

**EVALUATION OF SURGICAL CONDITION
DURING LAPAROSCOPIC GYNAECOLOGICAL
SURGERY IN PATIENT WITH MODERATE VS
DEEP NEUROMUSCULAR BLOCK IN LOW
PRESSURE PNEUMOPERITONEUM.**

DR UMAIRAH BINTI ESA

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE
REQUIREMENT FOR THE DEGREE OF MASTER OF MEDICINE
(ANAESTHESIOLOGY AND INTENSIVE CARE)

UNIVERSITI SAINS MALAYSIA

2022

ACKNOWLEDGEMENTS

All praise be to Allah, the Almighty, as for His Will and Blessings,

I would like to deliver my utmost gratitude and heartfelt appreciation to Associate Professor Dr. Rhendra Hardy Mohamad Zaini, my research supervisor, for his guidance throughout the entire course. My deepest appreciation also goes to Associate Professor Mohd Zulfakar Mazlan, academic supervisor/co-supervisor, for all his encouragement, and support.

Thank you very much to all my lecturer, colleagues, staff, and everyone who have contributed to the research.

To Dr Anas Rosedi- my beloved husband, my knight in shining armour, my partner in crime who are with me through thick and thin, thank you very much.

My Children, Thank you for great understandings

My family, thank you for unconditional support.

Thank you.

TABLE OF CONTENT

ACKNOWLEDGEMENTS.....	i
TABLE OF CONTENT	ii
LIST OF TABLES.....	vi
LIST OF FIGURES	vii
LIST OF SYMBOLS AND ABBREVIATIONS	viii
APPENDICES	ix
ABSTRAK.....	x
ABSTRACT.....	xii
CHAPTER 1 INTRODUCTION	1
1.1 Background.....	1
1.2 Problem Statements	1
1.3 Aim	2
1.4 Significant of the study	2
1.5 Literature Review	3
CHAPTER 2 STUDY PROTOCOL.....	7
2.1 General Objective	7
2.2 Specific Objectives	7
2.3 Null hypothesis	8
2.4 Research Methodology	9

2.4.1 Research design	9
2.4.2 Sampling Method.....	9
2.4.3 Study period.....	9
2.4.4 Sampling time frame.....	9
2.4.5 Study location	9
2.4.6 Study Population.....	9
2.5 Subject Criteria	11
2.5.1 Inclusion criteria	11
2.5.2 Exclusion Criteria	11
2.5.3 Withdrawal criteria	11
2.6 Sample Size Estimation	12
2.7 Sampling method and subject recruitment.....	16
2.8 Research tool.....	19
2.9 Operational Definition	20
2.10 Data collection	23
2.11 Proposed Data Analysis	23
2.12 The Gantt Chart	24
2.13 Study flowchart	25
2.14 Ethical Considerations	26
2.14.1 Subject vulnerability	26
2.14.2 Declaration of absence of conflict of interest	27
2.14.3 Privacy and Confidentiality	27

2.14.4 Community sensitivities and benefits	27
2.14.5 Honorarium and incentives	27
2.14.6 Ethics Approval	28
Chapter 3 Manuscript.....	32
3.1 Title Page	32
3.2 Abstract.....	33
3.3 Introduction.....	35
3.4 Material and Method	36
3.4.1 Study Design, respondent, and randomisation.....	36
3.4.2 Measurement of primary and secondary outcomes	37
3.4.3 Sample Size.....	38
3.4.4 Statistical analysis.....	38
3.5 Results.....	38
3.5.1 Demographic and Clinical Characteristic	39
3.5.2 Rate of Increasing Intraabdominal Pressure	39
3.5.4 Surgical Space Condition.....	39
3.5.5 Post Operative Pain Score.....	39
3.6 Discussion.....	42
3.6.1 Demographic.....	42
3.6.2 Intraabdominal Pressure	42
3.6.3 Surgical Space Condition.....	43
3.6.4 Pain	44

3.7 Conclusion	46
3.8 References.....	47
3.9 List of Table and Figures	51
Chapter 4 The Malaysian Journal of Medical Sciences, Guidelines for Authors.....	58
APPENDICES	77
Appendix A- Data Collection Form.....	78
Appendix B Patients Informed Consent Form.....	79
Appendix C- Raw Data In SPSS.....	94

LIST OF TABLES

Table 1 : Literature Review	5
Table 2 : Sample size calculation based on objective.....	12
Table 3 : Demographic	52
Table 4: Rate of increasing intraabdominal pressure.....	53
Table 5: Highest intrabdominal pressure(mmHg)	53
Table 6: Surgical Space Condition	54
Table 7: Abdominal Pain Score between Deep NMB and Moderate NMB.....	55
Table 8: Multiple comparison on mean abdominal pain score over time between deep NMB and moderate NMB.....	55
Table 9: Shoulder Tip Pain Score between Deep NMB and Moderate NMB.....	56
Table 10: Multiple comparison on mean shoulder tip pain score over time between deep NMB and moderate NMB.....	57

