were chosen. All patients were premedicated with Inj. Glycopyrrolate 0.2 mg one hour before surgery. Induction of anaesthesia and intubation was done after midazolam 0.05 mg/kg, sodium thiopental 3 – 5 mg/kg and vecuronium 0.1 mg/kg. Before pneumoperitoneum the control group received i.v., normal saline 0.5 ml/kg and the study group received i.v., magnesium sulphate in the dose of 50 mg/kg, diluted in normal saline to 0.5 ml/kg and made as a 10% solution. The infusion was given slowly over 2 -3 minutes.

No opioids or any analgesics was given in both groups throughout the surgery. In both groups the anaesthesia was maintained with N_2O and O_2 in the ratio 1:1 at 4 litres per minute and a end tidal sevoflurane concentration of 1.5 – 2.5 %.

Standard monitoring devices were used and during pneumoperitoneum, the intra abdominal pressure was maintained at 14 mm Hg.

Arterial pressures, heart rate, serum magnesium, plasma renin activity and catecholamine, cortisol and vasopressin levels were measured in both groups.

Results: Systolic and diastolic blood pressures were higher in the control group than the study group at 10, 20, 30 minutes post pneumoperitoneum. The vasopressin and catecholamine levels were also significantly higher in the control group than the magnesium group. There was no significant difference in the rennin and cortisol levels between the two groups.

Conclusion: Magnesium sulphate attenuates the arterial pressure increase and the catecholamine response to pneumoperitoneum during laparoscopic surgeries.

2. Indian Journal of Anaesthesia 2008; 52 (6):800-804.

Dilip Kothari, Amrita Mehrotra, Bhanu Choudhary, Alok Mehra.

"Effect of Intravenous Magnesium Sulfate and Fentanyl Citrate on Circulatory Changes During Anaesthesia and Surgery: A Clinical Study."

In this study the circulatory effects of fentanyl citrate and magnesium sulphate were compared during general anaesthesia and surgery. Sixty ASA I and II patients were chosen with 30 in each group. The magnesium group was given

intravenous magnesium sulphate 20mg/kg 5 minutes before induction, 10 mg/kg 5 minutes before skin incision and 10 mg/kg every 30 minutes thereafter. The fentanyl group was given intravenous fentanyl citrate 1.25 mcg/kg, 0.5 mcg/kg and 0.5 mcg/kg at similar intervals. General anaesthesia was standardised in both groups with controlled ventilation, O_2 , N_2O and 0.2% halothane and relaxants in both groups. The baseline pulse rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was monitored and was subsequently recorded at regular intervals. There was a rise in all the hemodynamic variables immediately after intubation in both groups and returned to near baseline values thereafter. There was no statistically significant difference between the variables in both groups. Therefore this study suggests that magnesium sulphate could be used as a safe and cheap alternative to fentanyl citrate during surgeries under general anaesthesia.

3. Journal of Research in Medical Sciences 2005; 10(2): 82-86.

K. Montazeri MD, M. Fallah MD.

A Dose – Response Study of Magnesium Sulfate in Suppressing Cardiovascular Responses to Laryngoscopy & Endotracheal Intubation.

This study was done with the aim of estimating the optimal dose of magnesium sulphate that attenuates the cardiovascular responses to laryngoscopy and tracheal intubation. 120 ASA I patients between age group 15 and 50 years,

undergoing elective surgeries were chosen and were divided into six groups of twenty each. Each group received 10, 20, 30, 40 and 50 mg/kg of intravenous magnesium sulphate and the sixth group received 1.5 mg/kg of lidocaine. In all the groups the drug was given 1 minute before induction of anaesthesia. Induction was standardised with fentanyl 1 mcg/kg, atracurium 0.5 mg/kg and sodium thiopental 5 mg/kg in all groups.

Pulse rate and blood pressure was measured 5 minutes before giving any drug, just before laryngoscopy and 1, 3, and 5 minutes after intubation. Train of four was measured 45 minutes after induction of anaesthesia.

Results: There was no significant difference in the monitored parameters between the magnesium groups, but there was a significant difference between the magnesium and lidocaine groups.

Conclusion: The cardiovascular response suppression effect was more effective with magnesium sulphate than with lidocaine.

4. ANAESTHESIA ANALGESIA 1989;68:772-6.

Intravenous Magnesium Sulfate Inhibits Catecholamine Release Associated with Tracheal Intubation.

Michael F. M. James, FFARCS, R. Eryk Beer, FFA(SA), and Jan D. Esser, MMED.

The effect of 60 mg/kg of magnesium sulphate on cardiovascular response and catecholamine release associated with tracheal intubation was studied. 15 patients in each group were chosen. Group A patients received 60 mg/kg of 50% magnesium sulphate intravenously over 1 minute, while group B received normal saline. After intubation, the heart rate was unchanged and the rise in systolic blood pressure was insignificant in group A. Epinephrine levels were unchanged from baseline in the control group. Thus, this study concludes that magnesium sulphate attenuates the arterial pressure increase and catecholamine response to laryngoscopy and intubation.

5.J Urol. 1996 Apr;155(4):1368-71.

Catecholamine release caused by carbon dioxide insufflation during laparoscopic surgery.

Mikami O, Kawakita S, Fujise K, Shingu K, Takahashi H, Matsuda T.

This study evaluated the epinephrine and norepinephrine levels in 29 patients who underwent laparoscopic surgeries. The levels were found to be significantly higher five minutes after CO_2 insufflations than during Veress needle insertion or just before pneumoperitoneum. This study concluded that catecholamine release was associated with pneumoperitoneum during laparoscopic surgeries.

6.Br J Anaesth. 1997 Mar;78(3):264-6.

Role of vasopressin in the haemodynamic response to laparoscopic cholecystectomy.

Walder AD, Aitkenhead AR.

In this study 10 patients undergoing laparoscopic cholecystectomy were studied, with 5 patients undergoing elective limb surgeries under general anaesthesia as control. The parameters monitored were arterial pressure, heart rate, right atrial pressure, cardiac index, adrenaline, noradrenaline and arginine vasopressin concentrations. Arginine vasopressin levels were found to be elevated in the study group after insufflation of pneumoperitoneum and it caused significant hemodynamic changes.

7.British Journal Of Anaesthesia

Volume 104, (Number 4): 465-7; October 2009.

Magnesium: an emerging drug in anaesthesia.

The role of magnesium has been advanced and exemplified in the past century. Extensive obstetric research indicated that it is the best drug for the treatment of eclamptic seizures, although the mechanism is unknown. Apart from it, numerous studies have been conducted to establish its cardiovascular effects. These studies show that it is an effective arteriolar dilator, without causing venodilation, thus improving cardiac output and filling. When the

catecholamine levels are high, it is shown to be an excellent alpha adrenergic antagonist while preserving its beta agonistic effects. It is used for the treatment of torsades de pointes and also protects against catecholamine induced arrhythmias. It is a very safe drug with a therapeutic ratio of 10:1. Plasma concentrations of upto 6 mmol/L are hemodynamically safe and a concentration of 9 mmol/L causes only moderate hypotension.

8.Br. J. Anaesth. (1989) 62 (6): 616-623.

Use of magnesium sulphate in the anaesthetic management of phaeochromocytoma: a review of 17 anaesthetics

M. F. M. James, M.B., CH.B., F.F.A.R.C.S.

Seventeen patients with pheochromocytoma, undergoing elective surgery under general anaesthesia were included in this study. In these patients intravenous magnesium sulphate was used as the principal anti adrenergic agent. It was found to be effective in controlling the cardiovascular changes to induction and anaesthesia in 15 of them, and 4 of them required additional nitroprusside intraoperatively. The catecholamine levels were studied and magnesium was found to significantly reduce the catecholamine levels too.

9.Br. J. Anaesth. (2002) 89 (4): 594-598.

Evaluation of effects of magnesium sulphate in reducing intraoperative anaesthetic requirements

L. Telci, F. Esen, D. Akcora, T. Erden, A. T. Canbolat and K. Akpir.

In this study 81 patients undergoing elective spinal surgeries were included in two parallel groups. One group received 50 mg/kg of intravenous magnesium sulphate preoperatively and an infusion of 10 mg/kg/hr intraoperatively. The other group received equal volumes of normal saline. Anaesthesia was maintained with propofol and remifentanil. It was found that the requirement of propofol, remifentanil and vecuronium was significantly lesser in the magnesium group compared to the control group.

10.Br. J. Anaesth. (2005) 94 (4): 438-441.

Effects of magnesium sulphate and clonidine on propofol consumption, haemodynamics and postoperative recovery

A.Altan, N. Turgut, F. Yildiz, A. Turkmen and H. Ustun

Sixty ASA II patients undergoing elective spine surgeries were divided into three groups. Group I received 30 mg/kg of intravenous magnesium sulphate before induction and a infusion of 10 mg/kg/hr intraoperatively. Group II received 3 mcg/kg of clonidine before induction and an infusion of 2 mcg/kg/hr.

The third group received normal saline in equal volumes. Anaesthesia was maintained with propofol, fentanyl and cisatracurium.

Induction of anaesthesia was rapid in the magnesium group and the requirements of propofol and fentanyl were lower in both magnesium and clonidine group.

Conclusion: Clonidine causes hypotension and bradycardia. Magnesium, inspite of causing a delayed recovery can be used as an adjuvant intraoperatively.

11.Br. J. Anaesth. (1991) 66 (2): 216-223.

Attenuation of the pressor response to tracheal intubation in hypertensive proteinuric pregnant patients by lignocaine, alfentanil and magnesium sulphate

R. W. Allen, M.B., CH.B., F.F.A.R.C.S.I., M. F. M. James, M.B., CH.B., F.C.ANAES. and P. C. Uys, M.B., CH.B., F.F.A.(S.A.).

The attenuation of the pressor response to intubation was studied in pregnant patients with gestational hypertension. A comparison was done between lignocaine 1.5 mg/kg, magnesium sulphate 40 mg/kg and alfentanil 10 mcg/kg in 69 pregnant patients. The systolic arterial pressure was found to be higher in the lignocaine group, 5 minutes after intubation and there was no increase in the

arterial pressure in the other two groups. Of the three drugs, alfentanil caused the least increase in heart rate, but with some amount of fetal depression.

12.Anesthesiology: November 2002 - Volume 97 - Issue 5 - pp 1137-1141.

Choi, Jae Chan; Yoon, Kyung Bong; Um, Dae Ja; Kim, Chan; Kim, Jin Soo; Lee, Sang Gyu.

This study was done with the aim of evaluating whether intravenous magnesium sulphate decreases the requirement of propofol infusion during maintainance of anaesthesia. 54 patients undergoing elective abdominal hysterectomy were chosen and divided into two groups. The control group received normal saline, while the study group received magnesium sulphate 50 mg/kg bolus and a maintainance dose of 8 mg/kg/hr. The infusion rate of propofol was adjusted according to the heart rate and mean arterial pressure.

Conclusion: The propofol infusion rate was significantly lower in the magnesium group than the control group. This proves that magnesium sulphate has an effect on anaesthesia and analgesia.

13.Can J Physiol Pharmacol. 1987 Apr;65(4):729-45.

Mg2+-Ca2+ interaction in contractility of vascular smooth muscle.

Altura BM, Altura BT, Carella A, Gebrewold A, Murakawa T, Nishio A.

Studies on both arteriolar and venular smooth muscles of all types of blood vessels was done. It has been shown that only magnesium has the ability to inhibit the basal, myogenic and hormonal tone in vascular smooth muscles of all types of blood vessels. Due to the heterogenecity of the Ca2+ binding sites and the receptors (ligand- ,voltage- and leak- operated), the organic calcium channel blockers have a selective action on specific receptors. Magnesium is found to have a special calcium antagonistic action, though it is three to five times less potent than the calcium channel blockers.

METHODOLOGY

SOURCES OF DATA:

The data was collected from 60 ASA I patients scheduled to undergo laparoscopic surgeries (laparoscopic appendicectomy and cholecystectomy) under general anaesthesia, aged between 18 and 50 years. The study was conducted in Government Rajaji hospital, Madurai Medical College.

INCLUSION CRITERIA:

- Patients undergoing elective laparoscopic surgeries
- Age 18 to 60 years
- Both sex
- ASA I patients

EXCLUSION CRITERIA:

- Age <18 years , and >60 years
- ASA II or more patients
- Hypermagnesemia
- Allergy to magnesium sulphate
- Heart block
- Diabetes mellitus
- Systemic hypertension
- Cardiovascular or kidney disease
- Endocrine or metabolic disease

- Severe haemorrhage during the surgery
- Conversion to open procedure
- Need for any anti-hypertensive during the surgery
- Duration of surgery less than 30 minutes

METHODS:

The study is a randomised, prospective, double blinded control study. After obtaining approval from the institutional review board and informed consent sixty ASA I patients undergoing elective laparoscopic surgeries were enrolled in the study.

Pre – anaesthetic evaluation:

1. History of diabetes, hypertension or any cardiovascular disease.
2. History of any respiratory tract infection, wheezing or chronic chest infections.
3. History of seizures or neuromuscular disease/weakness.
4. History of any drug intake or allergic reactions to any drugs.
5. History of previous surgeries and any significant events.
6. Relevant investigations – haemoglobin, blood sugar, blood urea, serum creatinine, serum electrolytes, urine analysis.
7. Informed consent from patients.

All patients were premedicated with Diazepam 10 mg orally the night before surgery. Glycopyrrolate 0.2 mg i.m., and ranitidine hydrochloride 50 mg i.v., was given 1 hour before surgery. After shifting the patient into the operating room, pulseoximeter, NIBP and ECG leads were connected. Intravenous line was secured. A nasogastric tube was inserted and suction was applied to empty the stomach before intubation.

