Metabolic effects of carbon dioxide insufflation during laparoscopic surgery: Changes in pH, arterial partial pressure of carbon dioxide (PaCO2) and end tidal carbon dioxide (EtCO2).

A Dissertation Submitted In Partial Fulfilment Of The Requirements Of Masters In Medicine Anaesthesia and Critical Care Medicine

University Of Zimbabwe- College of Health Sciences

BY

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2013
Release Form

I Dr Emmerson. N. Mutetwa declare that this submission is my own work. In submitting it for my Masters degree in Medicine (Anaesthesia and Critical Care Medicine) I attest that it has not been submitted in part or in whole to any university or other institution of higher learning.

Signature...........................................................       Date......................................

I/We................................................................................having supervised and read this dissertation am/are satisfied that this is original work of the author under whose name it is being presented. I/We confirm that the work has been completed satisfactorily and is ready for presentation to the examiners. (Delete sections that are not applicable)

SIGNATURE

Supervisor........................................................................Date...................................

Supervisor........................................................................Date...................................

Chairman..........................................................................Date...................................

Department................................................................--------Date...................................
Abstract

Purpose: The purpose of this study was to assess the effects of low tidal volume ventilation on patients undergoing laparoscopic surgery on partial pressure of carbon dioxide, arterial to end tidal carbon dioxide gradient and acid base excess.

Methods: 30 patients undergoing laparoscopic surgery under General Anaesthesia were ventilated with tidal volume of 6 ml/kg and respiratory rate of 12breaths/minute and End tidal CO2, PaCO2, pH, Bicarbonate and ABE measurement was done before, during and after CO2 pneumoperitoneum and analyzed. Respiratory adjustments were done for End tidal CO2 levels above 60mmHg or haemodynamic changes attributable to elevated CO2.

Results: Pneumoperitoneum resulted in a significant elevation in PaCO2 (p<0.001) and a fall of pH (p <0.001), ion bicarbonate (p = 0.011), and base excess (p <0.001). A correlation was found between the EtCO2 and PaCO2 during pneumoperitoneum. No ventilatory adjustments were instituted on any of the patients as they maintained EtCO2 below 60mmHg throughout pneumoperitoneum.

Conclusion: Besides the expected respiratory acidosis, a metabolic acidosis can also be present during pneumoperitoneum. EtCO2 is still a good non invasive monitor for estimation of PaCO2 during low tidal volume ventilation during pneumoperitoneum.
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Abbreviations

ASA – American Society of Anaesthesiologists

ABE – Acid Base Excess

ABG – Arterial Blood Gases

BMI – Body Mass Index

BP - Blood Pressure

CO₂ – Carbon Dioxide

CPP – Cerebral Perfusion Pressure

ECG – Electrocardiogram

EtCO₂ – End Tidal Carbon Dioxide

FRC- Functional Residual Capacity

HCO₃⁻ - Bicarbonate

IAP – Intra-Abdominal Pressure

ICP- Intra-Cranial Pressure

JREC- Joint Parirenyatwa Hospital and College of Health Science Research Ethics Committee

mmHg – Millimetres of Mercury

MRCZ-Medical Research Council Of Zimbabwe
MV – Minute Ventilation

NIBP – Non Invasive Arterial Blood Pressure

PACO$_2$ – Alveolar Partial Pressure of Carbon Dioxide

PaCO$_2$ – Arterial Partial Pressure of Carbon Dioxide

PEEP – Positive End Expiratory Pressure

TcPCO$_2$ – Transcutaneous Carbon Dioxide

PvCO$_2$ – Venous Partial Pressure of Carbon Dioxide

SaO$_2$ – Arterial Saturation of Oxygen

SpO$_2$ – Arterial Saturation of Oxygen by Pulse Oximetry

SVR – Systemic Vascular Resistance

USA – United States of America

VILI – Ventilator Induced Lung Injury

V/Q – Ventilation- Perfusion
Introduction

Laparoscopy involves inspecting the abdomen and pelvis using an endoscope. Carbon dioxide (CO₂) is the gas that is commonly used to insufflate the abdomen so as to facilitate the view. Laparoscopy was first performed at the beginning of the 20th century by Georg Kelling, Dimitri Ott and Christian Jacobeus and it has become an important tool in patient management¹. It became popular among gynaecologists for its effectiveness and simplicity². It was however only performed for the diagnosis of liver disorders via visualization and biopsy and abdominal trauma in general surgery until Lukichev in 1983 and Muhe in 1985 performed laparoscopic cholecystectomies in humans.¹²

Over the past two decades the use of laparoscopy has increased due to the advances in video imaging, powerful light-sources, automatic pressure-driven insufflators, and high-flow suction-irrigation technology, making it possible to perform difficult intra-abdominal manoeuvres more easily.¹² Advantages of laparoscopy include less post-operative pain, reduced incidence of pulmonary complications, rapid recovery of bowel function, less intra-operative bleeding, less postoperative wound infection and fewer metabolic derangements. This ultimately reduces hospital stay with significant cost reduction. Additionally small incisions heal well and are less obvious or disfiguring resulting in improved cosmetic appearance.³

More extensive procedures are now being performed in older patients with multiple co-morbidities, including those with significant cardiopulmonary disease. Laparoscopic techniques have been attempted for multiple types of surgery, some with proven benefit, some with possible benefit and some with uncertain benefit(Table 1).⁴
Table 1: Current general surgical laparoscopic practice.

| Operations with proven benefit | - Diagnostic & staging laparoscopy for malignancy  
| - Cholecystectomy  
| - Adrenalectomy  
| - Splenectomy  
| - Anti-reflux surgery  
| - Cardiomyotomy for achalasia  
| - Obesity surgery  
| - Laparoscopic colonic surgery  
| - Live donor nephrectomy |
| Operations with possible benefit | - Laparoscopic abdominal aneurysm surgery  
| - Laparoscopic distal and central pancreatic surgery  
| - Laparoscopic left hepatic resections  
| - Laparoscopic localisation and enucleation of benign insulinomas  
| - Laparoscopic pancreatic necrosectomy  
| - Gastric and oesophageal resections  
| - Laparoscopic rectal surgery (anterior resection)  
| - Appendectomy  
| - Laparoscopic hernia surgery  
| Operations with uncertain benefit | - Right hepatectomy  
| - Pancreatoduodenectomy |
Gynaecological laparoscopy has also increased with Taiwan reporting an increase in laparoscopic hysterectomies from 6% to 38%, benign ovarian tumours from 32% to 72% and ectopic pregnancy from 19% to 74% between 1997 and 2007.5

Table 2: Common gynaecologic procedures6

<table>
<thead>
<tr>
<th>Tubal surgery</th>
<th>Ovarian surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Tubal ligation</td>
<td>• ovarian cystectomy</td>
</tr>
<tr>
<td>• Salpingectomy</td>
<td>Uterine surgery</td>
</tr>
<tr>
<td>• salpingostomy</td>
<td>• myomectomy</td>
</tr>
</tbody>
</table>

Diagnostic surgery

<p>| | |</p>
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<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• adhesions</td>
<td></td>
</tr>
<tr>
<td>• endometriosis</td>
<td></td>
</tr>
<tr>
<td>• pelvic inflammatory disease</td>
<td></td>
</tr>
</tbody>
</table>

The incidence of complications during laparoscopy varies significantly, depending on the type of procedure as well as, the training and experience of the surgeon. Common complications associated with laparoscopy include those related to creation of a pneumoperitoneum, patient positioning, surgical instrumentation and many others(Table 3).2
Table 3: Complications of laparoscopy

<table>
<thead>
<tr>
<th>Respiratory</th>
<th>Cardiovascular</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hypercarbia &amp; Acidosis</td>
<td>• Arrhythmias</td>
<td>• Shoulder pain</td>
</tr>
<tr>
<td>• Pneumothorax</td>
<td>• Hypotension</td>
<td>• Retinal haemorrhage</td>
</tr>
<tr>
<td>• Atelectasis</td>
<td>• Cardiac arrest</td>
<td>• Oliguria</td>
</tr>
<tr>
<td>• Subcutaneous emphysema</td>
<td>• Deep-vein thrombosis</td>
<td>• Transient ischemic attack</td>
</tr>
<tr>
<td>• Pneumomediastinum</td>
<td>• Pulmonary oedema</td>
<td>• Bowel ischemia/oedema</td>
</tr>
<tr>
<td>• Pleural effusion</td>
<td>• Myocardial infarction</td>
<td>• Hypothermia</td>
</tr>
<tr>
<td></td>
<td>• Gas embolism</td>
<td>• Necrotizing fasciitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Tumour inoculation</td>
</tr>
</tbody>
</table>