LIST OF FIGURES

Figure 1: Neuromuscular Monitoring	20
Figure 2 : Numerical Rating Scale for pain	21
Figure 3 : ASA classification.....	22
Figure 4: Gantt Chart	24
Figure 5: Study Flowchart	25
Figure 6: Study flowchart according to CONSORT guideline.....	51
Figure 7: Plot Line for pain score between deep NMB and moderate NMB.	55
Figure 8 : Plot Line for shoulder tip pain score between deep NMB and moderate NMB	56

LIST OF SYMBOLS AND ABBREVIATIONS

ASA	American Society of Anaesthesiology
NMB	Neuromuscular Block
TOF	Train of Four
PTC	Post Tetanic Count
HUSM	Hospital Universiti Sains Malaysia
=	equal to
±	standard deviation
<i>p</i>	<i>p</i> -value
°	degree
%	percent
<	less than

APPENDICES

APPENDIX A	Data Collection Form
APPENDIX B	Patient Informed Consent Document
APPENDIX C	Raw SPSS Data In CD

ABSTRAK

Pengenalan

Kesan ketara sekatan otot kuat dalam pembedahan laparoscopi masih didalam perbincangan dan siasatan terutamanya dalam pembedahan laparoscopi tekanan rendah. Dalam kajian ini, kami menyiasat kesan sekatan otot kuat pada penggunaan tekanan perut, kualiti ruang pembedahan, sakit perut selepas pembedahan dan sakit hujung bahu selepas pembedahan dalam pembedahan ginekologi laparoscopi.

Kaedah

Kajian ini adalah kajian secara rawak dan terkawal sama ada sekatan otot sederhana (TOF) 1 atau 2) sekatan otot kuat(post tetanic(PTC) 1 atau 2). Dalam kedua-dua kumpulan, rocuronium digunakan. Rocuronium digunakan secara yang berselang-seli digunakan dalam sekatan otot sederhana manakala infusi intravena digunakan untuk mengekalkan sekatan otot kuat. Sekatan otot kedua dua kumpulan dikembalikan dengan sugammadex. Pada permulaan pembedahan, tekanan dalam perut ditetapkan pada 8 mmHg. Pakar bedah dibenarkan untuk meningkatkan tekanan didalam perut jika keadaan pembedahan tidak memuaskan . Keadaan pembedahan dinilai pada skala 4 mata (1: cemerlang, 2: baik tetapi tidak optimum, 3: lemah tetapi boleh diterima, 4: tidak boleh diterima) pada akhir pembedahan. Sakit perut selepas pembedahan dan sakit hujung bahu dinilai menggunakan skala penarafan berangka untuk kesakitan. 0 ditakrifkan sebagai tiada kesakitan hingga 10-sakit teruk di kawasan pemulihan (masa 0), 30 minit dan 24 jam selepas pembedahan.

Keputusan

Seramai 70 pesakit telah menyertai kajian ini. Tiada perbezaan dalam kadar peningkatan tekanan intraabdominal antara dua kumpulan p-value: 0.172. Pembedahan dengan

sekatan otot kuat berjaya dilengkapkan dengan tekanan perut yang lebih rendah dengan purata penggunaan tekanan perut tertinggi 10.31mmHg (1.39) manakala 11.54mmHg (1.69) pada sekatan otot sederhana. Purata skor keadaan ruang pembedahan adalah lebih baik secara signifikan dalam kumpulan sekatan otot kuat pada 2.4(0.7) berbanding tekanan otot sederhana pada 3.2(0.66), $p < 0.005$. Terdapat skor sakit perut selepas pembedahan yang jauh lebih rendah dalam sekatan otot kuat tetapi tidak terdapat perbezaan yang signifikan dalam skor sakit hujung bahu antara dua kumpulan.

Kesimpulan

Tekana otot kuat membolehkan penggunaan tekanan dalam perut yang lebih rendah dalam pembedahan laparoscopi tanpa mengganggu keadaan ruang pembedahan dan mengurangkan skor sakit perut selepas pembedahan dalam 24 jam berbanding dengan sekatan otot sederhana.

ABSTRACT

Introduction

The significant effect of deep neuromuscular block in laparoscopic surgery is still controversial and under investigation especially in lower pressure laparoscopic surgery. In this study, we investigate the effect of deep neuromuscular block on intraabdominal pressure, surgical space quality, post operative abdominal pain and post operative shoulder tip pain in laparoscopic gynaecological surgery.

Material and method

This is a randomized, double blinded control trial which randomized the patient to either the moderate NMB (train-of-four count (TOF) of 1 or 2) or deep NMB (post tetanic count(PTC) of 1 or 2). In both groups, rocuronium was used. Intermittent bolus of rocuronium was use in moderate NMB while intravenous infusion was used to sustain neuromuscular blockade in deep NMB. Each group was then reversed with sugammadex. At the beginning of surgery, the intra-abdominal pressure was set at 8 mmHg. Surgeon was allowed to increase the intraabdominal pressure if the surgical condition was unfavourable. Surgical condition was rated on a 4- point scale (1: excellent, 2: good but not optimum, 3: poor but acceptable, 4: unacceptable) at the end of surgery. Post operative abdominal pain and shoulder tip pain was assessed using numerical rating scale for pain. Score 0 define as no pain to 10 as severe pain at recovery area as time 0, 30 minutes and 24 hours post operative.