Preoxygenation was done with 100% oxygen for 3 minutes. All patients were induced with fentanyl citrate 2 mcg/kg, thiopentone sodium 3-5 mg/kg and suxamethonium 1.5 mg/kg for muscle relaxation. Proper sized cuffed oral endotracheal tube was inserted, cuff was inflated and connected to closed circuit for controlled ventilation. Immediately before pneumoperitoneum the patients were randomly allocated into two groups using sealed envelopes chosen by the patients preoperatively. The control group received normal saline 0.5 ml/kg i.v. The study group received 0.5 ml/kg of 10% magnesium sulphate (50 mg/kg) i.v., over 2 – 3 minutes. The drug was given 1 minute before pneumoperitoneum in both groups.

Anaesthesia was maintained with 66% nitrous oxide and 33% oxygen and 1 – 2 % sevoflurane. Atracurium 0.5 mg/kg bolus was given and 0.1 mg/kg was used

for maintainance of muscle relaxation. Fentanyl citrate 0.5 mcg/kg was given every 30 minutes thereafter. Ventilation was adjusted to maintain a end tidal CO_2 of 35 – 40 mm Hg. Carbondioxide pneumoperitoneum was established and the intra abdominal pressure was maintained between 13 – 15 mm Hg. Ringer lactate solution was administered in according to the fasting period, maintainance volume and blood losses. Neuromuscular monitoring was done using train of four to look for any prolongation of the muscle relaxant action.

The hemodynamic parameters were measured by an anaesthetist who was unaware of the study, to make it double blinded. The systolic and diastolic blood pressures and the pulse rate was measured at the following intervals :

Baseline / preoperative

- 0 minute/ before pneumoperitoneum
- 5 minutes after pneumoperitoneum
- 10 minutes after pneumoperitoneum
- 15 minutes after pneumoperitoneum
- 20 minutes after pneumoperitoneum
- 30 minutes after pneumoperitoneum
- 45 minutes after pneumoperitoneum
- 60 minutes after pneumoperitoneum

At the end of surgery glycopyrrolate 0.01 mg/kg and neostigmine 0.05 mg/kg was used for reversal of muscle relaxation. After thorough suctioning and nasogastric tube aspiration the tracheal tube was removed.

Patients in whom the pneumoperitoneum was terminated within 30 minutes and those who needed other i.v., antihypertensives were excluded from the study. Post operative sedation was monitored for 6 hours using the Ramsay's sedation score. Patients were monitored for other signs of hypermagnesemia and serum magnesium levels were measured in the post operative period in the magnesium group.

RAMSAY'S SEDATION SCORE:

1. anxious and agitated or restless or both
2. cooperative and oriented
3. responds to oral commands only
4. brisk response
5. sluggish response
6. no response

LEVEL 1 – 3: patient awake

LEVEL 4 – 6: patient asleep, responds to light glabellar tap or loud auditory stimulus

SIGNS OF HYPERMAGNESEMIA:

- weakness/ flaccid paralysis/ depressed reflexes
- nausea and vomiting
- impaired breathing
- decreased respiration
- arrhythmias and asystole
- decreased or absent tendon reflexes
- hypotension, flushing
- bradycardia
- hypocalcemia and paralytic ileus

STATISTICAL TOOLS:

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2010)** developed by Centre for Disease Control, Atlanta.

Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

RESULTS:

Table 1:

Age distribution

Age group	Magnesium group		Control group	
	No	%	No	%
Upto 20 years	7	23.3	7	23.3
21-30 years	11	36.7	11	36.7
31-40 years	5	16.7	5	16.7
41-50 years	5	16.7	4	13.3
> 50 years	2	6.7	3	10.0
Total	30	100	30	100
Range	18 - 54 years		18 - 56 years	
Mean	30.9 years		31.1 years	
SD	11.3 years		11.7 years	
'p'	0.9646 Not significant			

Table 1 shows that there was no significant difference in the age distribution between both groups.

Figure 1a

Age Distribution mean

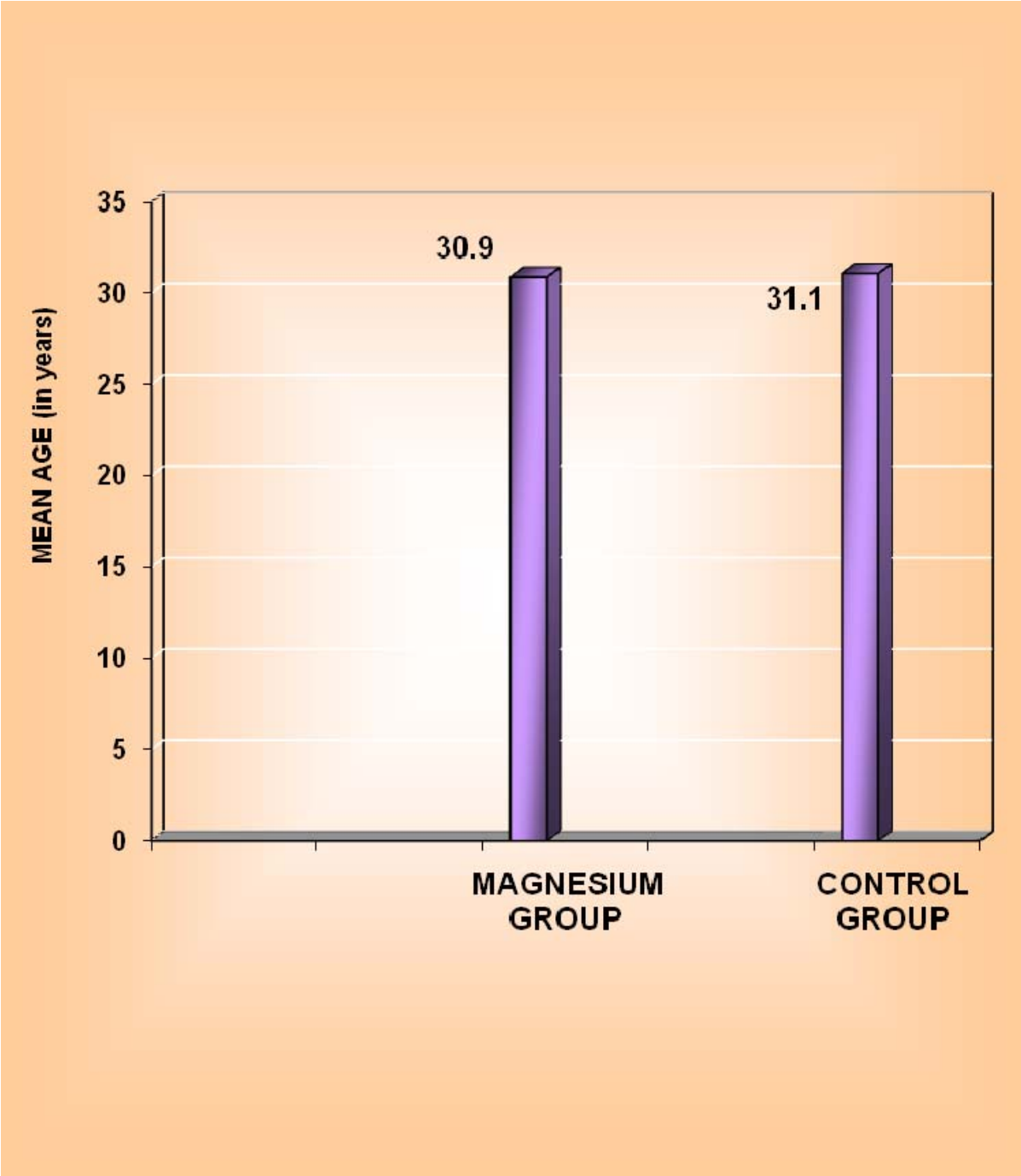


Figure 1b

Age distribution no of cases

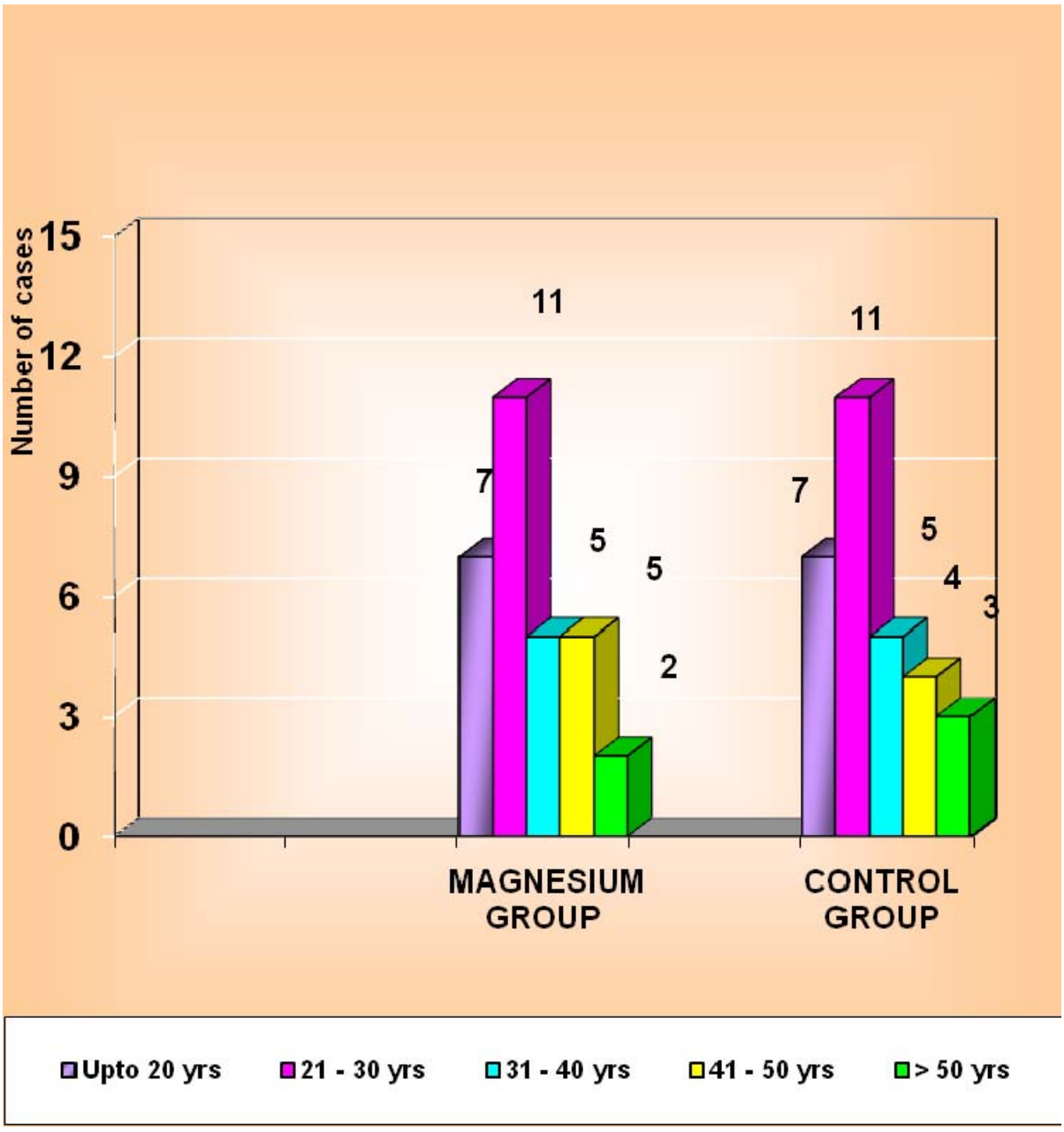


Table2:

Sex distribution

Sex	Magnesium group		Control group	
	No	%	No	%
Male	14	46.7	17	56.7
Female	16	53.3	13	43.3
Total	30	100	30	100
'p'	0.6054 Not significant			

Table 2 shows that there was no significant difference in the sex distribution between both groups.