Since the year 2000 in the USA, there has been an increase in the use of laparoscopy accounting for 40% of urologic procedures, 50% of general surgical procedures and 70% of gynaecologic procedures. However development has been slow in the setting of public hospitals in Zimbabwe accounting for less than 0.01% (75 out of 7674) of the non-ophthalmologic surgical operations carried out at Parirenyatwa Group of Hospitals in the year 2011(Table 4)(Table 5). An active drive to improve availability of laparoscopic facilities is underway at both referral hospitals in Harare, including the acquisition of new state of the art equipment and the establishment of operating theatres dedicated to laparoscopy.
### Table 4: laparoscopic surgery at Parirenyatwa Hospital

<table>
<thead>
<tr>
<th>Gynaecology</th>
<th># of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Diagnostic laparoscopy for chronic pelvic pain</td>
<td>22</td>
</tr>
<tr>
<td>• Laparoscopy and dye studies for infertility</td>
<td>13</td>
</tr>
<tr>
<td>• Laparoscopy for ovarian cystectomy</td>
<td>3</td>
</tr>
<tr>
<td>• Laparoscopy for ectopic pregnancy</td>
<td>2</td>
</tr>
<tr>
<td>• Tubal surgery for sub-fertility</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>General surgery</th>
<th># of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Laparoscopic cholecystectomy</td>
<td>16</td>
</tr>
<tr>
<td>• Laparoscopic aspiration of liver cysts</td>
<td>2</td>
</tr>
<tr>
<td>• Laparoscopy for diagnosis of intra-abdominal pathology</td>
<td>10</td>
</tr>
<tr>
<td>• Laparoscopic inguinal hernia repair</td>
<td>2</td>
</tr>
<tr>
<td>• Laparoscopic assisted sigmoid cholectomy</td>
<td>3</td>
</tr>
<tr>
<td>• Laparoscopic appendectomy</td>
<td>1</td>
</tr>
</tbody>
</table>

### Table 5: Laparoscopic surgery as a % of total surgical operations

<table>
<thead>
<tr>
<th></th>
<th>Gynaecology</th>
<th>General surgery</th>
<th>Urology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of cases</td>
<td>2540</td>
<td>1606</td>
<td>576</td>
</tr>
<tr>
<td>Laparoscopic cases</td>
<td>41</td>
<td>34</td>
<td>00</td>
</tr>
<tr>
<td>% of Total</td>
<td>0.016</td>
<td>0.021</td>
<td>00</td>
</tr>
</tbody>
</table>
However laparoscopic procedures done in Harare’s private health facilities may be a little more than the 0.01 documented for Parirenyatwa. This is as a result of uninterrupted availability of laparoscopy consumables.

The learning curve presents a challenge to both surgeons and anaesthetists due to inexperience in the field. Excluding direct surgical complications the many metabolic derangements related to prolonged pneumoperitoneum make it necessary to improve measures taken by anaesthetists in order to reduce morbidity and mortality. This study aims to examine the metabolic changes associated with pneumoperitoneum and develop recommendations to anaesthetists to manage mechanical ventilation during laparoscopy.


**Literature review**

**The ideal insufflating gas**

The ideal insufflating gas is inexpensive, chemically stable, highly soluble, rapidly eliminated, non combustible and with minimal physiological effects. Carbon dioxide is the closest to such a gas, maintaining its role as the primary insufflating gas in laparoscopy.\(^9,^{10}\)

Oxygen and air are not used because they support combustion especially with bipolar diathermy and laser. Helium and argon are relatively insoluble and can result in serious complications should intravascular gas embolization occur. Nitrous oxide has been found to be advantageous for some procedures, however its main drawbacks are related to the fact that it can cause expansion of gas filled spaces including air embolus and that it does not suppress combustion.\(^11\)

A novel approach to laparoscopy involves a gasless technique which relies on an abdominal wall lift to create an intra-abdominal space. This is done at atmospheric pressure thus avoiding problems related to increased intra-abdominal pressure (IAP), hypercarbia, and gas embolization with better physiological parameters.\(^12,^{13}\)

**Complications and physiological effects of pneumoperitoneum**

In the 1960s and 1970s, laparoscopic complications rate was 0.6-2.4%, one third of which could be attributed to physiologic problems.\(^14\) In a 1993 USA national survey of 77 000 laparoscopic cholecystectomies 50% of the mortality was attributed to non technical issues.\(^15\)

A review of greater than 200,000 laparoscopies suggested that serious complications resulting in further surgical intervention can be expected in 1 in 660 cases and 1 death in 2000 cases.\(^16,^{17}\) The major physiological consequences are related to carbon dioxide
insufflation, elevated intra-abdominal pressure and patient positioning which mainly affect the cardiovascular, respiratory and renal systems (Table 5). The cardiovascular effects of laparoscopy include an increase in heart rate, systemic vascular resistance, alterations in blood pressure, arrhythmias and cardiac arrest. The haemodynamic effects are dependent on several variables among them the IAP attained, volume of carbon dioxide absorbed, intravascular volume, ventilator technique and the anaesthetic agents used. However with regards to the haemodynamic changes the IAP and patient position have the greatest impact. The reverse trendelenberg position decreases venous return and cardiac output in hypovolaemic patients leading to hypotension. However, activation of the neuro-hormonal system can increase secretion of vasopressin and catecholamines with activation of the renin angiotensin system resulting in an increase in systemic vascular resistance and hypertension.

Further, several changes occur to the respiratory system due to the increase in the IAP and patient positioning. There is a reduction in lung volumes, an increase in peak and plateau airway pressures, and a decrease in pulmonary compliance with abdominal insufflation. The high airway pressures and decreased compliance may be associated with pulmonary barotraumas for example pneumothorax. Basal atelectasis and ventilation perfusion mismatch may occur resulting in intrapulmonary shunting and impaired gas exchange. However, oxygenation is usually not affected during pneumoperitoneum. Although some studies have reported little change in pulmonary compliance with the trendelenberg and reverse trendelenberg positions, others suggest that the reverse trendelenberg may reduce the adverse effects associated with trendelenberg position.
Table 6: Physiological effects of pneumoperitoneum

<table>
<thead>
<tr>
<th>cardiovascular</th>
<th>Respiratory</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ Venous return</td>
<td>↓ lung volumes FRC</td>
<td>↓renal function</td>
</tr>
<tr>
<td>↓ cardiac output</td>
<td>↑ airway resistance</td>
<td>↑ risk of regurgitation</td>
</tr>
<tr>
<td>↑ SVR</td>
<td>↓ pulmonary compliance</td>
<td>↑ ICP</td>
</tr>
<tr>
<td>↓ BP</td>
<td>↑ airway pressure</td>
<td>↓ CPP</td>
</tr>
<tr>
<td>Brady/tachycardia</td>
<td>↑ risk of barotraumas</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↑ V/Q mismatch</td>
<td></td>
</tr>
</tbody>
</table>

Carbon dioxide physiology

Insufflated CO₂ is rapidly absorbed from the peritoneal cavity into the circulation. CO₂ is more rapidly absorbed during extra-peritoneal than intra-peritoneal insufflations and its diffusion is not influenced by the duration of intra-peritoneal pressure.⁹,¹⁰ Extra-peritoneal insufflation also results in higher PaCO₂ values in the post operative period. The maximal absorption rate of CO₂ is reached already at a low IAP of 10mmHg.³⁴,³⁵ The absorbed Insufflated CO₂ is only excreted through the lungs and therefore elimination continues in the postoperative period. Up to 120L CO₂ can be stored in the body with bone as the greatest reservoir.⁹