Results

A total of 70 patient completed the study. There was no difference in rate of increasing intraabdominal pressure between two groups (p-value: 0.172), but deep NMB required less pneumoperitoneum to complete the surgery with mean highest intraabdominal

pressure of 10.31mmHg (1.39) whereas 11.54mmHg (1.69) in the moderate NMB. Mean surgical space condition score was significantly better in deep NMB group at 2.4(0.7) compared to moderate NMB at 3.2(0.66), ($p<0.005$). There was significantly lower post operative abdominal pain score in deep NMB but there is no significant difference in shoulder tip pain score between two groups.

Conclusion

Deep NMB enable the usage of lower intraabdominal pressure in laparoscopic surgery without interfering with surgical space condition and reduce the post operative abdominal pain score in 24 hours compare to moderate NMB

CHAPTER 1

INTRODUCTION

1.1 Background

Laparoscopic surgery has increasing popularity and slowly replacing conventional open surgery as it offers more benefit to patient and health care practitioner. The overall risk of complications during laparoscopic surgery is known to be lower than during laparotomy. Laparoscopic hysterectomy compared to open vaginal hysterectomy reduces postoperative pain, reduce post op analgesics requirement and shorter duration of hospital admission.(1)

1.2 Problem Statements

Traditionally pneumoperitoneum was created at 15mmHg.(2) High intra-abdominal pressure created during laparoscopic surgery can affect cardiovascular, pulmonary, and renal physiology. Besides the risk of post-operative nausea and vomiting, it is also stated that the pneumoperitoneum created during laparoscopic surgery is an important factor in the cause of postoperative shoulder pain.(3). Insufflation of intraabdominal carbon dioxide may cause post-operative shoulder pain up to 70% in some study in gynaecologic laparoscopic surgery. (4)

The usage a lower pressure pneumoperitoneum might decrease postoperative pain, decrease post-operative shoulder tip pain(5) and reduce the risk of laparoscopic related complication.(6) Many studies used lower insufflation of intraabdominal pressure as an intraoperative intervention to reduce the complication. (7), (6) However, a lower intraabdominal pressure may impair surgical space and increase the risk of conversion to open surgery.

Though many factors contribute to the quality of surgical space include non-modifiable such as obesity, previous abdominal surgery, and modifiable factors such as anaesthesia related factor, patient position and intraabdominal pressure. Numerous studies also have been carried out showing that deep neuromuscular block improves surgical condition in different type of laparoscopic surgery includes laparoscopic gynaecology surgery and robotic assisted laparoscopic surgery. (Kim et al., 2016), (9), (10).

1.3 Aim

The primary aim of this study is to determine the rate of increasing intraabdominal pressure use in laparoscopic gynaecology surgery when it started with low pressure pneumoperitoneum between patient that been paralyze using deep neuromuscular block (Deep NMB) and moderate neuromuscular block (Moderate NMB). Thus, to determine whether the usage of deep neuromuscular block help in reducing intrabdominal pressure use during laparoscopic surgery without interfering the surgeon surgical view. Next aim is to investigate whether the use of deep neuromuscular block improve surgical condition compared to moderate neuromuscular block. Finally, this study also aims to assess post operative pain and shoulder tip pain between these two groups for 24 hours post operatively.

1.4 Significant of the study

Laparoscopic surgery increases tremendously in the past decade in the era of enhance recovery after surgery (ERAS), despite its many advantages increase intraabdominal pressure by intraabdominal carbon dioxide inflation produce respiratory, cardiac side effect. There are previous studies done that show deep neuromuscular blockage in laparoscopic surgery increase quality of surgical view in upper abdominal surgery, bariatric surgery, and extraperitoneal surgery like nephrectomy. However, there are still a lot of heterogeneity in previous study to compare superiority of deep neuromuscular

block than moderate neuromuscular block. There is also lack of study in local clinical health care setting pertaining this subject. Therefore, further studies are still required to evaluate the benefit of deep neuromuscular block especially in local population.

1.5 Literature Review

In the past decade, many studies have been done to evaluate the benefit of deep neuromuscular blocker in many types of laparoscopic surgery such as to the surgical space quality, duration of operation, post-operative pain, and intraoperative complications.