Figure 2a

Sex distribution

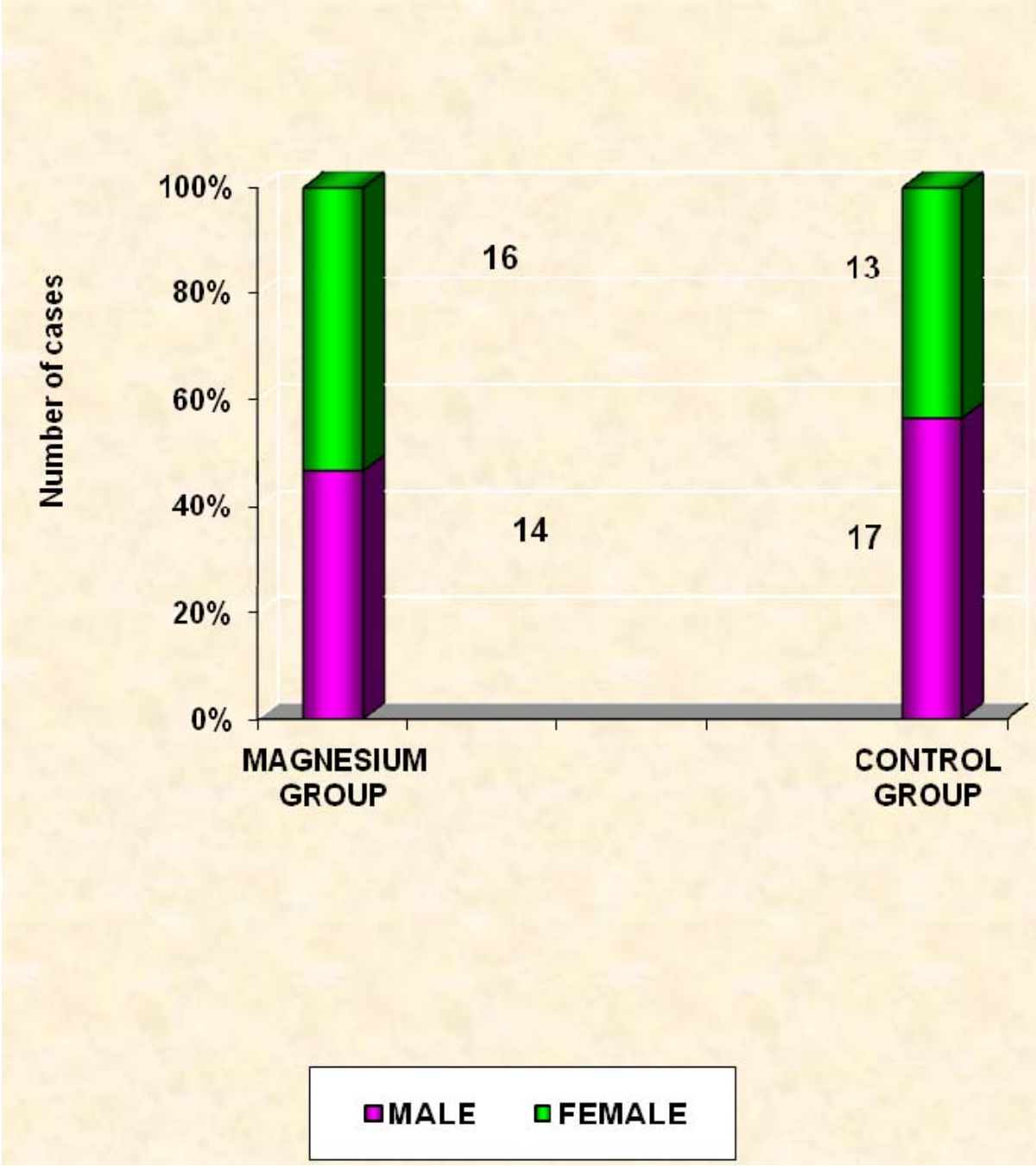


Figure 2b

Sex Distribution in percentage

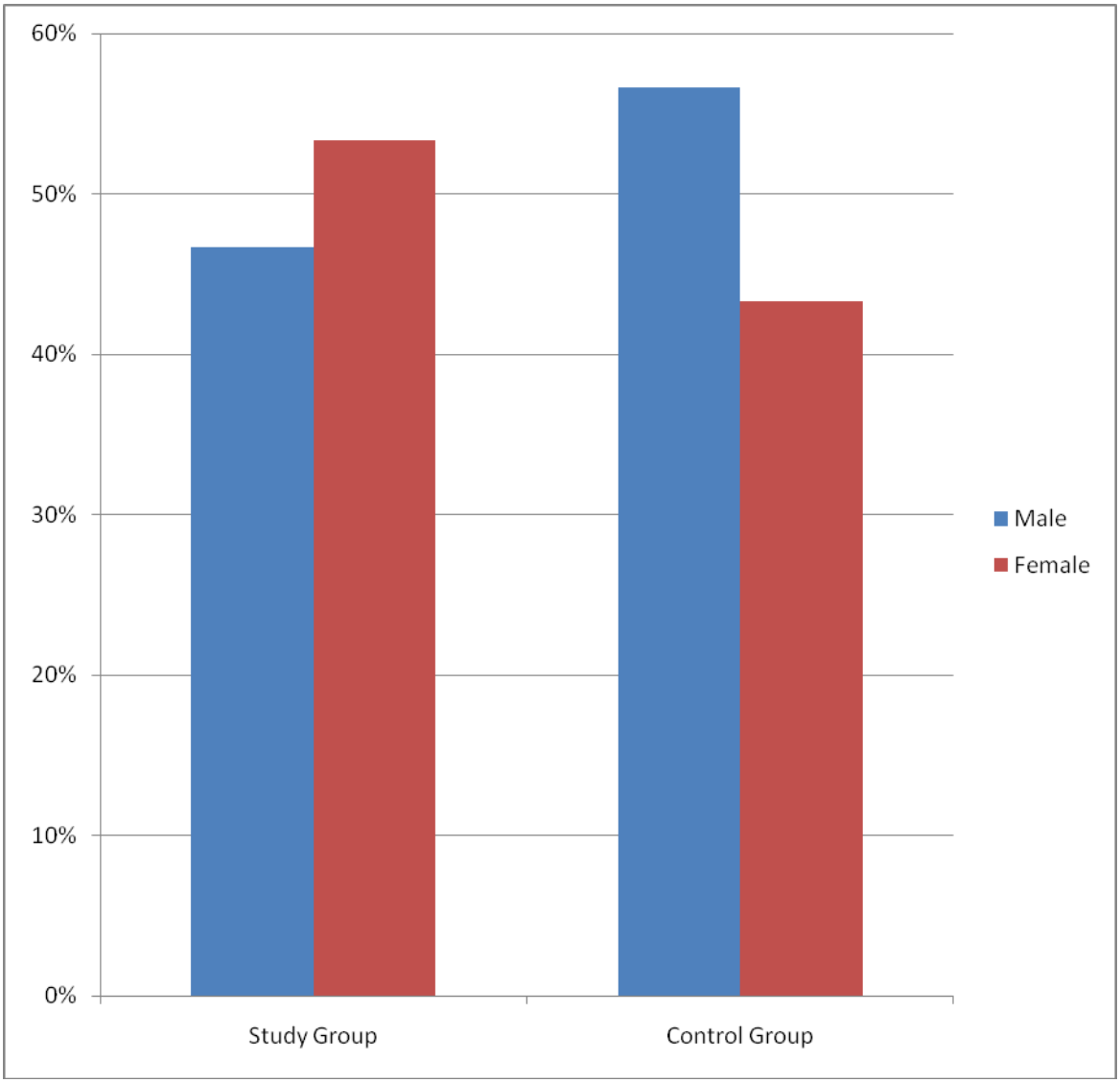


Table 3:

Duration of surgery

Duration of surgery (in minutes)		
	Magnesium group	**Control group**
Range	62 - 119	62 - 120
Mean	85.2	85.4
SD	16.1	15.7
'p'	0.9764	
	Not significant	

Table 3 shows that there is no significant difference in the duration of surgery between both groups

Figure 3

Mean duration of surgery

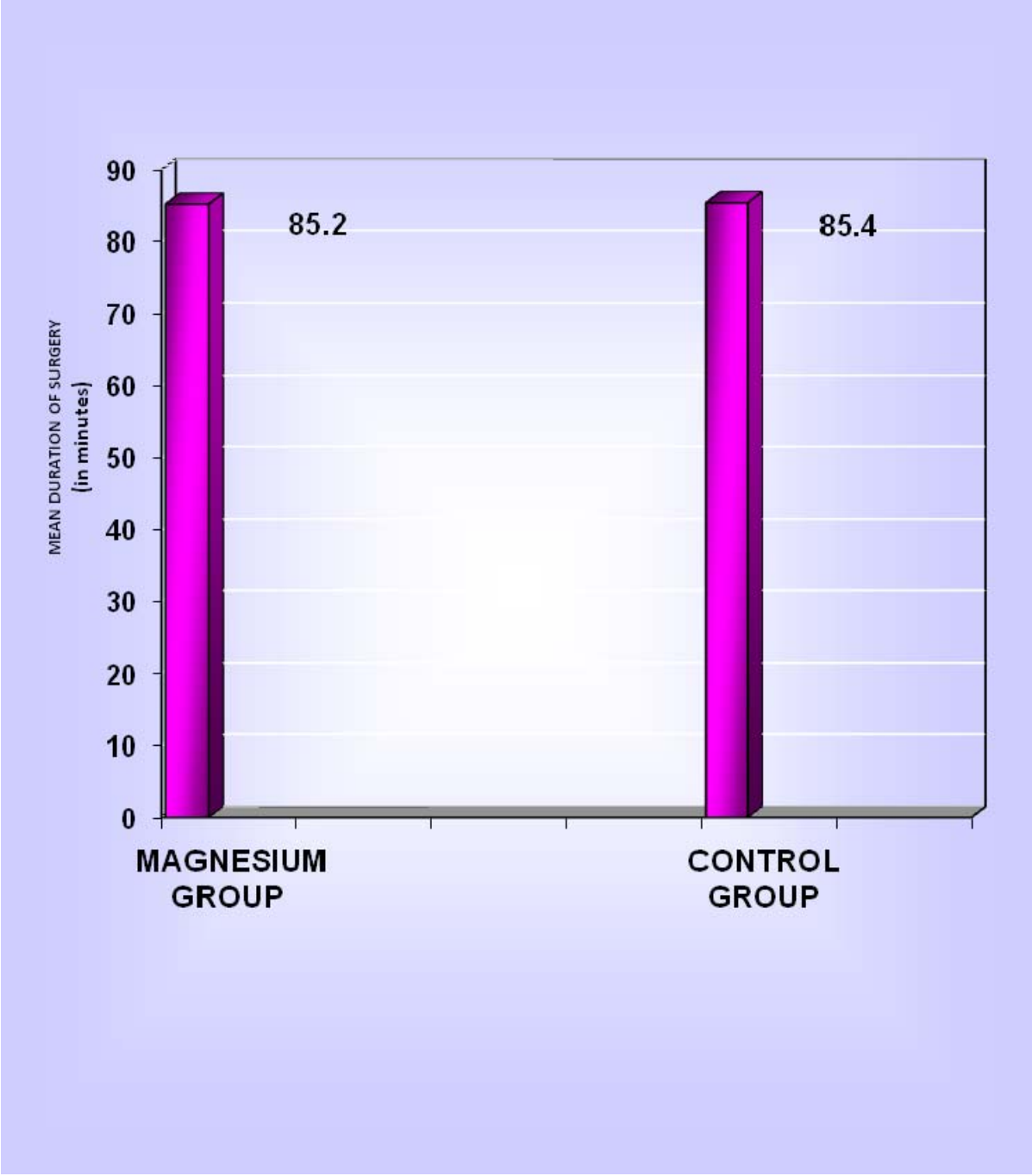


Table 4:

Changes in systolic B.P

SBP at	Systolic BP in				'p'	Significance
	Magnesium Group		Control group			
	Mean	SD	Mean	SD		
Baseline	118.0	8.9	116.7	7.7	0.6451	Not significant
0 minute	120.8	13.1	120.3	8.9	0.8704	Not significant
5 minutes	122.7	10.9	122.5	7.0	0.9408	Not significant
10 minutes	123.0	12.4	129.5	10.6	**0.0305**	**Significant**
15 minutes	125.0	11.7	132.5	14.1	**0.0263**	**Significant**
20 minutes	126.6	10.5	136.7	11.2	**0.0001**	**Significant**
30 minutes	128.8	12.1	136.4	12.0	**0.0338**	**Significant**
45 minutes	125.4	13.2	136.4	14.4	**0.0025**	**Significant**
60 minutes	127.4	10.1	136.3	11.5	**0.0015**	**Significant**

Table 4 shows that there is a significant difference in the systolic blood pressure between the magnesium group and the control group at 10, 15, 20, 30 45 and 60 minutes post pneumoperitoneum.