During laparoscopy with CO₂ insufflation, PaCO₂ is expected to progressively increase until a plateau is reached. Mullet et al noted a rapid increase in PaCO₂ and EtCO₂ in the first 8 to 10 minutes of insufflation which reached a plateau at 15 to 40 minutes in patients undergoing mechanical ventilation.³⁴,³⁶,³⁷,³⁸ Within 5 minutes of insufflation the partial pressure of CO₂ in
arterial blood (PaCO₂), mixed venous blood (PvCO₂), and alveolar gas (PACO₂) rise by 10 mmHg in young healthy patients.⁴⁷,⁴⁹

Gandara et al noted a decrease in pH, bicarbonate and base excess with the rise in PaCO₂ signifying a metabolic acidosis. This was unrelated to the duration of pneumoperitoneum or amount of carbon dioxide insufflated during laparoscopy and with no significant differences between anaesthetic techniques. They further noted a PaCO₂ increase to a maximum at 60 minutes and a decrease in pH to the lowest level in the recovery room. Twenty seven percent (27%) of the patients had hypercarbia during laparoscopy whilst fifty six percent (56%) were hypercarbic in the recovery room.⁴⁰ Ciofolo et al. performed gynaecological laparoscopy under epidural anaesthesia in which they noted a stable PaCO₂ but there was a significant increase in the minute ventilation. Ciofolo et al also concluded that epidural anaesthesia was a safe alternative to general anaesthesia for outpatients laparoscopy.⁴¹

The change in PaCO₂ is not significantly affected by position whether trendelenberg or head up tilt. IAP is the main determinant of change with continuous rise in PaCO₂ associated with pressure changes from 0-25mmHg but no further changes thereafter.⁴² However, Seif et al. found that lowering the insufflation pressure from 15 to 10 mmHg does not contribute to the correction of acid–base balance alterations during laparoscopic cholecystectomy.⁴³ Several factors are involved in the rise in PaCO₂, among them are carbon dioxide absorption from the abdominal cavity, and impaired pulmonary elimination of carbon dioxide due to changes in ventilatory mechanics. Impaired organ perfusion has been suggested as a cause of metabolic acidosis in laparoscopic surgery. However the main mechanism of acidosis is the absorption of carbon dioxide. This is further supported by the fact that there is much less increase in PaCO₂ and acidosis with nitrous oxide or helium pneumoperitoneum despite similar conditions.⁴⁴,⁴⁵
Respiratory monitoring

In addition to monitoring of airway pressures during laparoscopy it is advantageous to monitor EtCO2. Expiratory CO2 monitoring has evolved as a safety monitoring tool and as an important physiological monitor during anaesthesia. Excluding ventilation perfusion mismatch, and sampling errors, PaCO2 should approximate PACO2 which will approximate EtCO2 making capnography a real time non invasive reflection of ventilation.46 The normal PaCO2 to EtCO2 gradient is in the range of 2-5mmHg. During laparoscopy, this gradient increases to 5-10mmHg secondary to increases in dead space because of lung compression and distortion.

Baraka et al noted that at 40 minutes the maximum EtCO2 is reached and correlates well with PaCO2 during laparoscopy. They concluded that EtCO2 was a reliable monitor of PaCO2 during laparoscopy in the absence of acute intraoperative physiological disturbances.47 The same findings were reported by Nyarwaya et al who noted a constant PaCO2-EtCO2 gradient throughout the operation and was not affected by time, IAP, or head up tilt. All the patients maintained an intra-operative saturation above 95% making SpO2 and EtCO2 reliable monitors during carbon dioxide insufflation.48 However, in some individuals there may be variations in the correlation between EtCO2 and PaCO2 especially when the etCO2 increases beyond 41mmHg.49,50 This discrepancy was mainly noted in patients who are ASA II and III, in which there was a greater increase in PaCO2 and widening of the PaCO2-EtCO2 gradient.51,52

Patients with limited capacity to eliminate carbon dioxide due to cardiopulmonary disease may be at greater risk of developing hypercarbia even in the presence of lower EtCO2. Therefore EtCO2 may underestimate PaCO2 in these patients. Fitzgerald et.al, noted this in patients with chronic obstructive pulmonary disease and Wulkan et.al. made the same
conclusion after investigating children with cyanotic heart disease during laparoscopy possibly due to the shunting of venous blood away from the pulmonary circulation.\textsuperscript{53,54} The PaCO\textsubscript{2}-EtCO\textsubscript{2} gradient has also been shown to increase with atelectasis in a porcine model of pneumoperitoneum.\textsuperscript{55} Sprung et.al. showed that in obese patients increasing the tidal volume may decrease PaCO\textsubscript{2}-EtCO\textsubscript{2} gradient, with the opposite seen in normal weight patients. This has been attributed to the fact that there is potentially greater lung recruitment in the obese but an increase in shunting in patients with normal weight.\textsuperscript{56} The main use of EtCO\textsubscript{2} during laparoscopy is to indirectly assess the rise over time of PaCO\textsubscript{2} and to titrate minute ventilation.

In a more recent study by Ozyuvaci et al where transcutaneous, arterial and end-tidal measurements of carbon dioxide were compared during pneumoperitoneum they noted that EtCO\textsubscript{2} was significantly lower than PaCO\textsubscript{2} whilst transcutaneous carbon dioxide (TcPCO\textsubscript{2}) was much closer to PaCO\textsubscript{2} concluding that TcPCO\textsubscript{2} was a more valid and practical measurement compared with EtCO\textsubscript{2} but both could be used to estimate PaCO\textsubscript{2}.\textsuperscript{57}

**Ventilation during laparoscopy**

The physiological consequences of pneumoperitoneum require careful management of ventilation during laparoscopic surgery. It has been estimated that to avoid hypercarbia and respiratory acidosis during laparoscopy, the minute ventilation has to be increased by up to 30-60\% of baseline. Tan and Hirnoven found that this is more efficiently done by increasing tidal volume rather than respiratory rate.\textsuperscript{29,58} Historically high tidal volume ventilation using (10-12ml/kg) has been used to maintain normocapnia during laparoscopy. However Ventilator induced lung injury (VILI) in the normal lungs has become a point of debate even in the operating room. Conventional mechanical ventilation of normal lungs has been shown to induce pro-inflammatory cytokine gene transcription. Webb and Tierney demonstrated that
ventilator induced pulmonary oedema develops when end-inspiratory lung volume is excessive. Dreyfuss et al. provided further proof that high tidal volume is deleterious to the lung when he reported on the effects of high airway pressure, high tidal volume and PEEP. Many studies and reviews have supported the use of low tidal volume ventilation to ventilate normal lungs citing reduction in shearing forces in the alveoli with a resultant decrease in release of pro-inflammatory cytokines. Consequently this reduces systemic inflammatory response during major surgery, thus preventing alveolar collapse and VILI.

In a meta analysis by Serpa Neto et al and Fuller et al they found that low tidal volume ventilation was associated with a lower incidence of pulmonary infection, shorter hospital stay, higher mean PaCO₂, lower pH but similar PaO₂ to FiO₂ ratio when compared to higher tidal volume ventilation. Overall only 4% of patients who received low tidal volumes went on to develop lung injury while 13% of those who received high tidal volumes had acute lung injury.

There might be a need to increase respiratory rate to overcome the rise of PaCO₂ and EtCO₂. In obese patients with flow limitations, the development of intrinsic PEEP during laparoscopy may occur resulting in difficult management. Current experimental data and clinical trials support the safety of allowing permissive hypercapnia. Slow changes in pH do not compromise haemodynamics. Potkin et al reviewed that survival is possible in acute severe respiratory acidosis as long as tissue anoxia and ischaemia are prevented. However, the limits of tolerance to hypercapnia and respiratory acidosis are unclear. Bidani et al. in their review showed that a PaCO₂ levels of 60 to 70 mm Hg and arterial pH level of 7.2 to 7.25 are safe for most patients.