Dubois et. Al in 2014 compare the surgical condition in deep neuromuscular block and shallow neuromuscular block in laparoscopic hysterectomy using 4-point surgical scale. It shows that better surgical rating scale in deep neuromuscular block. In 98 of the subjects 34 of subject show excellent surgical condition where only 21 patients in shallow group score excellent.(11)

Madsen et. Al had done multiple randomized controlled trial in 2015 and 2016 evaluating different outcome comparing deep neuromuscular block and moderate neuromuscular block in laparoscopic gynaecological surgery. In 2015, they investigated whether deep neuromuscular block compared with no neuromuscular block would increase surgical space by measuring distance from sacral promontory to the inserted trocar at pneumoperitoneum of 12 mmHg and 8mmHg.(10) At 12 mmHg pneumoperitoneum, deep neuromuscular block improved surgical space with a mean of 0.33 cm (95% confidence interval 0.07–0.59) ($P = 0.01$) which is statistically insignificant but at 8mmHg deep neuromuscular block significantly improved surgical space with a mean of 0.3 cm (95% confidence interval, 0.06–0.54) ($P = 0.005$). in this study, surgical condition during suturing fascia in deep neuromuscular block is significantly better

compared to moderate block($p=0.03$) estimated by the gynaecologist on a 4-point subjective rating scale.

In the next randomized controlled study, Madsen study the incidence of post-operative shoulder tip pain and recovery after laparoscopic hysterectomy in low pressure pneumoperitoneum 8mmHg with deep neuromuscular block (post tetanic count 0 to 1) compared with standard-pressure pneumoperitoneum (12 mmHg) with moderate neuromuscular block. In this study the incidence of shoulder tip pain is significantly reduce in group lower pneumoperitoneum with deep neuromuscular block ($p = 0.34$) after 4 days but after 14 days, the p value is 0.74 which is insignificant.(3)

Meta-analysis in 2017 by M. H. Bruintjes include seven studies pooled in analyses surgical space condition. Overall surgical space condition improved in deep neuromuscular block by mean difference of 0.65 (95% CI: 0.47–0.83) on a scale of 1–5. Between study heterogeneity was 46%. In this meta-analysis also, 5 studies pooled to analyse post-operative pain in the post anaesthesia care unit (PACU) during the first hour after surgery, which show overall significant reduction of early postoperative pain in the group with deep neuromuscular blockage by mean difference 0.52 (95% CI: –0.71 to –0.32) on an 11-point scale. (12)

Subsequent meta-analysis in 2018 by park et al analyse eleven RCTs involving 844 patients. The frequency of excellent or good operating conditions was higher with deep block compared with a moderate block (odds ratio 2.83, 95% confidence interval 1.34 to 5.99, $P = 0.007$, $I^2 = 59\%$). However further studies are required to address the heterogeneity.(13)

Recent meta-analysis in 2020 includes eight study in analysis of the surgical space conditions which provides evidence that low intraabdominal pressure+ deep

neuromuscular block does improve surgical space conditions compared with low intraabdominal pressure + moderate neuromuscular block however there is no difference in post-operative pain and duration of surgery.(14) However different intraabdominal pressure used, and degree of neuromuscular blocker use is different which make the study cannot have a solid conclusion which protocol is preferable. All meta-analysis conclude that we still need further randomized controlled studies are warranted to address the heterogeneity and power shortage demonstrated by the meta-analysis.

Table 1 : Literature Review

Article code [no.]	Laparoscopic procedure	NMB level experimental group	NMB level control group	Number of patients	Surgical rating scale	Other outcome measure
Dubois ¹³ 2014	Hyst	Deep	Shallow	100	1–4	Duration
Martini ¹⁸ 2014	Prost/Nephr	Deep	Moderate	24	1–5	Duration, pain, comp
Staehr-Rye ¹⁹ 2014	Chol	Deep	Moderate	48	1–4	Dur, pain, Intraabdominal pressure
Yoo ²⁰ 2015	Prost	Deep	Moderate	66	1–5	Duration, pain, intraabdominal pressure comp
Madsen ⁹ 2015	Gyn	Deep	No NMB	14	1–4	Intraabdominal pressure

Table 1: Continue

Blobner 2015 ²¹	Chol	Deep	No NMB	50	0– 100%	Duratio n, pain, IAP, comp
Barrio 2016 ²²	Chol/Gyn	Deep	Moderate	41	NA	
Kim 2016 ⁹	Colorectal	Deep	Moderate	61	1–5	Dur, pain, LOS, IAP, comp
Koo 2016 ¹⁰	Chol	Deep	Moderate	64	1–4	Dur, pain, IAP, comp
Madsen 2016 ¹⁴	Hyst	Deep	Moderate	99	NA	Dur, pain, LOS, IAP, comp
Torens ma 2016 ²³	RYGB	Deep	Moderate	100	1–5	Duratio n, pain
Ozdemi r 2017 ¹²	Donor nephrectom y	Deep	Moderate	34	1-5	Pain, abdomi nal pressur e

CHAPTER 2

STUDY PROTOCOL

2.1 General Objective

To evaluate the effect of deep neuromuscular blockade on surgical conditions during laparoscopic gynaecological under low-pressure pneumoperitoneum.