Figure 4a

Mean systolic BP

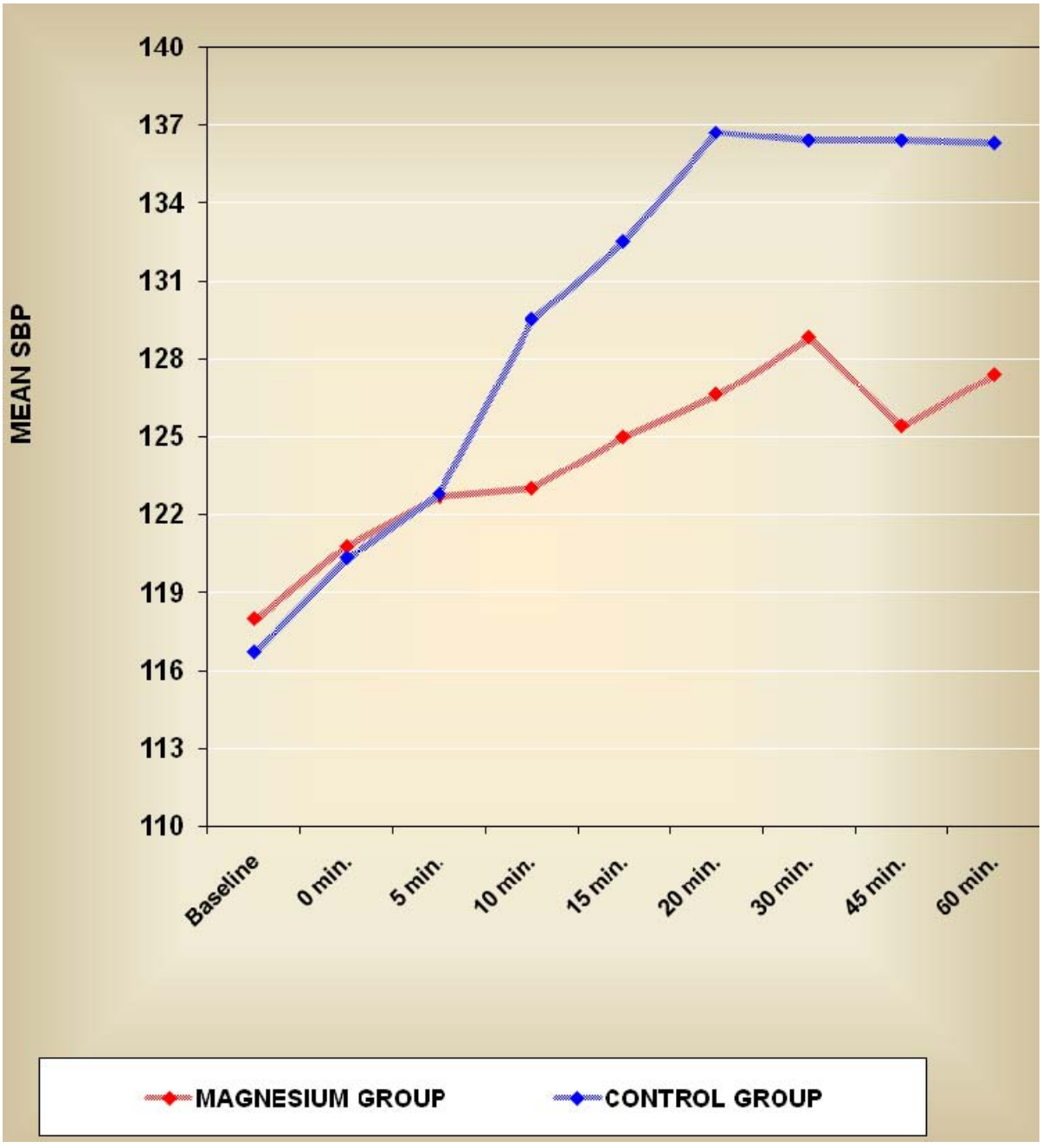


Figure 4b
Mean systolic BP

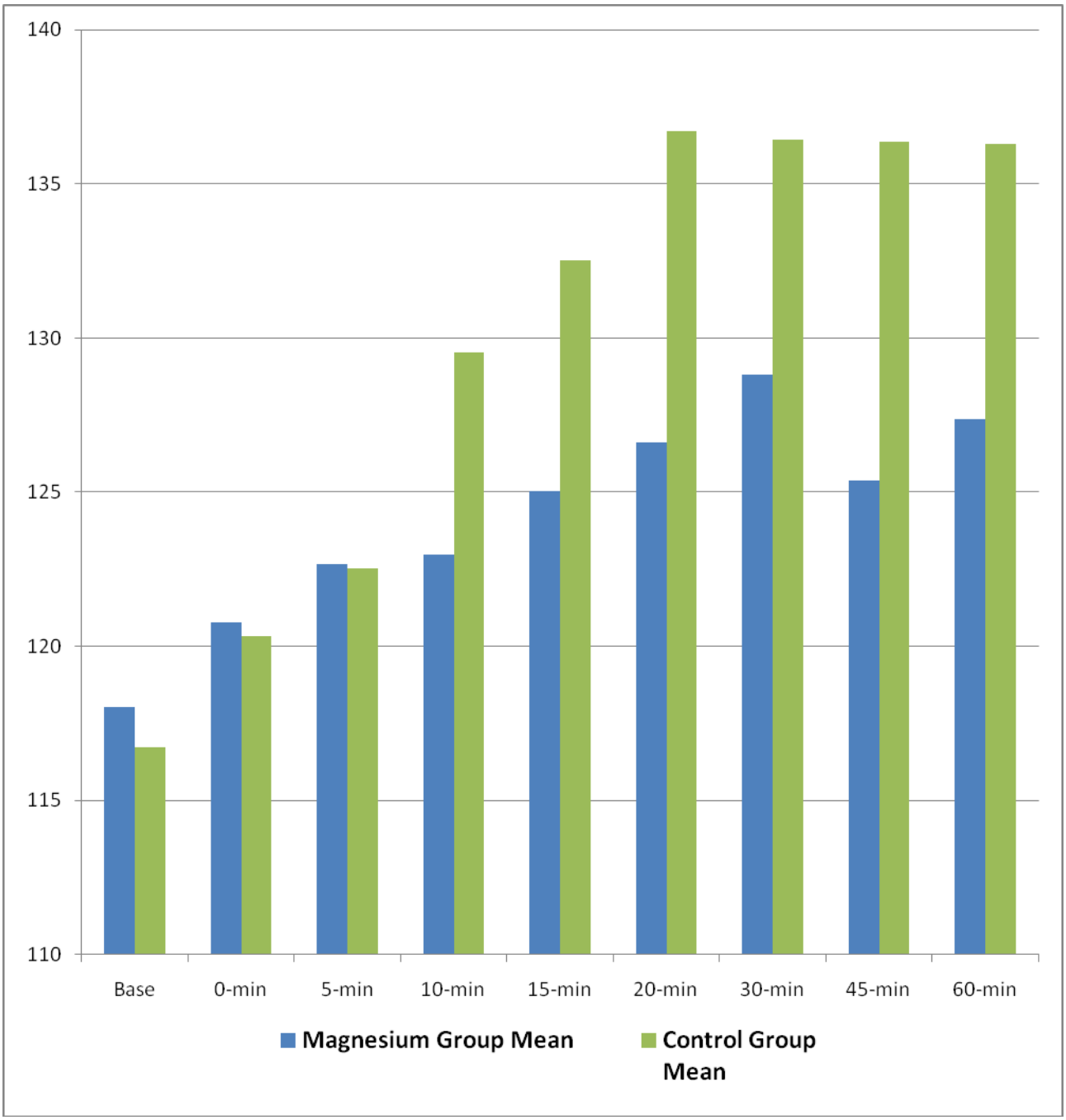


Table 5:

Intra operative Changes in Systolic B.P from baseline

SBP at	Systolic BP in				'p'	Significance
	Magnesium Group		Control group			
	Mean	SD	Mean	SD		
Baseline	118.0	8.9	116.7	7.7	0.6451	Not significant
Maximum reached during Intra operative period	134.1	8.6	143.1	9.9	**0.0009**	**Significant**
Changes during Intra operative period	16.1	8.9	26.4	10.5	**0.0003**	**Significant**
Percentage of Changes during Intra operative period	14.0	8.3	22.9	9.6	**0.0007**	**Significant**

Table 5 shows that the changes in the systolic BP in the magnesium group was 14 % from the baseline and in the control group it was upto 22.9% from the baseline which is statistically significant.

Figure 5

Intraoperative changes in systolic BP from baseline

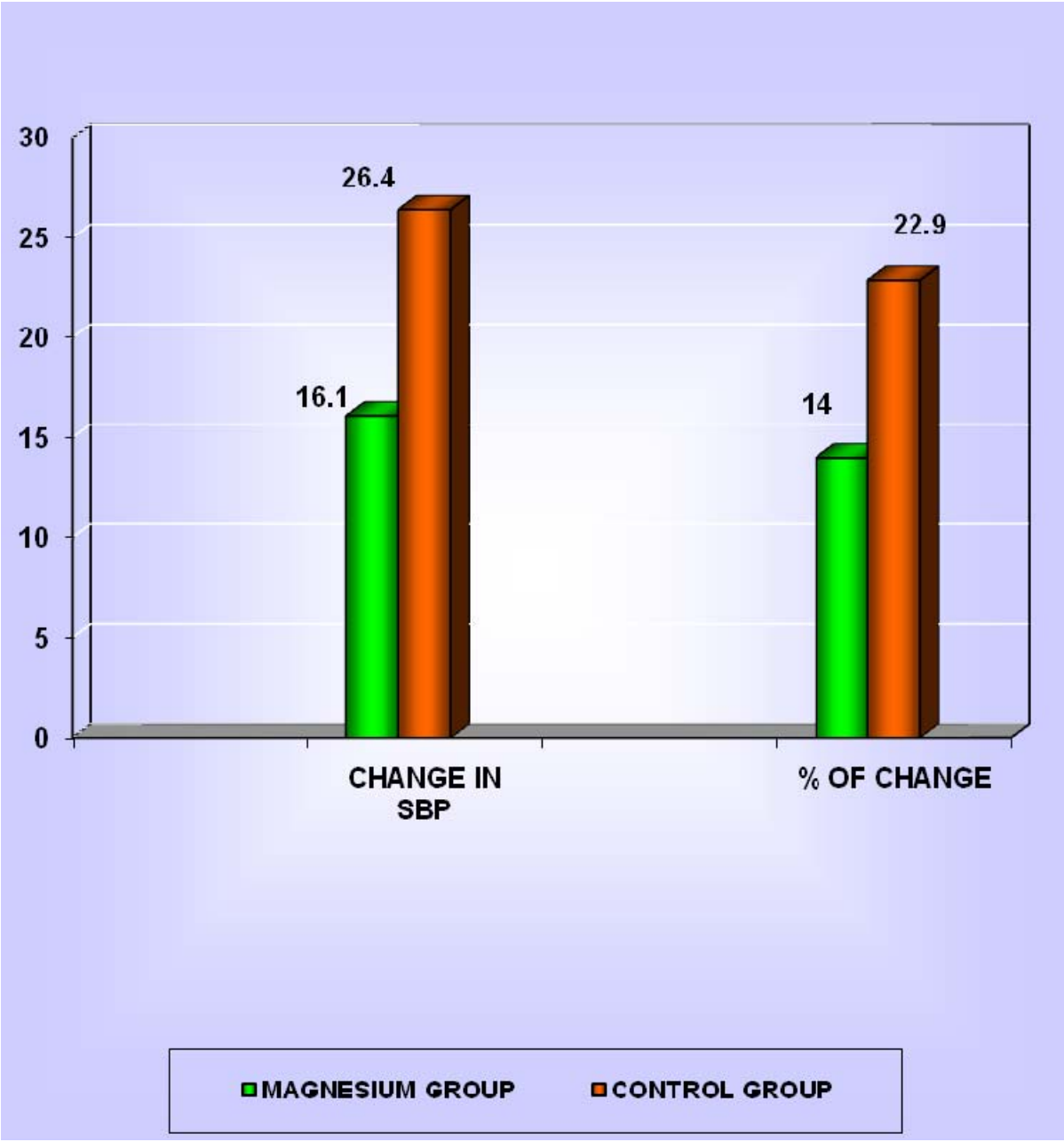


Table 6:

Changes in diastolic blood pressure

DBP at	Diastolic BP in				'p'	SD
	Magnesium Group		Control group			
	Mean	SD	Mean	SD		
Baseline	77.2	6.9	76.4	6.2	0.8779	Not significant
0 minute	76.4	10.9	79.6	4.8	**0.0026**	**Significant**
5 minutes	79.7	8.5	81.2	6.9	**0.0465**	**Significant**
10 minutes	81.3	6.8	85.1	5.2	**0.0304**	**Significant**
15 minutes	81.4	7.2	84.8	7.4	**0.0412**	**Significant**
20 minutes	80.6	9.7	85.7	8.5	**0.0065**	**Significant**
30 minutes	82.5	9.1	86.0	9.0	**0.0274**	**Significant**
45 minutes	79.7	7.6	85.3	8.3	**0.016**	**Significant**
60 minutes	78.4	6.9	84.1	8.4	**0.0087**	**Significant**

Table 6 shows that there was a significant difference in the diastolic BP between the magnesium group and the control group from the beginning of pneumoperitoneum.