The respiratory mechanical changes related to pneumoperitoneum due to the increase in the IAP can result in basal atelectasis, increased ventilatory pressures and decreases in lung compliance. Use of high inspired concentrations of oxygen is also an important cause of
atelectasis during anaesthesia.\textsuperscript{72} Strang et al however concluded that the PaO\textsubscript{2}/FiO\textsubscript{2} ratio did not correlate with the degree of shunt that occurs during pneumoperitoneum after they noted a worsening atelectasis without worsening PaO\textsubscript{2}/FiO\textsubscript{2} ratio.\textsuperscript{73} Nguyen et al demonstrated that the ratio of the alveolar dead space to tidal volume and the alveolar to arterial oxygen gradient did not change significantly during pneumoperitoneum suggesting that pulmonary oxygen exchange is not significantly affected by pneumoperitoneum.\textsuperscript{74}

With evidence suggesting that the presence of peritoneal acidity during pneumoperitoneum results in a reduction in sepsis and that less aggressive ventilation with hypercapnia might outweigh the cardio-respiratory side effects of CO\textsubscript{2} insufflation, more evidence from clinical trials is required before any recommendations are made.\textsuperscript{75,76,77,78}
Statement of the problem

Laparoscopic surgery is increasing in the setting of both public and private hospitals in Zimbabwe. However arterial blood gas monitoring is not routinely done due to unavailability of ABG analyzers and the related costs. There is limited data related to the complications associated with the procedure in the setting of protective lung ventilation with permissive hypercapnia. This study intends to study the metabolic effects of carbon dioxide pneumoperitoneum with low tidal volume ventilation (6ml/kg) and the reliability of EtCO$_2$ monitoring as a surrogate to PaCO$_2$ in the local population.

Research questions

1. What are the metabolic (arterial pH, bicarbonate and acid base changes) changes that occur with laparoscopic surgery using low tidal volume ventilation?
2. Is there a correlation between EtCO$_2$ and PaCO$_2$ during laparoscopy with low tidal volume ventilation?
3. Is there an additional metabolic component that contributes to the acidosis that occurs with CO$_2$ insufflation during laparoscopy?

Main objective

1. To determine the metabolic changes (PaCO$_2$, HCO$_3^-$, pH, acid base deficits) that occur with low tidal volume ventilation during laparoscopy

Other objectives

1. To determine the severity of hypercarbia with low tidal volume ventilation during laparoscopy
2. To determine the correlation between PaCO$_2$ and EtCO$_2$ during laparoscopic surgery
**Methodology**

**Inclusion Criteria**

1. Patients above age of consent (18 years) undergoing laparoscopic surgery.
2. ASA I and II patients.

**Exclusion Criteria**

1. Patient’s refusal
2. Patients for emergency laparoscopy
3. Obese patients BMI>30
4. Patients who are converted to an open procedure

**Approval of Study**

The Study was approved by the Joint Parirenyatwa Hospital and College of Health Science Research Ethics Committee (JREC) (see appendix 3) and the Medical Research Council of Zimbabwe (MRCZ) (see appendix 4). No patient was prejudiced on religious, political, cultural, social or educational grounds.

**Study type and setting**

A cross-sectional interventional study carried out at Parirenyatwa Group of Hospitals
Patient Recruitment

After obtaining informed consent, thirty (30) consecutive ASA I and II patients with BMI<30 were recruited into the study. Patients were recruited from surgical and gynaecological wards and out-patient clinics at Parirenyatwa Group of Hospitals on the first preoperative contact. Patients were counselled in their native language on the objectives of the study, the potential risks and benefits for joining the study. A consent form written in English and vernacular with the above explanations was given to the patients to read and sign indicating consent (see appendix 1).

Sample size

Statistical calculations were based on previous published data of mean carbon dioxide output during laparoscopic surgery. Sample size was determined assuming a standard deviation of 5 ml min\(^{-1}\) m\(^{-2}\) in carbon dioxide output during carbon dioxide pneumoperitoneum and a precision of within 2 ml min\(^{-1}\) m\(^{-2}\) to give a minimum of 25 participants.

\[
n = \left( \frac{z_{\alpha/2} \times s}{d} \right)^2 = \left( \frac{1.96 \times 5.0}{2.0} \right)^2 \approx 25
\]
**Anaesthetic technique**

Arterial catheter was placed in the radial location under local anaesthesia after the Allen’s test. General anaesthesia with endotracheal tube placement was instituted after standard ASA monitors had been placed. Volume controlled ventilation was instituted on all patients with a tidal volume of 6ml/kg and respiratory rate at 12 breaths per minute. Minute ventilation was increased if EtCO₂ rose beyond 60mmHg, or in the presence of hypoxia, or if there was clinical evidence of haemodynamic compromise (arrhythmias, hypertension, undue heart rate changes) from elevated PaCO₂. Increasing the respiratory rate was the only interventional strategy while the tidal volume remained unchanged.

**Sampling technique**

Arterial blood for metabolic measurements was sampled before induction of anaesthesia, every 15 minutes in the first hour after CO₂ insufflation, at 30 minutes interval for the second hour then hourly thereafter until the end of the procedure. The last sample was collected in the recovery room fifteen minutes after the patient was extubated and was ascertained to be adequately breathing spontaneously. The EtCO₂ and SPO₂ at the time of sampling were recorded (see appendix 2). The ABG sample was analysed using the Radiometer Copenhagen ABL555 machine.
Table 7: Normal values

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EtCO₂</td>
<td>35-45mmHg</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>35-45mmHg</td>
</tr>
<tr>
<td>pH</td>
<td>7.35-7.45</td>
</tr>
<tr>
<td>HCO₃</td>
<td>22-28mmol/L</td>
</tr>
<tr>
<td>ABE</td>
<td>-2.5 to +2.5</td>
</tr>
<tr>
<td>PaCO₂-etCO₂ gradient</td>
<td>2-5 mmHg</td>
</tr>
<tr>
<td>PaO₂/FiO₂ ratio</td>
<td>300-500</td>
</tr>
</tbody>
</table>

Expected outcome

1. Progressive increase in the PaCO₂ and EtCO₂ to a plateau

2. Mild to moderate hypercarbia

3. Correlation between PaCO₂ and EtCO₂
**Results**

A total of 30 participants were enrolled into the study. Table 8 shows the gender distribution of the study patients. The median age of the group was 38 years, IQR (Q₁=28; Q₂=47) and there was no significant difference in the median age for females (38 years, IQR (Q₁=28; Q₂=44)) and for males (41 years, (Q₁=32; Q₂=53.5)) (p value=0.886). The duration of pneumoperitoneum ranged from 45 minutes to 180 minutes, 21 patients reached 60 minutes and only 2 patients reached 180 minutes. Tables 10-15 show the change in variables measured over time where (n) is the number of procedures that reached the time indicated in minutes and R is recovery.

**Table 8: Gender distribution**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Frequency, n=30(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>4(13.3)</td>
</tr>
<tr>
<td>Female</td>
<td>26(86.7)</td>
</tr>
</tbody>
</table>

Table 9 below summarizes the distribution of the laparoscopic procedures of which the most frequent were laparoscopic cholecystectomies and laparoscopic ovarian cystectomies. There was an even distribution of general surgical patients (15) and gynaecological patients (15).
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>laparoscopic cholecystectomy</td>
<td>11</td>
<td>36.7</td>
</tr>
<tr>
<td>laparoscopic ovarian cystectomy</td>
<td>6</td>
<td>20.0</td>
</tr>
<tr>
<td>laparoscopic appendicectomy</td>
<td>3</td>
<td>10.0</td>
</tr>
<tr>
<td>laparoscopy for chronic pelvic pain</td>
<td>3</td>
<td>10.0</td>
</tr>
<tr>
<td>laparoscopic hysterectomy</td>
<td>2</td>
<td>6.7</td>
</tr>
<tr>
<td>diagnostic laparoscopy for uterine abnormality</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>laparoscopic assisted vaginal hysterectomy</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>laparoscopic incisional hernia repair</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>laparoscopic myomectomy</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>laparoscopy and dye studies</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Table 10 shows the change in PaO$_2$/FiO$_2$ ratio over time and figure is a plot of mean PaO$_2$/FiO$_2$ over time. The mean PaO$_2$ values decreased significantly from a mean of 388.1 (sd=54.8) at time zero to a mean of 342.3 (sd=99.2) in 15 minutes (P=0.033). Overall there was no statistically significant difference in mean PaO$_2$ values from time zero to 180 minutes (p=0.239). Mean PaO$_2$ values increased from 296.5 (sd=23.3) at 180 minutes to a mean of 381 (sd=91.7) during recovery. This increase was not statistically significant (p=0.210).