2.2 Specific Objectives

1. To compare the rate of increasing intra-abdominal pressure (IAP) by the surgeon when they decide that the surgical conditions are inadequate for the operation in patient receiving deep neuromuscular block compared to moderate neuromuscular block in laparoscopic gynaecological surgery.
2. To compare quality of surgical space condition in patient receiving deep and moderate neuromuscular block in laparoscopic gynaecological surgery.
3. To compare skin to sacral promontory distance in patient in patient receiving moderate neuromuscular block and deep neuromuscular block in laparoscopic gynaecological surgery.
4. To compare the post-operative pain and shoulder tip pain in patient receiving deep neuromuscular block and moderate neuromuscular block in laparoscopic gynaecological surgery

2.3 Null hypothesis

1. There is no significant difference in rate of increasing intra-abdominal pressure (IAP) by the surgeon when they decide that the surgical conditions are inadequate for the operation in patient receiving deep neuromuscular block compared to moderate neuromuscular block in laparoscopic gynaecological surgery.
2. There is no difference in quality of surgical space condition in patient receiving deep and moderate neuromuscular block in laparoscopic gynaecological surgery.
3. There is no difference in skin to sacral promontory distance in patient in patient receiving moderate neuromuscular block and deep neuromuscular block in laparoscopic gynaecological surgery.
4. There is no significant difference in the post-operative pain and shoulder tip pain in patient receiving deep neuromuscular block and moderate neuromuscular block in laparoscopic gynaecological surgery.

2.4 Research Methodology

2.4.1 Research design

Single Centre, double blinded randomized controlled trial.

In Hospital Universiti Sains Malaysia, the patient that fulfill inclusion criteria is randomized in a double-blind, randomize control trial comparing the rate of increasing intraabdominal pressure in low pressure pneumoperitoneum in laparoscopic gynecological study.

2.4.2 Sampling Method

Sample are randomized either in moderate group or deep group by simple randomization. Surgeon and participant are blinded to the study either in moderate or deep groups.

2.4.3 Study period

October 2020 – June 2022 (18 months)

2.4.4 Sampling time frame

October 2020 – October 2021(12 months)

2.4.5 Study location

Single Center-Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan

2.4.6 Study Population

1. Adult patient more than 18 years old underwent laparoscopic gynaecological surgery (laparoscopic hysterectomy, laparoscopic ovarian cystectomy, laparoscopic myomectomy, laparoscopic salpingectomy) in Hospital Universiti Sains Malaysia , Kubang Kerian, Kelantan
2. Sampling frame: Adult patient more than 18 years old, ASA I and ASAILI underwent laparoscopic gynaecological surgery (laparoscopic hysterectomy,

laparoscopic ovarian cystectomy, laparoscopic myomectomy, laparoscopic salphingectomy in Hospital Universiti Sains Malaysia , Kubang Kerian, Kelantan.

2.5 Subject Criteria

2.5.1 Inclusion criteria

1. Age more than 18 years old
2. ASA I or II
3. Patient underwent laparoscopic gynaecological surgery (laparoscopic hysterectomy, laparoscopic ovarian cystectomy, laparoscopic myomectomy, laparoscopic salpingectomy) in Hospital Universiti Sains Malaysia , Kubang Kerian, Kelantan.

2.5.2 Exclusion Criteria

1. Allergy to study drugs (rocuronium, suggamadex)
2. Serious cardiac and respiratory disease (reactive airway disease, upper respiratory tract infection)
3. Neurological or neuromuscular disease (epilepsy, family history and history of malignant hyperthermia etc.)
4. Pregnancy
5. Morbid obesity BMI>35

2.5.3 Withdrawal criteria

Conversion to open surgery

2.6 Sample Size Estimation

We used PS Power and Sample Size Calculations, Version 3.0, January 2009 and G*Power software (Version 3.1.9.2, Copyright © 1992-2014 by Franz Faul, Universitat Kiel, Germany) to estimate sample size. The calculation of sample size for each of the specific objectives as table below:

Table 2 : Sample size calculation based on objective

Specific objective	Statistical test	Sample size determination
1. Rate of increasing intraabdominal pressure	Chi-squared Test /Dichotomous	-Type 1 error: 0.05 -Power 0.8 -Po (control subject): 0.6 based on previous study by Dubois et al.(11) -P1 (study subject): 0.9 based on previous study Dubois et. all -We are planning a study of independent cases and controls with 1 control(s) per case. -We will need to study 32 experimental subjects and 32 control subjects to be able to reject the null hypothesis that the failure rates for experimental and control subjects are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05. We will use an uncorrected chi-squared statistic to evaluate this null hypothesis.

2. Surgical space T.test
quality

-With addition of 10% drop out, we need 70 sample to evaluate null hypothesis.

-Software: power sample size calculation size app.

-Type I error = 0.05

-Power = 0.8

-True difference of surgical space quality between group Moderate (control) and deep group is 0.5 based on previous study.(15)

-Standard deviation of surgical space quality is 0.4 on a prior study (15)

-Ratio of control to experimental patients = 1:1

-If the true difference in the experimental and control means is 0.5, we will need to study 11 experimental subjects and 11 control subjects to be able to reject the null hypothesis that the population means of the experimental and control groups are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05.