Figure 6a
Changes in diastolic BP

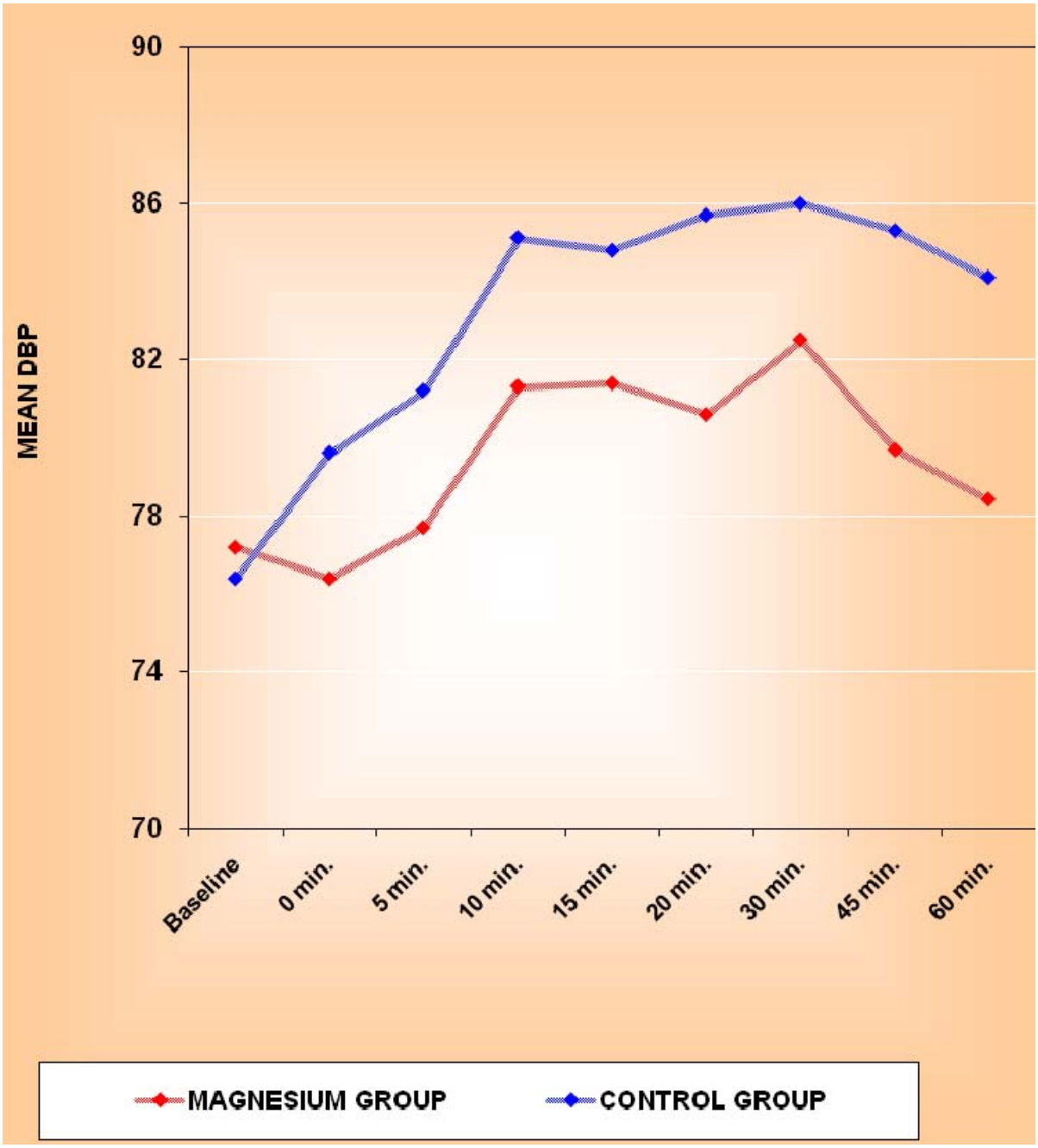


Figure 6b

Changes in diastolic BP

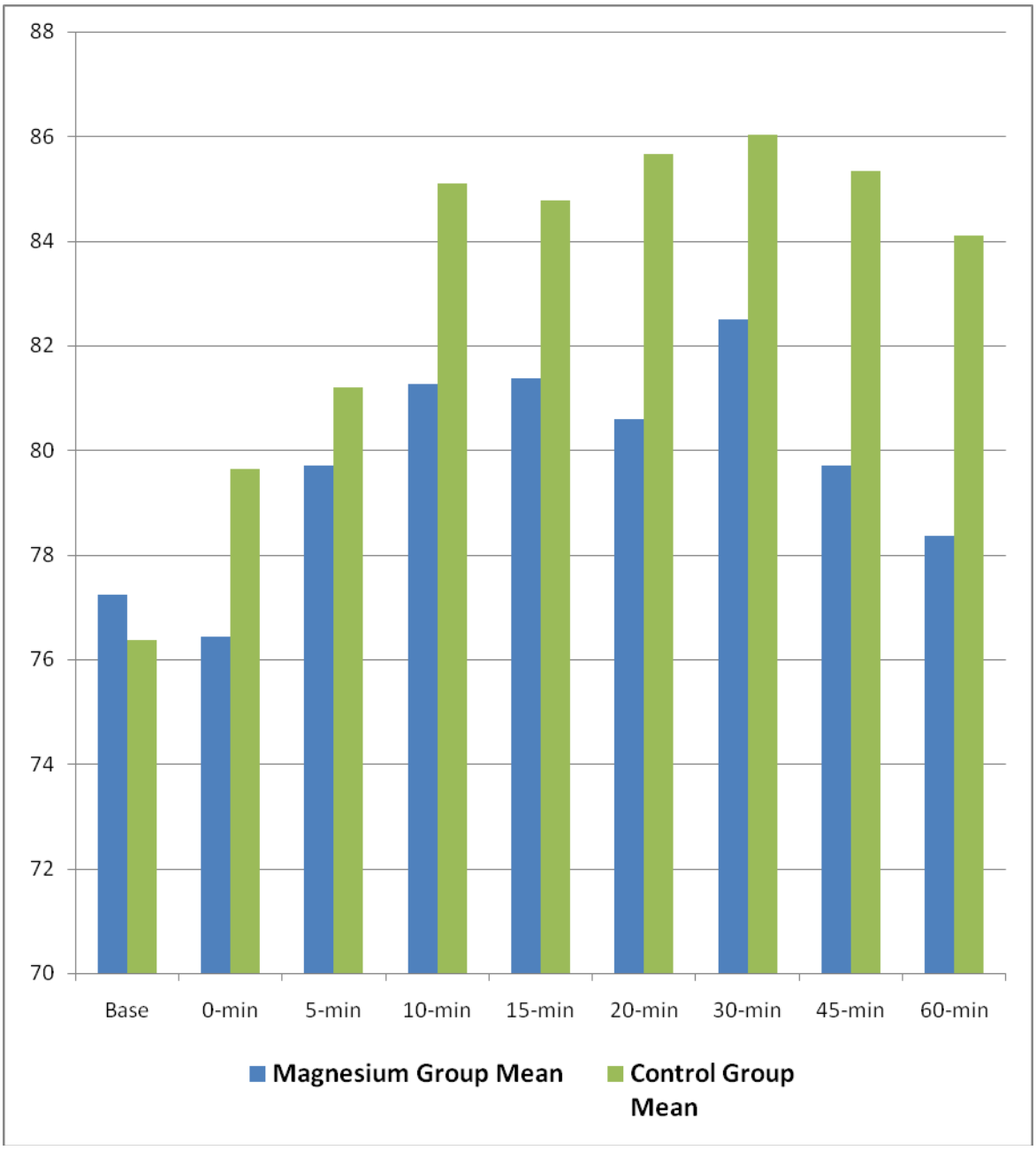


Table 7:

Intra operative Changes in Diastolic B.P from baseline

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DBP at	Diastolic BP in				'p'	Significance
	Magnesium Group		Control group			
	Mean	SD	Mean	SD		
Baseline	77.2	6.9	76.4	6.2	0.1779	Not significant
Maximum reached during Intra operative period	89.5	7.5	90.6	6.1	0.1649	Not significant
Changes during Intra operative period	12.3	6.1	14.2	5.5	0.2366	Not significant
Percentage of Changes during Intra operative period	16.3	8.6	19.0	8.0	0.3702	Not significant

Table 7 shows that the change in diastolic BP in the magnesium group was 16% from baseline and in the control group was 19% from baseline.

Figure 7

Intraoperative changes in diastolic BP from baseline

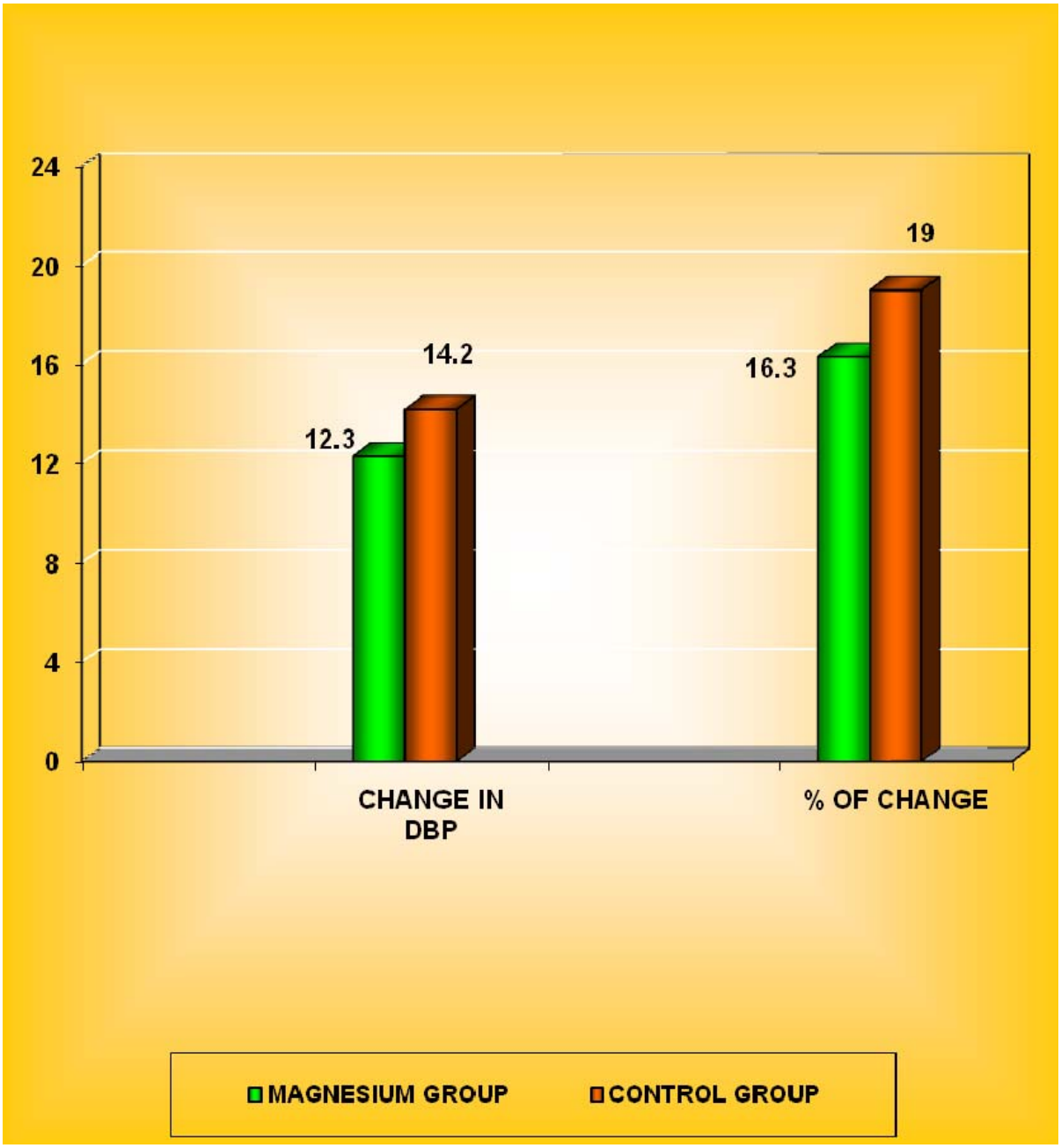


Table 8:

Changes in heart rate

Heart rate at	Heart rate at				'p'	SD
	Mag. Group		Control group			
	Mean	SD	Mean	SD		
Baseline	86.7	14.2	83.1	9.5	0.3338	Not significant
0 minute	88.0	14.0	85.3	7.3	0.3654	Not significant
5 minutes	86.3	11.0	89.1	7.2	0.2101	Not significant
10 minutes	86.6	11.5	94	6.3	**0.0217**	**Significant**
15 minutes	88.1	12.7	94.5	7.8	**0.0487**	**Significant**
20 minutes	88.0	11.7	93.7	11.5	**0.0415**	**Significant**
30 minutes	87.0	11.0	94	11.5	**0.0204**	**Significant**
45 minutes	88.7	10.6	95.8	10.5	**0.0461**	**Significant**
60 minutes	88.0	11.1	96	8.6	**0.0163**	**Significant**

Table 8 shows that there was a significant difference in the heart rate between both groups from 10 minutes after pneumoperitoneum