**Table 10: change in PaO$_2$/FiO$_2$ over time**

<table>
<thead>
<tr>
<th>Time(t)/min</th>
<th>0 (n=30)</th>
<th>15 (n=30)</th>
<th>30 (n=30)</th>
<th>45 (n=30)</th>
<th>60 (n=21)</th>
<th>90 (n=11)</th>
<th>120 (n=3)</th>
<th>180 (n=2)</th>
<th>R (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean PaO$_2$/FiO$_2$ mmHg (SD)</td>
<td>388</td>
<td>342</td>
<td>356</td>
<td>340</td>
<td>340</td>
<td>346</td>
<td>335</td>
<td>296</td>
<td>381</td>
</tr>
</tbody>
</table>

**Figure 1: graph of change in the PaO$_2$/FiO$_2$ ratio over time**
Table 11 shows the range and the mean values of the EtCO$_2$ recorded at various times during the pneumoperitoneum. Figure 2 is a graph of the mean EtCO$_2$ against time and shows a gradual EtCO$_2$ increase from 15 minutes to 180 minutes. However the changes were not statistically significant from 15 minutes to 180 minutes, (p=0.121).

**Table 11: Change in EtCO$_2$ over time**

<table>
<thead>
<tr>
<th>Time(t)/min</th>
<th>15 (n=30)</th>
<th>30 (n=30)</th>
<th>45 (n=30)</th>
<th>60 (n=21)</th>
<th>90 (n=11)</th>
<th>120 (n=3)</th>
<th>180 (n=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean EtCO$_2$/mmHg (SD)</td>
<td>40.7 5.9</td>
<td>41.7 6.0</td>
<td>43.1 6.3</td>
<td>44.0 6.8</td>
<td>45.2 6.9</td>
<td>45.3 4.2</td>
<td>48.0 4.2</td>
</tr>
<tr>
<td>Range</td>
<td>30-54 29-54</td>
<td>31-56 31-55</td>
<td>31-56 31-56</td>
<td>42-50 45-51</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 2: Graph of mean EtCO$_2$ over time**
Table 12 shows the mean values of the PaCO$_2$ recorded over time and Figure 3 shows the rate of change of PaCO$_2$ over time. The change in PaCO$_2$ values was significant from time 0 through 15-180 minutes (p<0.001) with a significant drop in PaCO$_2$ from 180 minutes to recovery (p=0.006). There was a significant difference in PaCO$_2$ between time zero (35.4, SD(4.2)) and recovery period (43.2, SD(4.6)) (p<0.001).

**Table 12: Change in PaCO$_2$ over time**

<table>
<thead>
<tr>
<th>Time(t)/min</th>
<th>0  (n=30)</th>
<th>15 (n=30)</th>
<th>30 (n=30)</th>
<th>45 (n=30)</th>
<th>60 (n=21)</th>
<th>90 (n=11)</th>
<th>120 (n=3)</th>
<th>180 (n=2)</th>
<th>R  (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean PaCO$_2$/mmHg (SD)</td>
<td>35.7 4.2</td>
<td>44.6 5.9</td>
<td>45.6 6.0</td>
<td>47.9 5.9</td>
<td>49.0 6.5</td>
<td>51.2 6.5</td>
<td>52.7 3.5</td>
<td>53 0</td>
<td>43.2 4.6</td>
</tr>
</tbody>
</table>

**Figure 3: Graph of change in PaCO$_2$ over time**
The \( \text{PaCO}_2 \)-\( \text{EtCO}_2 \) difference (Table 13) was illustrated by the graphs of \( \text{PaCO}_2 \) and \( \text{EtCO}_2 \) over time (Figure 4). There was gradual widening of the \( \text{PaCO}_2 \)-\( \text{EtCO}_2 \) gradient over time but the differences in mean \( \text{PaCO}_2 \) and \( \text{EtCO}_2 \) were not statistically significant from 15 minutes to 180 minutes, \((p=0.258)\). \( \text{EtCO}_2 \) and \( \text{PaCO}_2 \) are highly correlated \((r=0.90)\) and this correlation is significant \((p<0.001)\).

### Table 13: Mean difference between \( \text{PaCO}_2 \) and \( \text{EtCO}_2 \)

<table>
<thead>
<tr>
<th>Time (minutes) (n)</th>
<th>( t=15 ) (n=30)</th>
<th>( t=30 ) (n=30)</th>
<th>( t=45 ) (n=30)</th>
<th>( t=60 ) (n=21)</th>
<th>( t=90 ) (n=11)</th>
<th>( t=120 ) (n=3)</th>
<th>( t=180 ) (n=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(( \text{PaCO}_2 )-( \text{EtCO}_2 ))</td>
<td>Mean difference (SD)</td>
<td>4.4(3.5)</td>
<td>3.9(2.4)</td>
<td>4.8(2.6)</td>
<td>5.0(2.7)</td>
<td>6.0(3.0)</td>
<td>7.3(1.5)</td>
</tr>
<tr>
<td>Range</td>
<td>0-10</td>
<td>0-9</td>
<td>0-11</td>
<td>1-10</td>
<td>1-9</td>
<td>6-9</td>
<td>2-8</td>
</tr>
</tbody>
</table>

### Figure 4: Comparison between changes in \( \text{EtCO}_2 \) vs \( \text{PaCO}_2 \) over time

![Figure 4: Comparison between changes in \( \text{EtCO}_2 \) vs \( \text{PaCO}_2 \) over time](image-url)
Figure 5 is a plot of mean pH over time (mean values in Table 14) where a significant acidosis was observed from 15 minutes into the pneumoperitoneum. The pH significantly decreased from 0 minutes (7.42±0.05) to 7.33±0.04 at 15 minutes (p<0.001) and continued to decrease significantly from 0 minutes through 15-180 minutes (p<0.001) but the change in pH from 180 to recovery was not significant (p=0.344). There was significant difference between pH at time zero (7.42, SD (0.05)) and pH at recovery (7.32, SD (0.04)) p<0.001.

**Table 14: Change in pH over time**

<table>
<thead>
<tr>
<th>Time(t)</th>
<th>0 (n=30)</th>
<th>15 (n=30)</th>
<th>30 (n=30)</th>
<th>45 (n=30)</th>
<th>60 (n=21)</th>
<th>90 (n=11)</th>
<th>120 (n=3)</th>
<th>180 (n=2)</th>
<th>R (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean pH(SD)</td>
<td>7.42 ± 0.05</td>
<td>7.33 ± 0.04</td>
<td>7.32 ± 0.04</td>
<td>7.30 ± 0.04</td>
<td>7.30 ± 0.04</td>
<td>7.28 ± 0.05</td>
<td>7.27 ± 0.03</td>
<td>7.27 ± 0.04</td>
<td>7.32 ± 0.04</td>
</tr>
</tbody>
</table>
The mean HCO$_3^-$ values decreased significantly from 0 minutes (23.3±1.7) to 22.5±1.7 at 15 minutes (p=0.011) with a statistically non significant change thereafter (p>0.05) (Figure 6). The drop in HCO$_3^-$ from 180 minutes to recovery was also statistically non significant (p>0.05). However the drop in HCO$_3^-$ between time zero (23.3, SD (1.7)) and recovery time (21.3, SD (2.1)) was statistically significant, p<0.001.

Table 15: Change in bicarbonate (HCO$_3^-$) over time

<table>
<thead>
<tr>
<th>Time(t)</th>
<th>0 (n=30)</th>
<th>15 (n=30)</th>
<th>30 (n=30)</th>
<th>45 (n=30)</th>
<th>60 (n=21)</th>
<th>90 (n=11)</th>
<th>120 (n=3)</th>
<th>180 (n=2)</th>
<th>R (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean HCO$_3^-$ (SD)</td>
<td>23 (1.7)</td>
<td>23 (1.7)</td>
<td>22 (2.0)</td>
<td>22 (2.1)</td>
<td>22 (2.2)</td>
<td>22 (2.5)</td>
<td>22 (2.0)</td>
<td>23 (0.7)</td>
<td>21 (2.1)</td>
</tr>
</tbody>
</table>

Figure 6: Change in bicarbonate over time
The mean ABE value significantly fell from 1.0±2.1 below zero to 2.6± 1.8 below zero 
(p<0.001) in the first 15 minutes and continued to decrease significantly across the entire 
time range (Table 16, Figure 7) from 0-30 minutes (p=0.006), 0-60 minutes (p=0.002), 0-90 
minutes (p=0.002). However the change in ABE from 180 minutes to recovery was not 
statistically significant, (p=0.925). Change in ABE between time zero (-1.0, SD (2.1)) and 
recovery (-3.8, SD (2.4)), p<0.001 was statistically significant.

Table 16: Change in ABE over time

<table>
<thead>
<tr>
<th>Time(t)</th>
<th>0 (n=30)</th>
<th>15 (n=30)</th>
<th>30 (n=30)</th>
<th>45 (n=30)</th>
<th>60 (n=21)</th>
<th>90 (n=11)</th>
<th>120 (n=3)</th>
<th>180 (n=2)</th>
<th>R (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ABE (SD)</td>
<td>-1.0 (2.1)</td>
<td>-2.6 (1.8)</td>
<td>-3.0 (2.0)</td>
<td>-3.4 (1.9)</td>
<td>-3.3 (2.1)</td>
<td>-3.9 (2.4)</td>
<td>-3.3 (2.4)</td>
<td>-2.7 (1.8)</td>
<td>-3.8 (2.5)</td>
</tr>
<tr>
<td>Range (SD)</td>
<td>(-3.5)- (4.1)</td>
<td>(-5.6)- (2.4)</td>
<td>(-5.7)- (2.4)</td>
<td>(-6.6)- (1.8)</td>
<td>(-6.8)- (1.5)</td>
<td>(-7.8)- (0.3)</td>
<td>(-4.9)- (0.5)</td>
<td>(-3.9)- (1.4)</td>
<td>(-9.0)- (0.3)</td>
</tr>
</tbody>
</table>

Graph 7: Change in ABE over time
Discussion

Thirty (30) patients were enrolled in this study with a median age of 38 years and no statistically significant difference within the male cohort and female cohort. All the patients enrolled completed the study. Patients were selected from different specialties and underwent different types of surgery. Lister et al had proven that carbon dioxide physiology is not affected by patient positioning during laparoscopy but intra-abdominal pressure was the main determinant of carbon dioxide absorption thus an intra-abdominal pressure of 12mmHg was used for all patients throughout this study.

All the patients were ventilated using 100% oxygen due to the unavailability of medical air in the Parirenyatwa Group of hospitals theatres. All the patients maintained arterial oxygen saturations above 98%. No undue haemodynamic changes directly attributable to hypercarbia or acidosis were recorded and none of the patients required blood transfusion perioperatively.

Historically there was an emphasis on a careful ventilator strategy to avoid hypercarbia and respiratory acidosis during laparoscopic surgery. This was done by a combination of high tidal volume ventilation (10-12ml/Kg) and an increase in minute ventilation by up to 30-60% of baseline. Tan and Hirvenen proposed an increase in tidal volume rather than respiratory rate to efficiently control hypercarbia. However with the advent of ventilator strategies to protect the lungs, using low tidal volumes has been advocated. This strategy reduces the inflammatory process induced by mechanical ventilation but allows for permissive hypercapnia and respiratory acidosis.
The findings of this study had many similarities with other studies of a similar design. The mean PaO\textsubscript{2} to FiO\textsubscript{2} ratio was consistently above 300 throughout which signified adequate arterial oxygenation. However instances of a low ratio were recorded in some patients during the course of the pneumoperitoneum without a fall in oxygen saturation. The initial decrease could be attributed to the increased ventilation perfusion mismatched caused by the increased intra-abdominal pressure resulting in atelectasis exacerbated by absorption atelectasis from use of 100% oxygen. The stable PaO\textsubscript{2} observed for the duration of the pneumoperitoneum was in keeping with the findings of Strang et al and Nguyen et al who concluded that pneumoperitoneum did not cause any clinically significant changes in pulmonary gas exchange and impairment of arterial oxygenation.\textsuperscript{79,55}

There were rises in the PaCO\textsubscript{2} and EtCO\textsubscript{2} and a fall in pH signifying hypercarbia and hypercapnia with a resultant respiratory acidosis. However the rise was greater than that observed in the other studies where higher tidal volumes were used.

A rapid rise in the PaCO\textsubscript{2} was observed in the first 15 minutes of insufflation (figure 2). This was noted to be similar to the findings by Mullet et al who noted a rapid rise in PaCO\textsubscript{2} and EtCO\textsubscript{2} within the first 10 minutes of insufflation \textsuperscript{34}. There was an initial rise in PaCO\textsubscript{2} of approximately 10 mmHg in the first 15 minutes (p value<0.001) similar to the findings by Ishikawa et al and reviewed by Doyle et al\textsuperscript{39,37}. Similar to the findings of Mullet et al, Meininger et al, Ishikawa et al and Monagle et al there was a progressive increase in EtCO\textsubscript{2} and PaCO\textsubscript{2} during carbon dioxide insufflation in this study. The maximum rate of increase in this study occurred in the first 15 minutes of insufflation with a gradual increase thereafter.\textsuperscript{34,36,37,38} The rapid rise from the initial carbon dioxide load may be due to the delayed equilibration of the carbon dioxide between the blood and other tissues considering that the bone which is the biggest buffer has relatively poor blood supply. However a plateau was not observed in this study as there was a continuous and significant rise in the PaCO\textsubscript{2}
throughout the duration of the procedures (p value < 0.001) unlike in the other studies where there was a PaCO2 plateau between 15 and 45 minutes\textsuperscript{36,38,34,37}. The PaCO2 was observed to decrease 15 minutes post-extubation but did not return to baseline during this period (p<0.001). The fall from 180 minutes to 15 minutes into recovery was statistically significant (p value =0.006).

A plateau would suggest that the excess CO$_2$ absorbed from the peritoneal cavity would have reached equilibrium with CO$_2$ removed by ventilation so the findings of this study indicate that it might take longer for the insufflated CO$_2$ to equilibrate when using low tidal volume ventilation during laparoscopic surgery when compared to higher tidal volumes. However the decreasing number of subjects going beyond 60 minutes of pneumoperitoneum could be the limiting factor in determining a reliable PaCO$_2$ trend in this study.

The EtCO$_2$ was not measured preoperatively or postoperatively as it was technically difficult to get a reliable reading in spontaneously breathing un-intubated patient but a gradual increase in the EtCO$_2$ was observed from 15 minutes post insufflation through to 180 minutes post insufflation (figure 1). The trend and gradual rise of the EtCO$_2$ was similar to that observed by Baraka et al\textsuperscript{47}. However the change in the EtCO$_2$ from 15 to 180 minutes (p value =0.121) was not statistically significant. This suggested a plateau in the increase in EtCO$_2$ even with low tidal volume ventilation.

Maharjan et al compared the effect of low minute ventilation using tidal volumes of 10ml/kg and respiratory rate of 12 breaths per minute compared to 15 breaths and found a linear increase in both EtCO$_2$ and PaCO$_2$ with the low respiratory rate but unchanged levels in the high respiratory rate group\textsuperscript{80}. They suggested a 10-15% increase in minute ventilation to overcome hypercarbia by increasing respiratory rate. Kazama et al suggested an increase in minute ventilation by 1.54 times to maintain constant PaCO$_2$ while Mullet and colleagues
noted a 25% increase in PaCO$_2$. Wurst et al recorded a 30-40% increase in CO$_2$ output during laparoscopy. Similar trends in this study albeit at higher PaCO$_2$ values suggest that it might be possible to control PaCO$_2$ by just increasing the respiratory rate within the limits of permissive hypercapnia.

The range of the PaCO$_2$-EtCO$_2$ gradient was observed to be wider during laparoscopic surgery (figure 3) compared to the range in normal spontaneously breathing individuals. The observed range was 0-11mmHg with a mean between 4-7mmHg (normal gradient 2-5 mean 4mmHg) which was similar to the findings by Valenza et al. In this study there was progressive widening of the PaCO$_2$-EtCO$_2$ gradient which however was found to be statistically insignificant (p value=0.258). A correlation between PaCO$_2$ and EtCO$_2$ (r=0.90) was observed in this study. This is similar to findings of Nyarwaya et al and Baraka et al who also noted a correlation between the two. This implies that EtCO$_2$ is still a reliable non-invasive surrogate for monitoring PaCO$_2$ during laparoscopy. However in a recent study by Ozyuvaci et al where transcutaneous, arterial and end-tidal measurements of carbon dioxide were compared during pneumoperitoneum they noted that EtCO$_2$ was significantly lower than PaCO$_2$ whilst transcutaneous carbon dioxide (TcPCO$_2$) was much closer to PaCO$_2$ concluding that TcPCO$_2$ was a valid and practical measurement compared with EtCO$_2$ but both could be used to estimate PaCO$_2$.

There was a progressive decrease in the pH during pneumoperitoneum in keeping with the hypercarbia (figure 4). An increase towards baseline was observed during recovery but pH was still significantly lower than baseline 15 minutes into recovery (p<0.001). The pH was consistently above the 7.20 which was proposed by Bidani et al as the lower limit of safety in most patients where permissive hypercapnia is instituted. A significant degree of metabolic acidosis was also observed during pneumoperitoneum defined by a decrease in both the bicarbonate and the base excess. There was a significant decrease in bicarbonate in the first
15 minutes (p value=0.011) (figure 5) and a progressive decrease in base excess (p value <0.001) (figure 6) throughout the duration of pneumoperitoneum. Bicarbonate concentrations as low as 17mmol/L were recorded with base deficits as low as 9mmol/L. Gandara et al, Hirnoven et al and Shuto et al reported similar findings. The cause of the metabolic acidosis however could not be elucidated in this study as several components of the metabolic profile necessary to fully characterise the metabolic acidosis like the lactate levels, electrolytes, albumin and other anions were not measured. However it has been postulated that the metabolic acidosis is secondary to organ hypo-perfusion during pneumoperitoneum.
Study limitations

This study was limited by:

- The low turnout of study patients for laparoscopy due to several reasons-top being the high hospital fees. This resulted in the study taking longer than expected to complete.
- There were few laparoscopic operations of long enough duration (greater than 2 hours) to allow for adequate assessment of the effects of prolonged pneumoperitoneum on the metabolic status.
- The metabolic status was not fully characterised because some of the essential components like lactate were not measured and the anion and osmolar gaps could not be calculated due to unavailability of the relevant laboratory backup at Parirenyatwa hospital.

Conclusion

Use of low tidal volume ventilation is associated with increases in PaCO₂ and EtCO₂ and decreases in pH, bicarbonate and ABE which are within the limits of permissive hypercapnia.

A correlation was observed between the PaCO₂ and EtCO₂ throughout the duration of the insufflation making EtCO₂ a reliable monitor of CO₂ output during laparoscopy.

A metabolic component to the change in pH was also observed during insufflation but was not fully characterised in this study.
**Recommendations**

Low tidal volume ventilation can safely be employed during pneumoperitoneum within the limits of permissive hypercapnia.

An increase in respiratory rate rather than tidal volume should be considered to control the PaCO2.

The EtCO2 monitoring can safely be used for the monitoring of PaCO2; however ABGs should be done during pneumoperitoneum if available to ascertain the PaCO2-EtCO2 gradient.

This study included patients with various indications for laparoscopic surgery; a study with better patient stratification would be recommended.

A study in setting with good laboratory backup including measurements of lactate, urea, electrolytes and albumin and calculation of the anion and osmolar gaps would be recommended.

A study with longer term follow up of the patients after the surgery is also recommended to review the pulmonary and metabolic consequences of low tidal volume ventilation during laparoscopy.
Appendix 1

ABG STUDY QUESTIONNAIRE

Date enrolled ....../....../........

ID number .......................

PATIENT DETAILS:

1. Age/Zera: 
2. sex: 
3. Weight: 
4. Height: 
5. BMI: 
6. ASA: 
7. Procedure: 
8. Tidal Volume: 
9. Respiratory rate: 

Outcomes

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Appendix 2

SUBJECT INFORMED CONSENT

PROTOCOL TITLE: Metabolic effects of carbon dioxide insufflation during laparoscopic surgery: Changes in pH, arterial partial pressure of carbon dioxide(PaCO2) and end tidal carbon dioxide(etCO2).

NAME OF RESEARCHER: Dr Emmerson Mutetwa

PHONE: 0772936517 EMAIL: drenmutetwa@yahoo.co.uk

1. Project description

Laparoscopic surgery has become popular with both doctors and patients and has a proven safety record. Carbon dioxide, the gas used in the procedure causes some changes in the blood composition during the procedure but the changes have been noted to be mild and of no clinical significance if managed correctly in studies done in other countries. This study seeks to determine if the findings of these studies are the same with the local population.

2. Your rights

Before you decide whether or not to volunteer for the study, you must understand its purpose, how it may help you, the risks to you and what is expected of you. This process is called informed consent.

3. Purpose of research study

The purpose of the study is to determine the degree to which some selected composition of the blood change during laparoscopic surgery and determine whether the standard guideline measures adopted from other countries where research in this area has been apply for our local population.
4. Procedure involved in the study

The study will be carried out at Parirenyatwa Hospital and Harare Central Hospital theatres. Patients booked for laparoscopic surgery who satisfy the inclusion criteria will be selected. An arterial catheter will be inserted under local anaesthesia for blood sampling before anaesthesia, at designated periods during the operation and after the operation. The blood collected will undergo laboratory analysis for pH and carbon dioxide levels. The patient will undergo a standard anaesthetic management and the operation will be carried out in a standard way.

5. Discomforts and Risks

Arterial cannulation is a safe procedure which can be done painlessly by injecting a local anaesthetic on the site before cannulation. However some mild pain may be experienced during and after which can be managed effectively with the same pain medication which will be prescribed for the postoperative period. An Allen’s test, a procedure which assesses for the adequacy of collateral blood supply to the hand will be done before radial artery cannulation is performed to avoid complications of ischaemia to the hand.

6. Study withdrawal

You may choose not to enter the study or withdraw from the study at any time without loss of benefits entitled to you.

7. Potential benefits

There are no monetary or material gains in this study. You will not stay in hospital any longer than you will be required by your ward doctors. The anaesthetic and hospital costs are part of the standard care for your operation and you will not be charged extra for participating in this study. Materials specific for the study and laboratory fees will be catered for by the research team.
8. Confidentiality of records

Your part in this study is confidential. None of the information will identify you by name.

You will be identified by a unique study identification number. All data will be collected and analyzed according to these numbers. The coded identification numbers and all records will be locked in a filing cabinet. Any links of participant’s identification numbers to other identifying information will be stored separately in a locked cabinet with limited access.

Every effort will be made to keep your information confidential.

9. Problems/questions

Please ask questions about this research or consent now. If you have questions in future please ask Dr Emmerson Mutetwa on cell phone number 0772 936 517. If you have questions or concerns about your participation as a research subject, please contact the Medical research council of Zimbabwe on telephone 00263 4 791792 or 00263 4 791193

10. Authorization

I have read each page of this paper about the study (or it was read to me). I understand the possible risks and benefits of this study. I know that being in this study is voluntary. I choose to be in this study. I know I can stop being in this study and I will not lose any benefits entitled to me. I will get a copy of this consent form now.

Participant’s signature ......................................................... Date…./…../……

Participant’s name (printed) ......................................................

Researcher’s signature.......................................................... Date…./…../……

Witness’ signature.................................................................Date…./…../……
Appendix 3

Gwaro retenderano

Musoro weongororo: kusanduka kwemamiriro eropa (Metabolic changes) kubudikidza nekushandisa mweya wecarbon dioxide panoongororwa mudumbu nemuchina takananangana ne kusanduka kwe pH, huwandu hwecarbon dioxide muropa uye huwandu hwecarbon dioxide inobuditswa nemhunu achifema.

Zita remuwongorori wechirongwa: Dr Emmerson Mutetwa

Runhare rwavo: 0772936517

Email: drenmutetwa@yahoo.co.uk

1. Tsananguridzo yechirongwa

Operation yelaparoscopy (kuongororwa mamiriro emudumbu nemuchina) yagamuchirwa zvikuru navana chiremba pamwe nevarwere uye yakaonekwa kuti haina njodzi huru. Mweya we Carbon dioxide unoshandiswa pa operation iyi unokonzera shanduko mumamiriro eropa. Paongororo dzakaitwa kune dzimwe nyika zvakaonekwa kuti shanduko dzemamiriro eropa dzishomanana uye izi havzivakanise utano hwenyu kana zvikatariswa zvakanaka. Chironga ichi ndechekuda kuona kuti zvakaonekwa kunyika idzi zvichafanana here nezvichawanikwa munyika muno.

2. Kodzero dzenyu

3. Donzvo rechirongwa

Donzvo rechirongwa ichi nderekuda kuona nhanho yekusanduka kwezvimwe zviri muropa panenge pachiitwa operation yelaparoscopy. Uyezve nekuda kuona kuti nzira dzakatarwa nedzimwe nyika dzakaita ongororo dzinogona here kushandiswa muvanhu vemuno.

4. Zvichaitwa


5. Njodzi nekusagadzikana

Kuiswa tsono yekutosera ropa (arterial catheter) hazvina njodzi zhinji uye zvinogona kuitwa pasina marwadzo kana wakatanga vabaya kajekiseni kechiveve panzvimbo yavanenge pasarudza kushandira. Zvisineyi munhu anogona kurwadziwa zvishoma nguva yaenenge akiwa tsono nemushure mekubiswa. Marwadzo aya anopedzwa nekutora mushonga unodzivirira marwadzo unenge wayorwa nachiremba kuti mumwe mushure moperation.

Musati maiswa tsono yekutosera ropa munoitwa inonzi Allen’s test yekuongorora kuti ropa rinofamba zvakakwana here muruoko urwu . Izvi zvinotirwa kudzivirira dambudziko rekushomeka kwero panoendu kuruuko.
6. Kubuda muchirongwa
Munogona kusarudza kusave nhengo ye chirongwa chino kana kumira kuve nhengo ye chirongwa chino pane nguva ipi zvayo musingarasikirwe nazvamaifanirwa kuwana.

7. Zvamungangowana
Hapana chamunobhadharwa nekuve muchirongwa chino. Hamuzogari muchipatara kupfurikidza nguva inenge yatarwa nemachiremba enyu. Munobhadhara mega muripo we operation iyi sezvinotarisirwa kuti muite panguva dzose. Hamubhadhare mari yekupinda muchirongwa chino, zvinhu zvese zvichashandiswa zvakanangangana nechirongwa pamwe nekuongororwa kweropa kulaboratory zvinobhadharwa nevechirongwa

8. Zvakavanzika

9. Mibvunzo kana zvinonetsa
Tinokumbira kuti muvhunze mibvunzo iripamusoro pechirongwa chino kana chegwaro retenderano ikozvino. Kana mazove nemibvunzo mumazuva anotevera vhunzai Dr Emmerson Mutetwa parunhare runoti 0772936517. Kana muchinge maita mibvunzo iri mayererano nekodzero dzenyu senhengo yechirongwa batai ve Medical Research council panhare dzinoti 00263 4 791 792 kana 00263 4 791 193.
10. Mvumo

Ndaverenga zvakanyorwa mugwaro rechirongwa iri (kana kuti ndaverengerwa zvakanyorwa).
Ndanzwisisa nezvenjodzi dzingangoitika uye nezvandingangowana muchirongwa ichi.
Ndinoziva kuti kupinda muchirongwa isarudzo yangu. Ndinosarudza kupinda muchirongwa.
Ndinoziva kuti ndinogona kubuda muchirongwa ichi uyezve handizorasikirwi nezvese
zvandinofanirwa kuwana.

Zita remurapwa.................................................. Zuva.......................  
Sainechi yemurapwa.................................................................

Sainechi yemuongorori..................................................Zuva...............  
Sainechi yechapupu..................................................Zuva.........................
References


12. Alijani, A., Hanna, G. B. & Cuschieri, A. Abdominal wall lift versus positive-pressure
capnoperitoneum for laparoscopic cholecystectomy: randomized controlled trial. Annals
undergoing laparoscopic cholecystectomy: differences between the pneumoperitoneum
15. Deziel, D. J. et al. Complications of laparoscopic cholecystectomy: a national survey of
4,292 hospitals and an analysis of 77,604 cases. The American journal of surgery 165, 9–
18. Hardacre, J. M. & Talamini, M. A. Pulmonary and hemodynamic changes during
changes during laparoscopic cholecystectomy. Anesthesia & Analgesia 76, 1067–1071
(1993).
cholecystectomy: haemodynamic and neuroendocrine responses after pneumoperitoneum
21. Odeberg, S. et al. Haemodynamic effects of pneumoperitoneum and the influence of
posture during anaesthesia for laparoscopic surgery. Acta anaesthesiologica scandinavica


42. Lister, D. R. *et al.* Carbon dioxide absorption is not linearly related to intraperitoneal carbon dioxide insufflation pressure in pigs. *Anesthesiology* 80, 129 (1994).


73. The Effect of CO2-Pneumoperitoneum on Ventilation Perfusion Distribution of the Lung - FULLTEXT02. at <http://uu.diva-portal.org/smash/get/diva2:406991/FULLTEXT02>


UNIVERSITY OF ZIMBABWE
COLLEGE OF HEALTH SCIENCES
MEMORANDUM

FROM: Chairman, Joint Research Ethics Committee
TO: Dr E Mutetwa, Department of Anaesthetics
   c.c: Chairman, Department of Anaesthetics

DATE: 11th June 2012
EXT: 2241/2242

RE: METABOLIC EFFECTS OF CARBON DIOXIDE INSUFFLATION DURING LAPAROSCOPIC SURGERY: CHANGES IN PH, ARTERIAL PARTIAL PRESSURE OF CARBON DIOXIDE (PAC0₂) AND END TIDAL CARBON DIOXIDE (ETCO₂)– JREC/153/12.

Thank you for your application with the above mentioned title seeking approval from the Joint Parirenyatwa Hospital and College of Health Sciences Research Committee (JREC). The Committee has successfully evaluated and discussed the material you supplied.

It was agreed that your application be approved as a research project which is ethically sound.

Wishing you an enjoyable and fruitful research.

Approval Date: 11th June 2012

Expiry Date: 10th June 2013

Professor MM Chidzonga
APPROVAL LETTER

Ref: MRCZ/B349 20 June, 2012

Dr E.N Mutetwa
UZ College of Health Sciences
P.O Box A178
Harare

RE: Metabolic effects of carbon dioxide insufflations during laparoscopic surgery: Changes in pH, arterial partial pressure of carbon dioxide(PaCO2) and end tidal carbon dioxide(etCO2)

Thank you for the above titled proposal that you submitted to the Medical Research Council of Zimbabwe (MRCZ) for review. Please be advised that the Medical Research Council of Zimbabwe has reviewed and approved your application to conduct the above titled study. This is based on the following documents that were submitted to the MRCZ for review:

a) MRCZ Application form
b) CVs for P.I and Co P.I
c) Full research proposal and summary
d) Questionnaire (English)
e) Informed Consent Form (English and Shona)

- APPROVAL NUMBER: MRCZ/B349
  This number should be used on all correspondence, consent forms and documents as appropriate.
- APPROVAL DATE: 20 June, 2012
- TYPE OF MEETING: Expedited
- EXPIRATION DATE: 21 June, 2013

After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the MRCZ website or our website should be submitted three months before the expiration date for continuing review.

- SERIOUS ADVERSE EVENT REPORTING: All serious problems having to do with subject safety must be reported to the Institutional Ethical Review Committee (IERC) as well as the MRCZ within 3 working days using standard forms obtainable from the MRCZ website: www.mrcz.org.zw
- MODIFICATIONS: Prior MRCZ and IERC approval using standard forms obtainable from the MRCZ website is required before implementing any changes in the Protocol (including changes in the consent documents).
- TERMINATION OF STUDY: On termination of a study, a report has to be submitted to the MRCZ using standard forms obtainable from the MRCZ website.
- QUESTIONS: Please contact the MRCZ on Telephone No. (04) 791792, 791193 or by e-mail on mrc.zimbabwe@yahoo.com

Other:
- Please be reminded to send in copies of your final research results for our records as well as for the Health Research Database.
- You are also encouraged to submit electronic copies of your publications in peer-reviewed journals that may emanate from this study.

Yours Faithfully

MRCZ SECRETARIAT
FOR CHAIRPERSON
MEDICAL RESEARCH COUNCIL OF ZIMBABWE

PROMOTING THE ETHICAL CONDUCT OF HEALTH RESEARCH