-Include 10% drop out we need 24 subjects to reject null hypothesis

-Software: PS – Power and Sample Size Calculation

3. Sacral promontory distance	T test	-Type I error = 0.05 -Power = 0.8 -True difference of sacral promontory distance between group Moderate (control) and deep group is 0.38 based on previous study.(16) -Standard deviation of surgical space quality is 0.5 based on a prior study.(16) -Ratio of control to experimental patients = 1:1 -In a previous study the response within each subject group was normally distributed with standard deviation 0.5. If the true difference in the experimental and control means is 0.38, we will need to study 28 experimental subjects and 28 control subjects to be able to reject the null hypothesis.(16) -Include 10% drop out. we need 62 sample to reject null hypothesis. -Software: PS – Power and Sample Size Calculation
4. Post-operative pain	T test	-Type I error = 0.05 -Power = 0.8 -True difference of pain score between group Moderate (control) and deep group is 1 based on previous study.(17)

-Standard deviation of surgical space quality is 1.4 on a prior study.(17)

-Ratio of control to experimental patients = 1:1

- In a previous study the response within each subject group was normally distributed with standard deviation 1.4. If the true difference in the experimental and control means is 1, we will need to study 32 experimental subjects and 32 control subjects to be able to reject the null hypothesis that the population means of the experimental and control groups are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05.

-Include 10% drop out. we need 70 sample to reject null hypothesis.

-Software: PS – Power and Sample Size Calculation

Objective 1 require highest sample to reject null hypothesis. To reject all the specific objective, the study needs 35 sample in moderate group and 35 sample in deep group to reject all the null hypothesis. Total 70 samples are required.

2.7 Sampling method and subject recruitment

- Approval from Ethics Committee of University Sains Malaysia (USM) health campus were obtained prior to the recruitment of the patients.
- Patient listed to underwent laparoscopic gynaecological surgery, are received 1 day prior to operation day.
- Potential adult patients were selected according to inclusion and exclusion criteria one day before operation done by principal investigator.
- Detailed explanation regarding study procedures were explained and written inform consents were obtained from patients by principal investigator one day before the operation.
- The fasting time for all patients at least 6 hours prior to surgery
- All consented patients were randomly assigned into two group:
 - Group 1 (Induction with rocuronium 0.6mg/kg + maintenance with intravenous infusion rocuronium 8-12mcg/kg/minute (0.48-0.72 mg/kg/hour maintain PTC 0-1(deep block). (Study Group)
 - Group 2 (Induction with rocuronium 0.6mg/kg + maintenance with intermittent rocuronium 0.2mg/kg bolus. Maintain PTC >1, TOF 0-2). Moderate block. (Control Group)
- In operation room, baseline measurement of non-invasive blood pressure, mean arterial pressure, heart rate, pulse oximeter, electrocardiogram and oxygen saturation were monitored at time T₀
- Prior to induction of anaesthesia, intravenous cannula inserted and either 0.9% sodium chloride or Ringer's lactate solution were commenced.

- General anaesthesia was commenced to both group with bolus intravenous fentanyl 100mcg, intravenous propofol 2mg/kg, intravenous rocuronium 0.6mg/kg as induction agent. Then intubate with PVC endotracheal tube.
- Neuromuscular monitoring at ulnar nerve was attached to both groups using TOF watch, intubation at TOF 0
- Anaesthesia was maintained with inhalational anaesthetic agent at minimum alveolar concentration (MAC 1.0)
- Surgical team was blind to the medication. Unblind investigator was responsible for drug administration and neuromuscular monitoring
 - Group 1 (Induction with rocuronium 0.6mg/kg + maintenance with intravenous infusion rocuronium intravenous infusion rocuronium 8-12mcg/kg/minute (0.48-0.72 mg/kg/hour. Maintain PTC 0-1)
 - Group 2 Induction with rocuronium 0.6mg/kg + maintenance with intermittent rocuronium bolus. Maintain PTC >1, TOF 0-2)
- Pneumoperitoneum was created initial at 8mmHg
- Intravenous paracetamol 1g given after induction, and intravenous morphine 0.05mg/kg given
- After the insertion of trocha, intraabdominal pressure was set at 8mmHg. Skin sacral promontory distance was measured with the laparoscopic grasper through the trocha which inserted infraumbilically in 25-degree Trendelenburg position. A sterile ruler was used to measure the distance from surgeon's mark to the end of grasper in centimetres.
- After the measurement, surgical procedure was continued as usual with intraabdominal pressure 8mmHg.