Figure 8a

Changes in heart rate

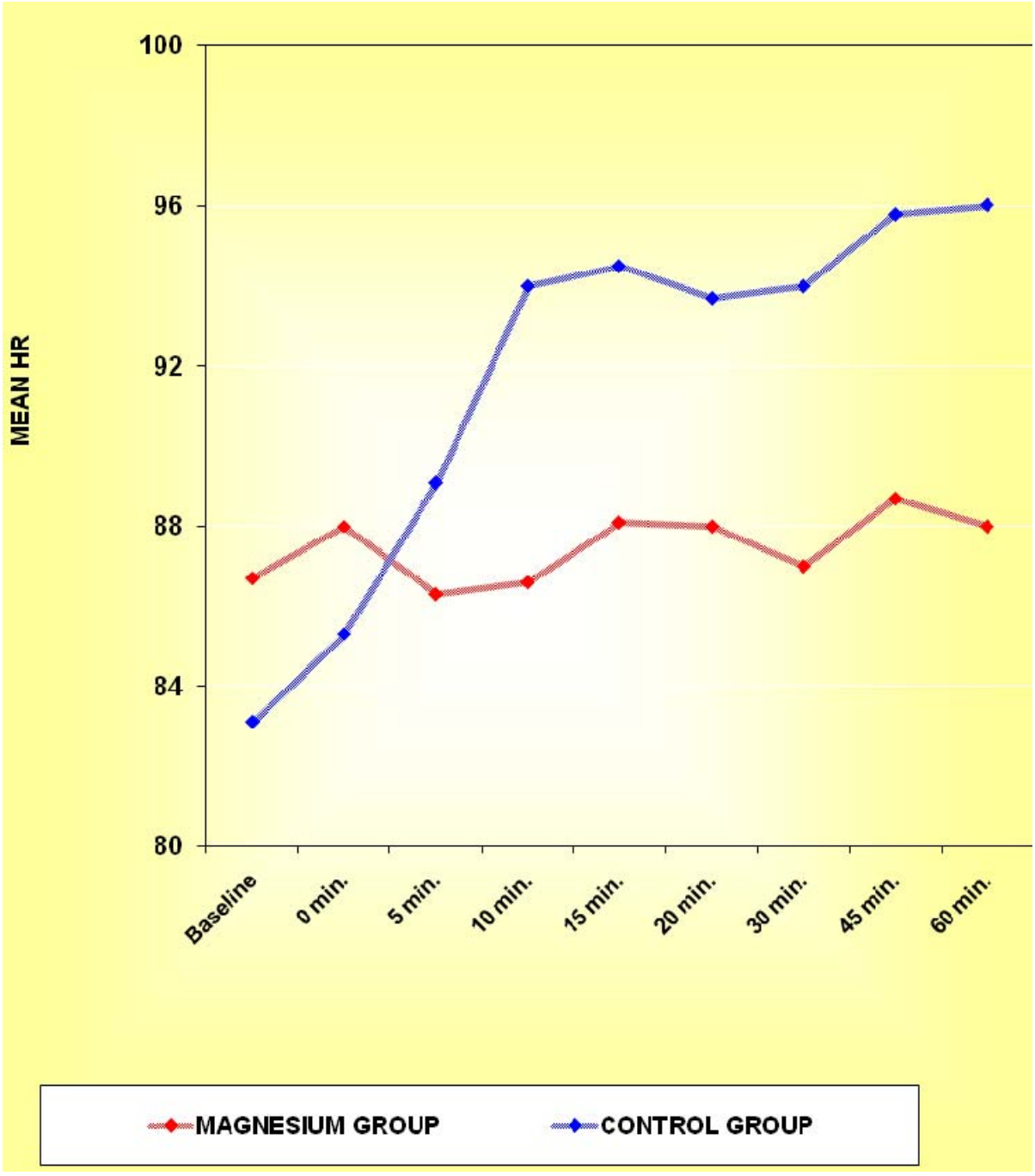


Figure 8b

Changes in heart rate

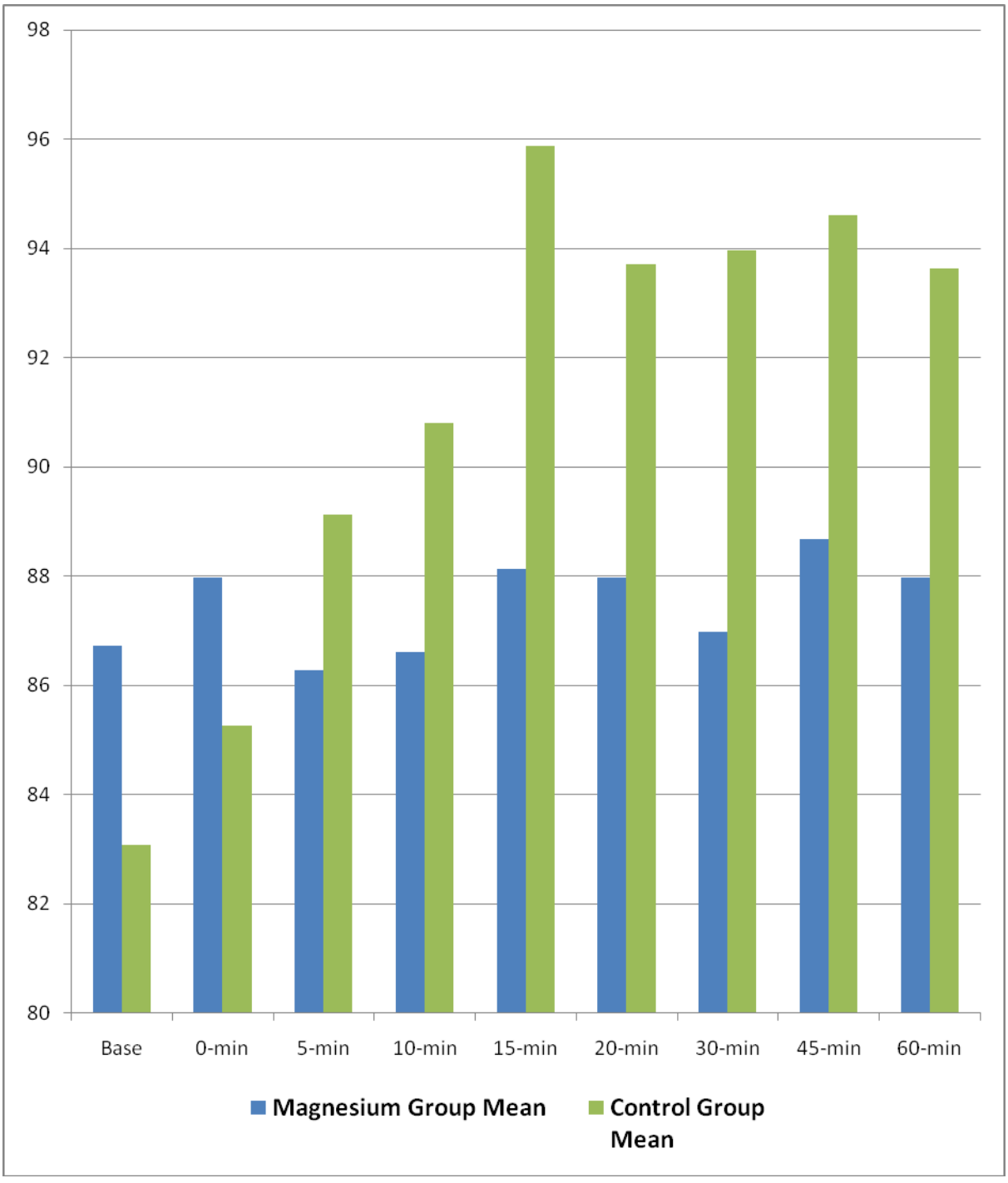


Table 9:

Intra operative Changes in Heart Rate from baseline

Heart Rate at	Heart Rate in				'p'	Significance
	Magnesium Group		Control group			
	Mean	SD	Mean	SD		
Baseline	86.7	14.2	83.1	9.3	0.3338	Not significant
Maximum reached during Intra operative period	95.2	12.9	100.5	8.3	0.239	Not significant
Changes during Intra operative period	8.5	9.1	17.4	7.2	**0.0001**	**Significant**
Percentage of Changes during Intra operative period	10.8	12.5	21.8	10.4	**0.0001**	**Significant**

Table 9 shows that the maximum change in heart rate in the magnesium group was 10.8% from the baseline and in the control group was 21.8% from the baseline which is statistically significant.

Figure 9

Intraoperative changes in heart rate from baseline

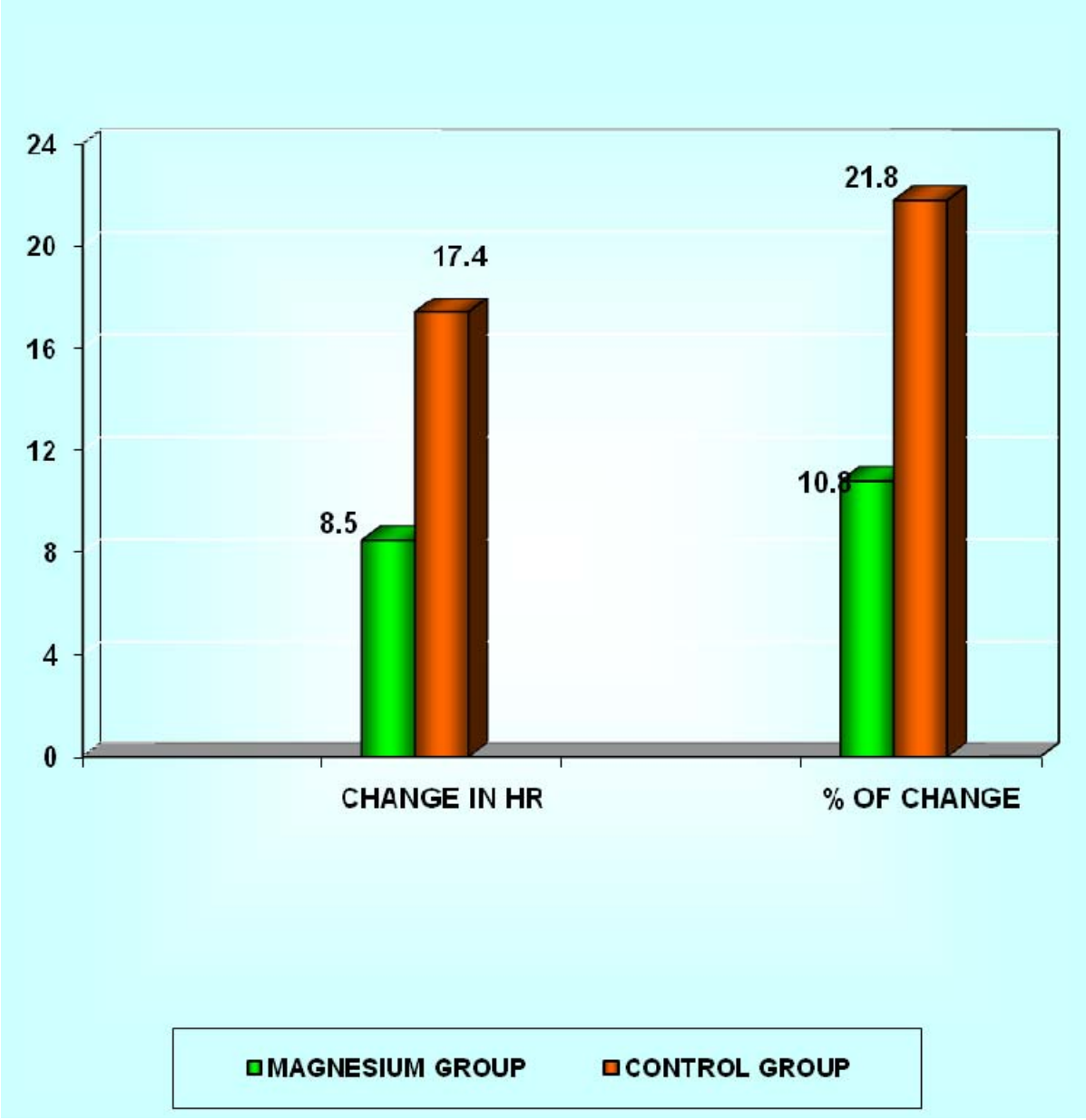


Table 10

Intraoperative fentanyl requirements

FENTANYL REQUIREMENT in mcg		
	Magnesium group	**Control group**
Range	80 - 160	80 - 140
Mean	109.7	116.7
S.D	18.8	14.7
P	0.1461 – Not significant	

Table 10 shows that there is no significant difference in the inraoperative fentanyl requirement between both groups

Figure 10

Intraoperative fentanyl requirements

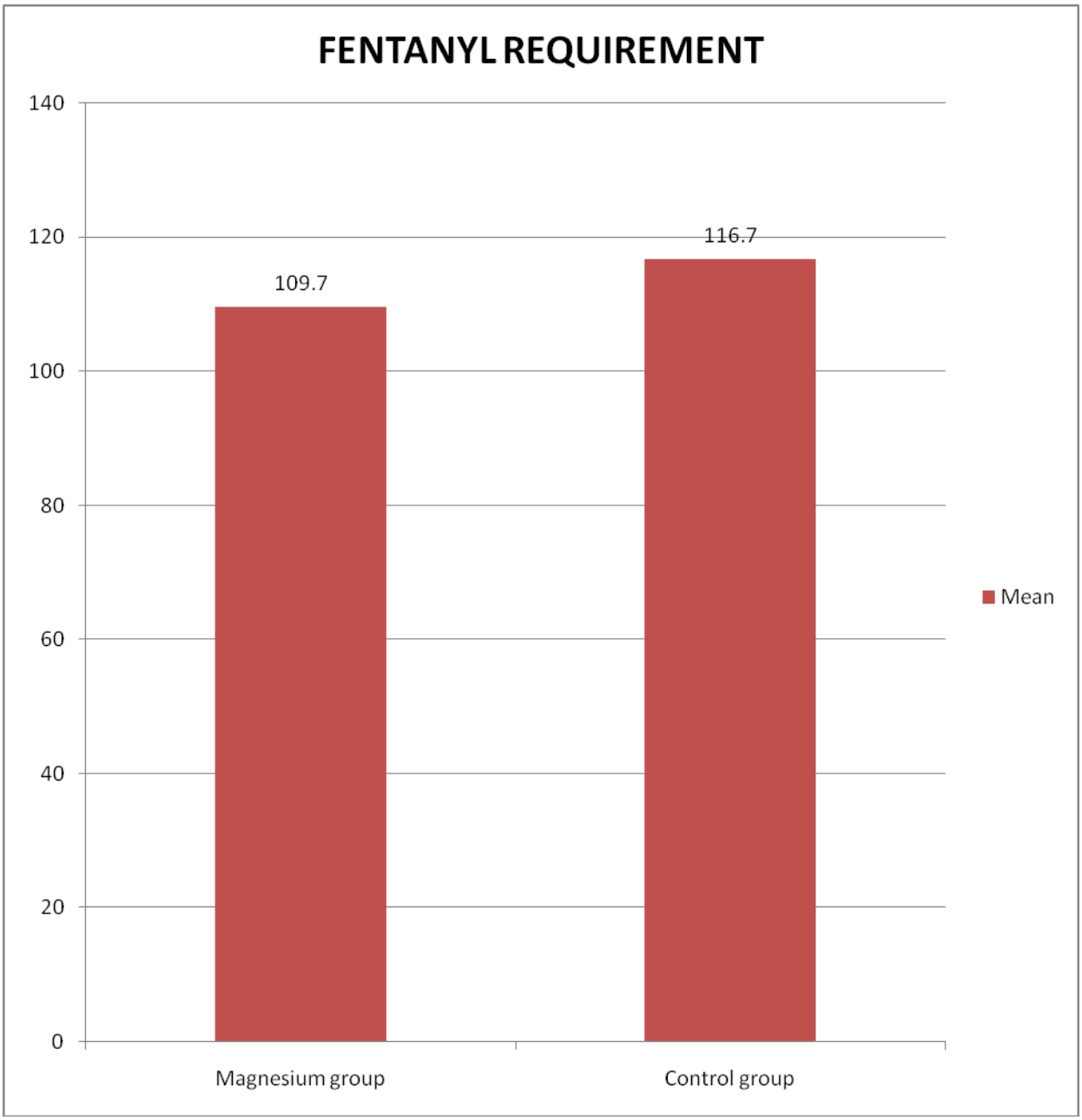


Table 11:

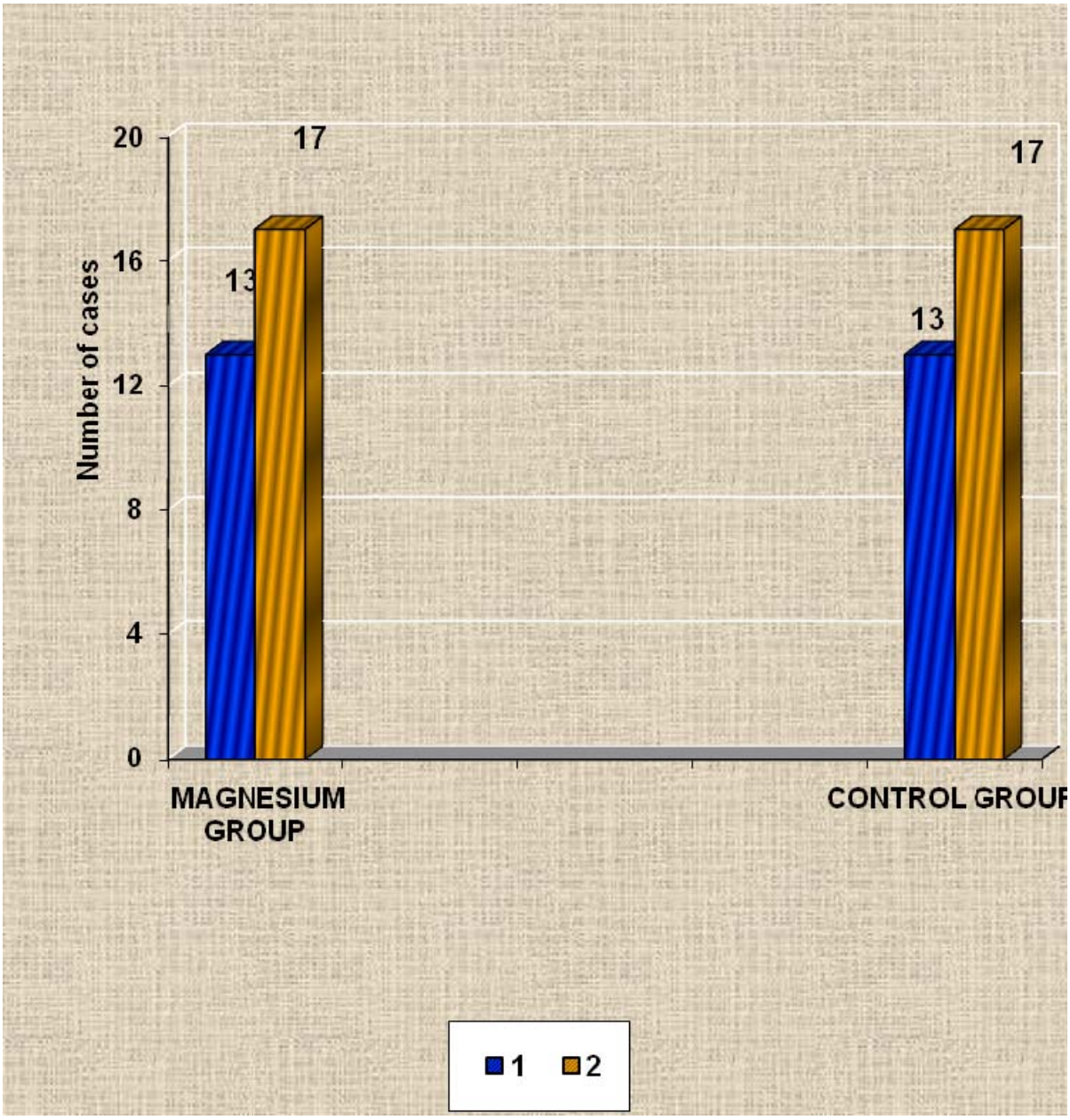
Sedation score

Sedation score	Magnesium group		Control group	
	No	%	No	%
1	13	43.3	13	43.3
2	17	56.7	17	56.7
Range	1 - 6		1 - 6	
'p'	1.0 Not significant			

Table 11 shows that there is no significant difference in the postoperative sedation between both groups

Figure 11

Sedation score



DISCUSSION

Pneumoperitoneum during carbondioxide insufflation is known to cause significant hemodynamic changes. It is due to rapid and immediate increase of plasma catecholamines, probably due to stretching of the peritoneum, increased intraperitoneal pressure and the stimulation of the peritoneum by carbondioxide. Many studies have been done to prove the catecholamine response as the cause for these hemodynamic changes. Various pharmacological agents and various techniques have been used to counteract these detrimental effects.

Several studies have been done with focus on the hemodynamic changes during laparoscopic surgeries. This randomised double blinded prospective study was conducted in 60 patients to evaluate the effects of magnesium sulphate in attenuation of the hemodynamic changes.

Though magnesium has been used for a number of conditions including eclampsia, asthma, seizures, arrhythmias and preterm labour its use in laparoscopic surgeries have not been studied. It has been used effectively for stress attenuation during laryngoscopy and intubation, for reducing the intraoperative anaesthetic requirements and has also been used for suppression of the cardiovascular responses during pheochromocytoma surgery.

Magnesium has been shown to inhibit the release of catecholamines both in vivo and in vitro and also act as a vasodilator by reducing the tone of the

vascular smooth muscles. So this study was conducted with the aim of using this property of magnesium in the very commonly done laparoscopic surgeries, to prove that it could be a cheap and effective alternative to maintain stable intraoperative hemodynamics.

Various doses of magnesium sulphate have been used for suppression of cardiovascular response to intubation. A dose of 10, 20, 30, 40, 50 and 60 mg/kg have all been used successfully during laryngoscopy and intubation. A bolus dose of 50 mg/kg of intravenous magnesium sulphate has been shown to effectively blunt the catecholamine response in various standard journals and publications. It is proven to produce a plasma magnesium concentration of 2 – 4 mmol/L, which is required to produce these effects.

There was no significant difference between the two groups in terms of age distribution, sex distribution and the duration of surgery. The mean age was 30.86 ± 11.32 years in the magnesium group and 31.06 ± 11.72 years in the control group. The ratio of number of male patients to the number of female patients was also comparable between both groups. The average duration of surgery was also not significant between both groups.

There was a significant difference between the systolic blood pressure between the magnesium group and the control group. But this difference occurred only 10 minutes post pneumoperitoneum. The systolic blood pressure was ranged

between 118.03 ± 8.85 to 127.37 ± 10.15 in the magnesium group and 116.73 ± 7.67 to 136.3 ± 11.53 in the control group.

There was also a significant difference between the diastolic blood pressures in both groups. The range of diastolic blood pressure was between 77.23 ± 6.88 and 78.37 ± 6.92 in the magnesium group and 76.37 ± 6.22 and 84.1 ± 8.39 in the control group.

There was a significant difference in heart rate between both groups from 10 minutes after pneumoperitoneum. The range of heart rate was between 86.7 to 88 per minute in the magnesium group and 83.1 to 96 per minute in the control group.

Throughout the intraoperative period the TOF response was monitored using a neuromuscular monitor and no prolongation of the blockade was found in the magnesium group. There was also no significant difference in the postoperative sedation between both groups. All patients were awake, alert and conscious at the end of surgery.

No significant adverse effects were observed in the study group throughout the intraoperative and postoperative period. At the end of surgery serum magnesium levels were done in the magnesium group. The levels were found to be normal within 2±0.2 mEq/L.

There were some limitations in the study. First, if plasma epinephrine, norepinephrine and vasopressin levels were monitored during the study it would have been a better evidence for the catecholamine and vasopressin suppression effect of magnesium sulphate. Second, the use of BIS monitor would have ensured that both groups had similar depth of anaesthesia.

SUMMARY

60 patients coming to Government Rajaji Hospital for elective laparoscopic surgeries were included in this study. The patients were randomly divided into two groups to receive intravenous magnesium sulphate 50 mg/kg in 0.5 ml/kg of normal saline or 0.5 ml/kg normal saline only as a placebo, after induction and intubation. All patients were induced with thiopentone sodium 3-5 mg/kg, succinyl choline 1.5 mg/kg and fentanyl 2 mcg/kg and the drug was given 1 minute before pneumoperitoneum. Anaesthesia was maintained with nitrous oxide, oxygen and sevoflurane. The monitors used were pulseoximeter, capnogram, ECG and NIBP. Neuromuscular monitoring was done using train of four to watch for any prolongation of neuromuscular blockade.

The systolic blood pressure, diastolic blood pressure and heart rate were monitored throughout the surgery. Intraoperative fentanyl requirements were also noted in both groups. The sedation scores, any signs of hypermagnesemia and serum magnesium levels were monitored in the postoperative period.

Hemodynamic stability is defined as heart rate between 60 and 100 and blood pressure fall or rise not more than 15% from the baseline.

Magnesium sulphate group was found to have a better hemodynamic stability than the control group. There was no significant adverse effect observed.

CONCLUSION

Hemodynamic changes during laparoscopic surgeries is a very commonly observed event. Various pharmacological agents have been used for stress attenuation during laparoscopy. Magnesium sulphate, though used to control stress response during intubation, is not a commonly used agent during laparoscopy. I decided to study the effect of magnesium sulphate in maintaining stable intraoperative hemodynamics during laparoscopic surgeries.

In all patients, premedication and induction was done using standardised drugs. Magnesium sulphate 50 mg/kg was given 1 minute before the creation of pneumoperitoneum, as a slow intravenous infusion. The control group was given an infusion of normal saline. The hemodynamic parameters that were monitored intraoperatively include the systolic blood pressure, diastolic blood pressure and heart rate.

The observations show that magnesium sulphate produces better intraoperative hemodynamics during laparoscopic surgeries.

I conclude that magnesium sulphate is an effective and cheap alternative to maintain good hemodynamic stability during laparoscopic surgeries.

ANNEXURES

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List of Abbreviations Used

ASA American societies of Anesthesiologists

CBF Cerebral blood flow

CNS Central nervous system

CSF Cerebrospinal fluid

GI Gastrointestinal

CVS Cardiovascular system

ICP Intra cranial pressure

IM Intramuscular

IV Intravenous

PONV Post operative nausea vomiting

SVR Systemic vascular resistance

IAP intra abdominal pressure

H1& H2 Histamine receptors 1 and 2

$5HT_3$ 5 Hydroxy Tryptamine

$EtCO_2$ End tidal carbon dioxide

TOF Train of four

ECG Electrocardiogram

NIBP Non invasive blood pressure

Proforma

MAGNESIUM SULPHATE ATTENUATES ARTERIAL PRESSURE INCREASE DURING LAPAROSCOPIC SURGERY

NAME: AGE: SEX: I.P. NO: WARD NO:

HT: WT: ASA:

DIAGNOSIS: PROCEDURE:

GROUP: M (magnesium sulphate) / C (control)

PRE MEDICATION:
INDUCTION AGENT:
INTUBATION:
MAINTAINANCE:
TOTAL FENTANYL GIVEN:
I.V. FLUIDS:

GROUP M:
Magnesium sulphate 50 mg/kg in 0.5 ml/kg normal saline given I.V over 2-3 min. immediately before pneumoperitoneum .
GROUP C:
0.5 ml/kg normal saline over 2-3 min.

	BASELINE	0 min	5 min	10 min	15 min	20 min	30 min	45 min	60 min
SpO2									
HR									
SBP									
DBP									
MAP									

OTHER OBSERVATIONS:
Presence of lacrimation, sweating, eye movement
Somatic responses-swallowing, grimacing, coughing, eye opening

INCIDENCE OF BRADYCARDIA OR HYPOTENSION:
Treatment given:

OTHER SIGNIFICANT EVENTS:

REVERSAL AND EXTUBATION:

POST OP:

SERUM MAGNESIUM LEVEL:

EXCLUSION CRITERIA:

-hypermagnesemia
-allergy to magnesium sulphate
-heart block
-diabetes mellitus
-hypertension
-Cardiovascular or kidney disease
-endocrine or metabolic disease
-Need for antihypertensives during surgery
-duration of surgery less than 30 min.