- There surgeon was allowed to change IAP to 10mmhg or 12mmhg if they decide that visual field is inadequate for the operation.
- At the end of surgery, infusion drug discontinued, and neuromuscular drug was reverse with Suggamadex base on TOF count for both groups.
- At the end of operation, surgeon rated the surgical condition at 4-point scale (1= excellent, 2= good, 3=acceptable, 4= poor)
- Intravenous dexamethasone 4mg was given after induction, and intravenous ondansetron was given 30 minutes after the end of surgery for anti-emetic.
- The entire laparoscopic surgery and intra-abdominal pressure levels were recorded to enable any subsequent analysis if necessary.
- Post operatively at Post anaesthesia care unit, post op pain and shoulder tip pain were evaluated at 30 minute and 24-hour Post operatively. Fentanyl was injected intravenously as needed in post anaesthesia care unit and dose will be recorded)
- Pain was measured using an 11-point numerical rating scale (NRS), ranging from 0 (no pain) to 10 (most pain imaginable).
- Postoperatively patient was monitored at recovery bay operation theatre for at least 30 minutes before discharge as standard post-operative monitoring before discharge to ward. Patient was monitor with continuous vital sign monitoring like standard post-operative procedure.
- The intubation procedure, anaesthesia conduct and extubating procedure was similar using standard procedure as normal general anaesthesia delivered to patient.

2.8 Research tool

1. TOF-Watch® SX- acceleromyography
2. Infusion pump
3. Data collection sheet
4. Standard monitoring devices such as non-invasive blood pressure, pulse oximetry(spO2), end-tidal carbon dioxide (etCO2) and electrocardiography (ECG) were used to ensure patient safety.
5. Standard General anaesthesia machine in operation theatre and standard laparoscopic set for surgeon to perform surgery.

2.9 Operational Definition

1. Neuromuscular monitoring will be placed on patient ulnar nerve.

Figure 1: Neuromuscular Monitoring

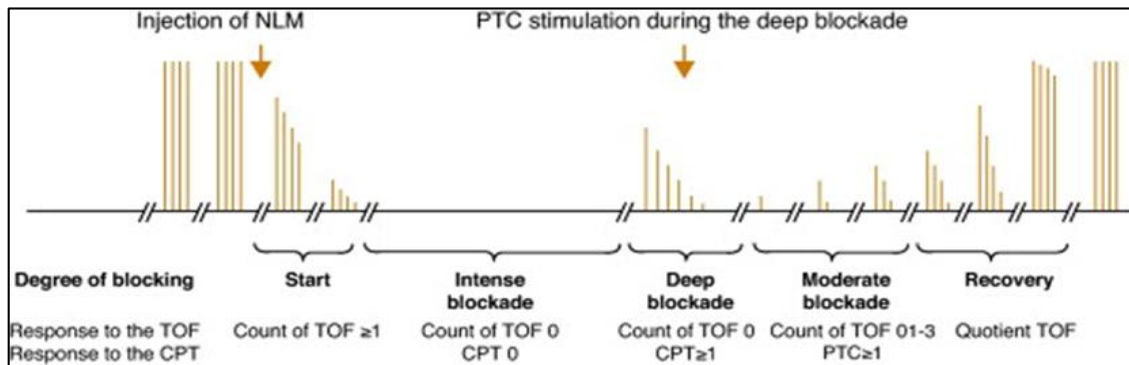


Table from: Joaquín Fabregat López, César Augusto Candia Arana, Caridad Greta Castillo Monzón, [Neuromuscular monitoring and its importance in the use of neuromuscular blockers](#), Colombian Journal of Anesthesiology, Volume 40, Issue 4, November – December 2012, Pages 293-303.

2. Moderate blocks define as train of four (TOF) 0-2 and Post tetanic count (PTC) > 1 whereas Deep block define as TOF 0 and PTC 0-1).
3. Low pressure pneumoperitoneum is defined as intraabdominal pressure 8mmHg. Rate of increasing intraabdominal pressure define as rate of conversion of intraabdominal pressure from 8mmHg to 10mmhg, 12mmhg.
4. Quality of surgical space condition define as 1: excellent, 2: good but not optimum, 3: poor but acceptable, 4: unacceptable.(11)
5. Numerical rating scale for pain. 0 define as no pain to 10-severe pain.

Figure 2 : Numerical Rating Scale for pain

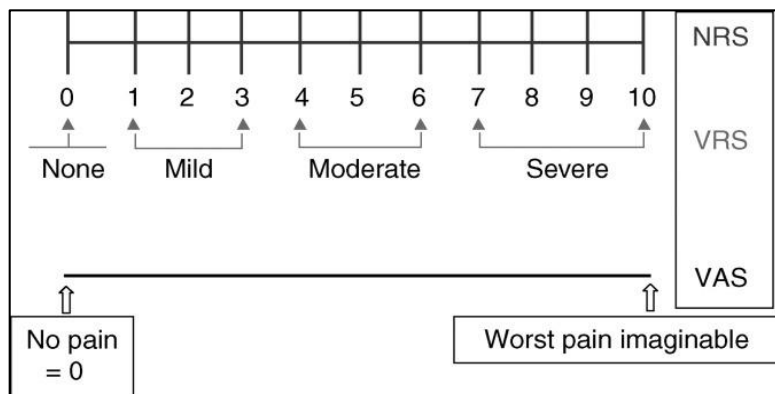


Table from: H. Breivik, P.C. Borchgrevink, S.M. Allen, L.A. Rosseland, L. Romundstad, E.K. Breivik Hals, G. Kvarstein, A. Stubhaug, Assessment of pain, British Journal of Anaesthesia, Volume 101, Issue 1, 2008, Pages 17-24, ISSN 0007-0912, <https://doi.org/10.1093/bja/aen103>.(<https://www.sciencedirect.com/science/article/pii/S0007091217342630>)

6. ASA classification

Figure 3 : ASA classification

ASA PS Classification	Definition	Adult Examples, Including, but not Limited to:	Pediatric Examples, Including but not Limited to:	Obstetric Examples, Including but not Limited to:
ASA I	A normal healthy patient	Healthy, non-smoking, no or minimal alcohol use	Healthy (no acute or chronic disease), normal BMI percentile for age	
ASA II	A patient with mild systemic disease	Mild diseases only without substantive functional limitations. Current smoker, social alcohol drinker, pregnancy, obesity (30<BMI<40), well-controlled DM/HTN, mild lung disease	Asymptomatic congenital cardiac disease, well controlled dysrhythmias, asthma without exacerbation, well controlled epilepsy, non-insulin dependent diabetes mellitus, abnormal BMI percentile for age, mild/moderate OSA, oncologic state in remission, autism with mild limitations	Normal pregnancy*, well controlled gestational HTN, controlled preeclampsia without severe features, diet-controlled gestational DM.
ASA III	A patient with severe systemic disease	Substantive functional limitations; One or more moderate to severe diseases. Poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, history (>3 months) of MI, CVA, TIA, or CAD/stents.	Uncorrected stable congenital cardiac abnormality, asthma with exacerbation, poorly controlled epilepsy, insulin dependent diabetes mellitus, morbid obesity, malnutrition, severe OSA, oncologic state, renal failure, muscular dystrophy, cystic fibrosis, history of organ transplantation, brain/spinal cord malformation, symptomatic hydrocephalus, premature infant PCA <60 weeks, autism with severe limitations, metabolic disease, difficult airway, long term parenteral nutrition. Full term infants <6 weeks of age.	Preeclampsia with severe features, gestational DM with complications or high insulin requirements, a thrombophilic disease requiring anticoagulation.
ASA IV	A patient with severe systemic disease that is a constant threat to life	Recent (<3 months) MI, CVA, TIA or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, shock, sepsis, DIC, ARD or ESRD not undergoing regularly scheduled dialysis	Symptomatic congenital cardiac abnormality, congestive heart failure, active sequelae of prematurity, acute hypoxic-ischemic encephalopathy, shock, sepsis, disseminated intravascular coagulation, automatic implantable cardioverter-defibrillator, ventilator dependence, endocrinopathy, severe trauma, severe respiratory distress, advanced oncologic state.	Preeclampsia with severe features complicated by HELLP or other adverse event, peripartum cardiomyopathy with EF <40, uncorrected/decompensated heart disease, acquired or congenital.
ASA V	A moribund patient who is not expected to survive without the operation	Ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction	Massive trauma, intracranial hemorrhage with mass effect, patient requiring ECMO, respiratory failure or arrest, malignant hypertension, decompensated congestive heart failure, hepatic encephalopathy, ischemic bowel or multiple organ/system dysfunction.	Uterine rupture.
ASA VI	A declared brain-dead patient whose organs are being removed for donor purposes			

* Although pregnancy is not a disease, the parturient's physiologic state is significantly altered from when the woman is not pregnant, hence the assignment of ASA 2 for a woman with uncomplicated pregnancy.

**The addition of "E" denotes Emergency surgery: (An emergency is defined as existing when delay in treatment of the patient would lead to a significant increase in the threat to life or body part)

Source ASA classification system. Assessed on 22 April 2022. Available from [ASA Physical Status Classification System | American Society of Anesthesiologists \(ASA\) \(asahq.org\)](https://www.asahq.org/Physical-Status-Classification-System)

2.10 Data collection

Data collection done by the primary investigator using assessment form. The details filled in the form include patient general demographic data (age, gender, weight). surgical procedure, time of surgery, skin sacral promontory distance, intraabdominal pressure, surgical condition score, pain at 0-minute, 30 minute and 24 hour and fentanyl requirement.

2.11 Proposed Data Analysis

Data will be entered and analysed using SPSS version 26. Descriptive statistics will be used to summarise the socio-demographic characteristics of subjects. Numerical data will be presented as mean (SD) or median (IQR) based on their normality distribution. Categorical data will be presented as frequency (percentage). Paired sample t test will be use compare continuous variable where chi square test will be used to test proportion. Our first objective will be analysed using chi square test. Second objective will be analysed using independent t test whereas pain score will be analysed using repeated measure annova. The significant level is when p -value <0.05 .

2.12 The Gantt Chart

Figure 4: Gantt Chart