Magnesium Group

					baseline			0 MIN			5 MIN			10 MIN			15 MIN			20 MIN			30 MIN			45 MIN			60 MIN			
Patient	Age	Sex	Surgery	Duration of Surgery in Minuts	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	Sedation_ Score
1	18	Female	Lap_App	65	110	70	96	108	68	98	113	76	88	110	74	90	128	80	84	128	81	87	138	89	86	120	77	93	118	77	85	1
2	24	Female	Lap_App	70	120	80	90	130	80	102	120	78	95	123	78	87	140	83	90	146	89	85	143	86	83	150	90	90	150	90	90	2
3	50	Male	Lap_Chole	119	140	90	120	150	110	110	148	91	110	150	90	105	140	90	110	150	110	108	148	100	106	146	90	104	146	90	104	2
4	33	Female	Lap_App	77	120	71	74	120	72	74	130	70	77	110	70	70	130	80	72	130	70	70	140	90	74	130	90	76	130	80	78	2
5	18	Male	Lap_App	80	120	90	96	119	86	90	121	99	86	119	88	88	125	90	92	120	80	90	120	80	90	120	80	90	120	80	90	1
6	19	Male	Lap_App	93	114	78	68	112	78	70	110	76	72	112	78	72	114	78	72	126	82	79	138	88	72	140	92	74	140	90	70	1
7	18	Female	Lap_Chole	100	110	80	88	130	70	92	110	70	86	100	70	88	110	70	90	120	80	88	110	70	84	108	80	86	120	70	84	1
8	50	Female	Lap_App	62	124	76	96	105	66	113	102	64	86	122	89	91	128	85	91	124	86	96	127	79	97	118	76	96	120	78	98	1
9	22	Male	Lap_App	65	120	70	68	128	70	66	130	80	70	120	80	64	100	70	62	110	70	64	110	60	66	100	70	64	120	70	64	2
10	44	Female	Lap_App	72	130	80	78	140	80	80	130	80	90	140	90	94	110	70	100	120	70	90	110	80	90	120	70	96	120	70	90	2
11	52	Male	Lap_App	80	106	66	68	116	74	86	128	78	92	134	80	96	136	78	94	134	76	98	134	78	98	136	76	96	130	74	96	1
12	30	Female	Lap_App	88	120	80	80	123	64	80	127	88	80	131	90	82	131	92	84	112	73	81	127	84	81	123	74	80	125	70	80	2
13	42	Male	Lap_App	90	110	70	97	99	70	72	128	83	70	130	80	75	136	90	79	130	80	82	136	90	82	130	70	90	130	80	94	1
14	26	Female	Lap_Chole	114	108	78	95	110	78	97	118	82	100	117	81	98	120	82	102	124	81	104	126	84	100	120	80	98	122	78	102	2
15	27	Male	Lap_Chole	103	120	80	85	122	80	90	124	82	92	126	81	98	129	83	99	127	82	98	124	80	96	120	80	97	121	79	97	2
16	23	Male	Lap_App	82	110	70	98	109	68	99	113	76	88	112	74	90	128	80	84	126	81	88	138	89	85	120	77	93	119	77	85	2
17	20	Male	Lap_App	68	120	80	90	130	79	102	120	78	93	123	78	87	140	82	90	146	87	85	144	86	83	149	90	90	150	89	90	1
18	22	Female	Lap_Chole	102	140	90	120	150	110	108	148	91	110	149	90	105	139	90	110	149	110	108	148	99	106	146	91	104	146	90	102	1
19	23	Female	Lap_App	87	120	71	74	120	72	74	130	70	77	110	70	71	130	80	72	130	70	70	140	89	74	130	90	75	130	80	78	1
20	32	Male	Lap_App	90	120	90	95	119	86	90	121	99	85	119	88	89	126	90	92	120	80	90	120	80	89	120	80	90	120	80	90	2
21	29	Female	Lap_Chole	95	114	78	68	110	78	70	112	76	72	112	78	72	114	78	72	126	82	79	138	88	73	140	92	75	140	89	70	1
22	54	Male	Lap_App	79	110	80	88	130	72	92	110	70	86	102	70	88	110	71	90	120	80	86	111	70	84	106	80	86	118	70	84	2
23	18	Female	Lap_App	66	124	76	96	107	66	113	102	64	89	122	89	91	127	85	91	124	86	96	127	79	97	118	76	96	120	78	97	2
24	28	Male	Lap_App	91	119	70	68	128	70	66	129	80	72	120	80	64	100	70	62	110	70	64	110	60	66	102	70	64	120	70	64	1
25	41	Female	Lap_Chole	117	130	80	78	138	80	80	131	80	89	140	90	94	110	70	102	120	70	90	110	79	90	120	70	96	119	70	90	2
26	39	Male	Lap_App	69	106	66	68	116	74	87	128	78	92	134	80	96	135	78	94	134	76	99	134	78	98	136	77	96	130	74	96	2
27	20	Female	Lap_App	89	120	79	80	123	64	80	127	87	80	130	90	82	131	92	84	112	73	81	127	85	81	123	74	80	124	70	80	2
28	28	Female	Lap_App	62	110	70	97	99	70	73	128	83	69	130	80	75	136	89	79	130	80	82	136	90	82	130	70	90	130	80	93	2
29	40	Female	Lap_App	93	108	78	96	110	78	95	118	82	100	116	81	98	120	82	102	125	81	103	126	84	100	120	80	98	122	78	102	2
30	36	Male	Lap_App	87	118	80	87	122	80	90	124	80	92	126	81	98	128	83	99	126	82	98	124	81	96	120	79	97	121	80	96	1

Control Group

					baseline			0 MIN			5 MIN			10 MIN			15 MIN			20 MIN			30 MIN			45 MIN			60 MIN			
Patient	Age	Sex	Surgery	Duration of Surgery in Minuts	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	Sedation_ Score
1	18	Male	Lap_App	68	130	80	88	110	70	88	110	70	90	160	90	95	158	92	92	162	100	102	165	101	104	158	94	100	154	90	93	1
2	24	Female	Lap_App	70	120	90	96	119	86	90	121	99	86	119	88	94	125	90	92	128	93	90	125	89	95	127	90	94	125	87	92	2
3	50	Female	Lap_Chole	120	120	70	68	128	70	66	130	80	70	120	80	92	100	70	88	110	70	64	110	60	66	100	70	86	120	70	94	2
4	33	Female	Lap_App	77	130	80	78	140	80	80	130	80	90	140	90	94	110	70	100	130	70	90	120	80	90	120	70	96	120	70	90	2
5	18	Male	Lap_App	78	106	66	68	116	74	86	128	78	92	134	80	96	136	78	94	134	76	98	134	78	98	136	76	96	130	74	96	1
6	19	Male	Lap_App	93	110	70	76	120	80	78	124	87	90	130	91	86	150	90	86	148	92	84	138	90	80	129	78	77	128	80	78	2
7	18	Female	Lap_App	95	110	70	82	120	80	86	118	69	90	123	79	87	138	83	95	140	87	92	138	89	90	143	92	94	140	90	90	1
8	56	Male	Lap_App	62	120	80	78	123	80	80	118	78	87	126	83	90	130	84	93	137	89	92	137	84	92	140	87	90	147	89	97	1
9	22	Male	Lap_App	65	107	78	76	100	78	83	110	80	84	125	80	89	127	83	87	137	83	86	135	83	82	136	87	87	134	84	89	2
10	44	Male	Lap_App	78	120	80	84	124	82	85	119	80	83	118	79	85	128	83	87	130	80	85	138	93	92	130	84	86	130	80	87	2
11	52	Female	Lap_App	82	110	70	78	120	80	86	124	83	89	135	90	92	134	89	95	138	90	96	140	90	94	147	89	96	138	87	98	1
12	30	Female	Lap_App	88	118	80	96	126	87	90	130	89	96	135	89	97	137	90	95	137	92	103	140	90	110	143	93	108	145	92	112	2
13	42	Male	Lap_App	90	124	80	98	126	83	97	129	80	102	130	90	110	138	93	112	140	90	108	145	92	108	144	90	109	141	89	107	1
14	26	Male	Lap_Chole	117	120	80	93	123	82	94	129	82	98	130	90	103	142	94	110	145	92	110	142	92	108	158	98	118	161	100	111	2
15	27	Male	Lap_App	99	108	70	85	110	80	87	117	81	89	120	80	97	138	83	90	137	80	98	137	82	101	136	79	102	132	78	98	2
16	23	Male	Lap_App	82	128	80	88	110	70	90	110	70	90	160	90	92	156	92	92	162	100	105	165	101	104	159	94	101	153	90	95	2
17	20	Female	Lap_App	70	120	89	96	119	86	91	121	99	86	117	88	88	123	90	92	128	93	90	124	89	95	126	90	96	125	87	92	1
18	22	Female	Lap_App	93	120	74	68	128	70	66	130	78	70	120	80	91	100	70	84	108	70	64	110	60	68	100	70	78	120	72	88	2
19	23	Male	Lap_App	87	130	80	78	138	80	80	132	80	92	140	90	94	108	70	102	130	72	90	120	80	90	120	70	96	120	70	90	1
20	32	Male	Lap_App	90	106	66	68	116	76	86	128	82	92	134	80	96	134	78	94	134	76	98	134	79	98	136	78	96	130	74	96	2
21	29	Female	Lap_Chole	100	110	70	80	120	80	78	124	87	90	130	91	99	150	90	86	148	92	84	138	90	80	129	78	79	128	80	94	1
22	54	Male	Lap_App	79	110	70	82	120	81	86	118	72	90	123	77	87	138	83	97	140	87	94	138	89	90	143	92	94	140	92	90	1
23	18	Female	Lap_App	62	120	80	78	123	80	80	118	78	87	126	82	90	130	84	95	137	89	92	139	84	90	140	87	90	147	89	97	2
24	28	Male	Lap_App	91	107	78	76	102	78	83	110	80	84	125	80	89	127	83	87	137	83	86	135	83	82	136	87	87	134	84	89	1
25	41	Male	Lap_Chole	117	120	80	84	126	82	87	119	80	83	118	77	96	128	83	87	130	80	85	138	90	92	130	86	86	132	80	87	2
26	39	Male	Lap_App	78	110	70	78	120	80	86	124	83	89	135	90	92	134	89	95	138	90	96	142	90	94	145	89	96	138	85	98	2
27	20	Female	Lap_App	89	118	80	96	126	87	90	130	89	96	135	89	97	137	89	95	137	92	103	140	89	110	143	93	108	145	92	113	2
28	28	Female	Lap_App	62	124	80	98	126	85	97	129	79	102	130	90	110	138	93	112	140	90	108	147	92	108	143	90	108	140	89	107	1
29	40	Male	Lap_App	96	118	80	93	123	82	95	129	82	98	128	90	103	144	94	110	145	92	110	142	90	108	158	97	118	160	101	112	2
30	36	Female	Lap_App	85	108	70	85	108	80	87	117	81	89	120	80	89	138	83	90	134	80	108	137	82	100	136	82	102	132	78	99	1

Ref. No. 5336 /E4/3/2012

Govt. Rajaji Hospital,
Madurai.20. Dated: .08.2012

Institutional Review Board / Independent Ethics Committee.
Dr. N. Mohan, M.S., F.I.C.S., F.A.I.S.,
Dean, Madurai Medical College & 2521021 (Secy)
Govt Rajaji Hospital, Madurai 625020.
Convenor
grhethicssecy @gmail.com.

Sub: Establishment-Govt. Rajaji Hospital, aMadurai-20-
Ethics committee-Meeting Agenda-communicated-regarding.

The Ethics Committee meeting of the Govt. Rajaji Hospital, Madurai was held at 11.00 Am to 1.00Pm on 28.06.2012 at the Dean Chamber, Govt. Rajaji Hospital, Madurai. The following members of the committee have been attended the meeting.

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1. Dr.N.Vijayasankaran,M.ch(Uro.) 094-430-58793 0452-2584397	Sr.Consultant Urologist Madurai Kidney Centre, Sivagangai Road,Madurai	Chairman
2. Dr.P.K. Muthu Kumarasamy, M.D., 9843050911	Professor & H.O.D of Medical, Oncology(Retired)	Member Secretary
3. Dr.T.Meena,MD 094-437-74875	Professor of Physiology, Madurai Medical College	Member
4. Dr. S. Thamilarasi, M.D (Pharmacol)	Professor of pharmacology	
5.Dr.Moses K.Daniel MD(Gen.Medicine) 098-421-56066	Professor of Medicine Madurai Medical College	Member
6.Dr.M.Gobinath,MS(Gen.Surgery)	Professor of Surgery Madurai Medical College	Member
7.Dr.S. Dilshadh, MD(O&G) 9894053516	Professor of OP&Gyn Madurai Medical College	Member
8.Dr.S.Vadivel Murugan., M.D, 097-871-50040	Professor of Medicine Madurai Medical College	Member
9.Shri.M.Sridher,B.sc.B.L. 099-949-07400	Advocate, 2, Deputy collectors colony 4th street KK Nagar, Madurai-20.	Member
10.Shri.O.B.D.Bharat,B.sc., 094-437-14162	Businessman Plot No.588, K.K.Nagar,Madurai.20.	Member
11.Shri. S.sivakumar,M.A(Social) Mphil 093-444-84990	Sociologist, Plot No.51 F.F, K.K Nagar, Madurai.	Member

Following Projects were approved by the committee

Sl. No	Name of P.G.	Course	Name of the Project	Remarks
1.	Dr. Dharani. S	M.D Anaesth	Magnesium sulphate for attenuation of pneumoperitoneum associated hemodynamic, changes during laparoscopy.	Approved

Please note that the investigator should adhere the following: She/He should get a detailed informed consent from the patients/participants and maintain Confidentially.

1. She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution to Government.
2. She/He should inform the institution Ethical Committee in case of any change of study procedure site and investigation or guide.
3. She/He should not deviate for the area of the work for which applied for Ethical clearance.
She/He should inform the IEC immediately, in case of any adverse events pr Serious adverse reactions.
4. She/he should abide to the rules and regulations of the institution.
5. She/He should complete the work within the specific period and apply for if any
Extension of time is required She should apply for permission again and do the work.
6. She/He should submit the summary of the work to the Ethical Committee on Completion of the work.
7. She/He should not claim any funds from the institution while doing the word or on completion.
8.She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

17.8.12

DEAN I/c.

To
All the above members and Head of the Departments concerned.
All the Applicants.

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Assignment title	Medical
Author	Dharani 20104001 M.D. Anaesthesiology
E-mail	drdharani26@gmail.com
Submission time	22-Dec-2012 01:31PM
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A COMPARATIVE STUDY TO ASSESS THE EFFICACY OF MAGNESIUM SULPHATE ON THE ATTENUATION OF HEMODYNAMIC RESPONSE TO PNEUMOPERITONEUM DURING LAPAROSCOPIC SURGERIES A STUDY OF 60 CASES DISSERTATION SUBMITTED FOR THE DEGREE OF DOCTOR OF MEDICINE APRIL 2013 BRANCH – X (ANAESTHESIOLOGY) THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY CHENNAI, TAMILNADU ACKNOWLEDGEMENT I express my sincere and heartfelt gratitude to my respected Professor and Guide Dr.S.C.Ganesh Prabu.M.D.,D.A., Director, Institute of Anaesthesiology, Madurai Medical College and Hospital for his continuous guidance, direct supervision and valuable support throughout the course of the present study. I am extremely grateful to, Dr. S....

A COMPARATIVE STUDY TO ASSESS THE EFFICACY OF MAGNESIUM SULPHATE ON THE ATTENUATION OF HEMODYNAMIC RESPONSE TO PNEUMOPERITONEUM DURING LAPAROSCOPIC SURGERIES

A STUDY OF 60 CASES

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

APRIL 2013

BRANCH – X (ANAESTHESIOLOGY)

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY