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DEPARTMENT OF ANESTHESIA

THESIS SUBMITED IN PART OF FULFILLMENT THE REQUIREMENT FOR MASTER OF SCIENCE IN ADVANCED CLINICAL ANESTHESIA OF ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCE AND SCHOOL OF MEDICINE DEPARTMENT OF ANESTHESIA

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Full tittle of research project	Comparison of defasciculation dose pancronium and mini-dose succinylcholine for preventing succinylcholine induced muscle fasciculation and post operative myalgia among surgical patient: A prospective, cohort study
Duration of project	July, 1 to September 1, 2019 GC
Study area	menelik II referral hospital, Addis Ababa
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Declaration

I, the undersigned declare that this thesis is my original work in partial fulfillment of the requirements for the master of science degree in anesthesia .I understand that plagiarism will not be tolerated and all directly quoted material has been appropriately referenced

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Date of submission:_____

This thesis work has been submitted for examination with my/our approval as Advisors and tuore on the master of science degree in anesthesia.

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Abstract

Background: Succinylcholine is a depolarizing skeletal muscle relaxant that remains the accepted standard for facilitating endotracheal intubation. This medication may cause some adverse effects in patients such as hyperkalemia, malignant hyperthermia, increased intra gastric and intracranial pressure, fasciculation during induction, and postoperative myalgia. Although postoperative myalgia are commonly encountered problem they may be very unpleasant experiences for the patient till 24–48 h after surgery.

Objective: Comparison of defasciculation dose pancronium and mini-dose succinylcholine for preventing succinylcholine induced muscle fasciculations and post operative myalgia among surgical patient in menelik II referral hospital.

Methodology: An institutional based prospective cohort study conducted on 96 patients undergoing elective surgery were divided in three equal groups :After pretreatment with either 0.01mg/kg defasciculating dose of pancronium as Group (n= 32) , 0.2mg/kg mini dose succinylcholine and 1ml NS group , patients were anesthetized with a 3-5mg/kg of Thiopental followed by succinylcholine 2mg/kg. Data on baseline characteristics, incidence and severity of muscle Fasciculation and post operative myalgia (after 24 hours) were collected.

Results: The demographic data of patients in three groups were comparable. The total incidence of succinylcholine induced fasciculation were 17(53.1%) , 8(25%) and 30(93.8%) in pancronium, mini-dose of succinylcholine pretreatment and NS Groups respectively (p=0.000).The severity of fasciculation was reduced more in mini-dose succinylcholine compared with pancronium group (0.012) and Normal saline group (0.000).The total incidence of myalgia was 6(18.8%) 3(9.4%)and 9(28.1%) in pancronium , mini-dose of succinylcholine and Normal saline Groups respectively (p=0.158).There is no difference on the severity of myalgia between groups (p=0.161)

Conclusion and recommendation: pretreatment with mini dose of succinylcholine is effectively reduced the incidence and severity of succinylcholine induced fasciculation in comparison with pancronium and Normal saline group. but there was no difference in the incidence and severity of post operative myalgia between the three groups. We recommended to use mini dose of succinylcholine as a pretreatment to reduce succinylcholine induced fasciculation.

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LIST OF ACRONMY AND ABBRAVATION

ASA	American Society of Anesthesiologist
ANOVA	Analysis of variance
BMI	Body mass index
BSC	Bachelor of Science
C	Control group
D	Defasciculating dose of pancronium group
DMRs	Depolarizing muscle relaxants
GA	General Anesthesia
I.V	Intra venous
M	mini dose of succinylcholine group
NDMRs	Non-depolarizing muscle relaxants
NMBA	Neuromuscular blockade agent
POM	Post operative mayalgia
RSI	Rapid sequence induction
SCh	Succinylcholine
SIMF	Succinylcholine induced muscle fasciculation
SD	Standard deviation
SPSS	Statistical package for social science

CHAPTER ONE INTRODUCTION

1.1. BACKGROUND

Succinylcholine is a short acting depolarizing muscle relaxant with rapid onset and short duration of action. Its use is associated with a number of side effects like fasciculation, postoperative myalgia, increased serum levels of creatinekinase and potassium, malignant hyperthermia, myoglobinuria, raised intraocular pressure and intracranial pressure (1) Fasciculations during induction and post-operative myalgia are unpleasant consequence of the use of succinylcholine. which is not acceptable in today anesthesia practice. It may be a source of greater distress to the patient than the surgical wound pain (11). The postoperative myalgia is generalized aches and pains that commonly occur at the first 24 hours after succinylcholine administration that mimic the muscular pains which is usually following violent exercise(11).

The exact mechanism is not known but stimulation of presynaptic acetylcholine receptors and contraction of intrafusal fibers of muscle spindles may contribute. It has been suggested that the underlying mechanism of muscle damage associated with administration of Succinylcholine may involve calcium-induced phospholipids degradation with release of damaging products of fatty acid metabolism (13)

Different pre-treatment modalities have been attempted to reduce the incidence and severity of fasciculations and myalgia. This includes precurarization with a small dose of non-depolarizing muscle relaxant(2), mini does of succinylcholine as a pretreatment(2), pre succinylcholine use of lidocaine(3), calcium gluconate(4), magnesium sulphate(5), nonsteroidal anti-inflammatory drugs (NSAIDs)(6),dexmedetomidine(7), benzodiazepines(3), remifentanil (8), etc .The efficacy of each is variable.

None depolarizing neuromuscular blockers presumably block prejunctional nicotinic receptors and thus prevent fasciculations, producing a decrease in postoperative myalgia. Administration of a small dose of non depolarizing neuromuscular blocker before succinylcholine is commonly practiced to lessen the incidence and severity of postoperative myalgia (11). The likelihood of blocking succinylcholine-induced muscle fasciculations is greatest with d-tubocurarine, followed by atracurium, pancronium, and vecuronium, due to the greater affinity of these drugs for

prejunctional cholinergic receptors.(15) Also prevention of succinylcholine-induced muscle fasciculations can be achieved by the administration of a small dose of succinylcholine used as a pretreatment before the subsequent full dose used for neuromuscular blockade for intubation, the effect of small dose succinylcholine pretreatment dose may be attributed to the induction of neuromuscular desensitization.(11) There are several advantages to succinylcholine pretreatment. First, pretreatment with NDMB may cause heavy eyelids, ptosis, blurred vision, diplopia, difficulty breathing, swallowing and speaking; bronchoconstriction caused by histamine release, and intensified need for a higher dose of succinylcholine, although succinylcholine pretreatment may not influence the patient's status during intubation (11).Even though a lot of researchers try to alleviate this problem they come with different result and other intolerable side effects (26), so that is why we eager to underwent this study to compare the effect of mini dose succinylcholine in comparison of defasciculation dose of pancronium for prevention of fasciculation and post operative myalgia.

1.2. STATEMENT OF THE PROBLEM

Succinylcholine has been a commonly used muscle relaxant for endotracheal intubation of surgical patients as it acts rapidly and has a short duration of action. It has been associated with a number of side effects e.g. fasciculation and postoperative myalgia, bradycardia, hyperkalemia and malignant hyperthermia. However, fasciculation immediately after induction of anesthesia and subsequent myalgia in postoperative period outnumber the rest.

Succinylcholine-induced fasiculation increase in intragastric pressure is thought to be a result, in part, of the fasciculation of abdominal muscles and a direct increase in vagal tone. it also increase in intra-ocular pressure.The cause is multifactorial, including increases in choroidal blood volume, extra-ocular muscle tone and aqueous humour out flow resistance.(12)

The reported incidence of Fasciculation is 95% of patients and succinylcholine-induced myalgia is around 50% (26). The duration of the discomfort is highly variable. It usually lasts for 2 or 3 days but occasionally persists for as long as a week. It usually appears on the first day after surgery, is most commonly described as the pain one might suffer after an unaccustomed degree of physical exercise, and is usually located in the neck, shoulder and upper abdominal muscles. It is generally agreed that iatrogenic postoperative myalgia is unacceptable in modern anaesthetic practice (10).

These side effects are very distressing for the patients especially for day case patients because postoperative myalgia may delay their discharge from the hospital(10).The pathophysiology of succinylcholine induced myalgia is poorly understood, that is why there is no standard treatment available for this complication.

In clinical practice the use of mini dose succinylcholine and defasciculation dose of pancronium produced conflicting results regarding to the effectiveness on preventing succinylcholine induced muscle fasciculations and post operative myalgia. Rasheed A(20) found a lower incidence of succinylcholine induced muscle fasciculations in mini dose succinylcholine compared with defasciculation dose of pancronium .while other study stated that Pretreatment with pancronium

decreased the incidence and severity of fasciculations significantly compared with mini-dose succinylcholine (15).

Therefore pretreatment with mini dose succinylcholine and pancronium are simple and routinely practiced in our setup. This can be the solution to select better pretreatment modality which minimum succinylcholine induced fasciculation and post operative myalgia.

1.3. SIGNIFICANCY OF THE STUDY

Although several regimens or pretreatments have been tried in an effort to decrease the incidence or severity of fasciculation and myalgia with succinylcholine, the effectiveness of such measures is debatable. most researcher found a lower incidence of succinylcholine induced fasciculation in defasciculation dose of pancronium than mini dose succinylcholine while other studies have found that mini dose is more effective or succinylcholine pretreatment yielded results identical to pretreatment with pancronium (15,17,20).So, the aim of our study is to prove this conflicting result.

Succinylcholine and pancronium widely available in our setup and applicable universally and easily so this study has provided rational and evidence-based case specific practical frame work that reduce the incidence of postoperative myalgia and fasciculation. it also make our patient more beneficiary by alleviating postoperative myalgia which suffers them post operatively and also decrease post operative analgesic consumption.

We hope that further comparative studies with similar design would have an impact on the future standard practice.

CHAPTER TWO

2.1. LITERATURE REVIEW

Study in Christian Medical College, Ludhian a, Punjab, India the study was conducted on 120 patients in the age group of 20-40 years of either sex belonging to ASA grade I or II. They were divided into two groups, Group R patients were given Rocuronium 0.06mg /kg and Group V patients were given vecuronium 0.01mg.kg intravenously 60seconds before the administration of thiopentone followed by succinylcholine.26 (43.3%) patients had mild fasciculation and 5(8.3%) patients had moderate fasciculation in Group V. 19(31.7%) patient had mild fasciculation and none of the patients had moderate fasciculation in Group R. Statistical analysis showed that fasciculations seen after succinylcholine chloride were significantly less in Rocuronium than Vecuronium group ($P< 0.01$). 3(5%) patients had mild myalgia and none of the patient had moderate or severe myalgia on the first post-operative day in Group V.6(10%) patients had mild myalgia and none of the patients had moderate or severe myalgia in Group R. statistical analysis showed that Both groups did not have statistically significant myalgia on the 1st post-operative day($p>0.01$).(24)

Study conducted in Institute of Liver and Biliary Sciences, New Delhi, India A total of 120 patients undergoing laparoscopic cholecystectomy were randomly assigned into three groups: Pregabalin group received 150 mg of pregabalin, gabapentin group received 600 mg of gabapentin and diclofenac group received 100 mg of diclofenac sodium orally 2 h prior to surgery. The myalgia occurred in 15(37.5%), 14(35%) and 13(32.5%) patients in pregabalin, gabapentin and diclofenac sodium group respectively ($P> 0.85$).Pre-treatment with pregabalin, gabapentin and diclofenac had equal efficacy in reducing the incidence and severity of succinylcholine-induced myalgia. (22)

Study in Himalayan Institute of Medical Sciences, Dehradun, India on 64 patients in Group P (pregabalin group) received 150 mg of pregabalin orally 1 h prior to induction of anesthesia with sips of water and patients in Group C (control group) received placebo. The intensity of fasciculations was assessed by an observer blinded on a 4-point scale. A blinded observer recorded postoperative myalgia grade after 24 h of surgery.The overall incidence of muscle

fasciculation was 83.9%in group P and 90% in group C was not significant between two groups ($p = 0.707$). while more patients in group C had moderate to severe fasciculation compared to group P ($p = 0.028$). severity of myalgia were significantly lower in group P ($p < 0.05$). (12)

According to the study conducted in India. The patients were randomly assigned to one of five groups: Group 1 (n = 21) received saline (NS), Group 2 (n = 20) received 0.03 mg/kg ROC, Group 3 (n = 20) received 0.05 mg/kg ROC, Group 4 (n = 20) received 0.01 mg/kg pancronium, and Group 5 (n = 20) received 0.03 mg/kg SCH. Thiopental 4-5 mg/kg IV was administered 3 min and 30 s after pretreatment. Fasciculations were absent in 90% of Group 2 patients, whereas 10% had vigorous fasciculations. In Group 3, 75% did not fasciculate, whereas 10% had mild and 15% had moderate fasciculations. Fasciculations were absent in 90% and mild in 10% of Group 4 patients. In Group 5, 10% had mild, 40% had moderate, and 20% had vigorous fasciculations. Pretreatment with ROC and pancronium decreased the incidence and severity of fasciculations significantly ($P < 0.0001$) compared with NS and mini-dose SCH. incidence and severity of myalgia between groups show no significant difference between groups ($p>0.05$)(25)

Study conducted in Madras Medical College, India on role of magnesium sulphate in attenuating succinylcholine induced fasciculation and post operative myalgia The study was conducted in 60 ASA grade I or II patients undergoing elective surgeries under general anaesthesia Patients were randomly allocated into 2 groups namely MG group(received Magnesium sulphate 40mg/kg diluted to 10ml with distilled water and NS group(Patients received 0.9% isotonic saline of volume 10ml) .15 patients had none, 8 had mild, 7 had moderate degree of fasciculation in MG group. 7 patients had mild, 20 had moderate and 3 had severe degree of fasciculation in NS group. P value is 0.0001 which is statistically significant. No patients had myalgia in MG group. 7 patients had mild and 3 patients had moderate degree of post op myalgia in NS group. P value of 0.002 which is statistically significant. (27)

study conducted in Liaquat National Hospital, Karachi, Pakistan 60 adult patients Group "A" received placebo and group "B" received Rocuronium 0.1 mg/kg, one minute prior to induction with Pentothal Sodium 5 mg/kg, Fasciculations were noticed in group "A" as 100 % (mild to

severe) and in group "B" 13.3% (mild) (P < 0.001). After 24 hours the incidence of myalgia was (23.33%) in the Rocuronium group and (93.33%) in the placebo group (P<0.001). (21)

According to study conducted in College of Physician and Surgeons, Karachi, Pakistan conducted on 80 patients in the age group of 20-60 years of either sex belonging to ASA grade I or II. They were divided into two groups, Group D patients were given pancronium 0.01mg /kg and Group M patients were given succinylcholine 0.2 mg/kg intravenously 60 seconds before the administration of thiopentone followed by succinylcholine. Incidence of succinylcholine induced fasciculation in pancronium group is 33% and in mini dose succinylcholine group is 15% (p=0.001).total incidence of post operative myalgia was 7 (10%) in defasciculating dose of pancronium and 4 (5.7%) were in mini dose of succinylcholine (p >0.10). (20)

According to the study conducted in Iran on succinylcholine induced myalgia in obstetric patient scheduled for caesarean section a prospective randomized double blind, placebo-controlled trial. One hundred twenty six participants undergoing elective cesarean section were randomized in two equal groups (63 participants in each): the diclofenac patch (containing 180 mg of diclofenac epolamine salt) and the placebo. In both groups, complaints from myalgia were in the neck or shoulder muscles or both. In diclofenac group, the incidences of myalgia was 15 (23.8%) versus incidences myalgia 33 (52.4%) in placebo group .The incidence and severity of myalgia were significantly lower in patients receiving diclofenac (p < 0.01).Request for rescue analgesia was significantly more frequent in the placebo group (26.4% of participants versus 10.9% of participants, p = 0.005).(13)

Study conducted in Iran one hundred thirty two patients were randomly allocated to three group. Anesthesia was induced with thiopentone 7mg/kg body weight. Group 1(n=44) was pretreated with 2mg pancronium 1 minute prior to full relaxation with Suxamethonium 1.5mg/kg. Group 2(n=44) received 0.02mg/kg succinylcholine. neuromuscular blockade was measured with regard to muscle fasciculation ,post operative myalgia ,succinylcholine pretreatment yielded results identical to pretreatment with pancronium.(31)

Study conducted in Amir Alam Hospital, Medical Sciences/University of Tehran, Iran. 79 patients were randomly assigned to three groups after premedication: Group 1 (n= 26) received

normal saline as a placebo, Group 2 (n= 27) received 0.01 mg/kg pancronium and Group 3 (n= 26) received 5 mg succinylcholine. Thiopental (4 mg/kg) was administered intravenously 60 seconds after pretreatment. There were no statistical differences among the three groups with respect to sex, weight or age. In Group 1, 3.8% of the patients showed no fasciculations, while 30.8% had mild, 53.8% had moderate and 11.5% had vigorous fasciculations. In Group 2, fasciculations were absent in 74.1% of the patients, while 25.9% of the patients had mild fasciculations. In Group 3, 23.1% patients had no fasciculations, while 42.3%, 30.8% and 3.8% of the patients showed mild, moderate and vigorous fasciculations, respectively, with succinylcholine pretreatment. Results showed that the incidence and severity of fasciculations were significantly decreased by pancronium pretreatment but not by pretreatment with succinylcholine or placebo ($p< 0.0001$ and $p= 0.0003$ respectively.There was no difference in the presence or severityof myalgia between the three groups ($p>0.05$) (15)

Study conducted in Ayatollah Kashani Hospital, Shahrekord, Southwest Iran, a Comparison of atracurium and methocarbamol for preventing succinylcholine-induced muscle fasciculation: A randomized controlled trial. Fifty-nine adults elective surgery BMI <30kg/kg were randomly assigned to two groups: Group A ($n = 29$) was administered with atracurium 0.02 mg/kg, and In Group B, 1g methocarbamol was administered , 27 patients (93.1%) suffered mild and two (6.9%) from moderate level of fasciculation in A group and In 20 (68.9%) suffered from mild, 5 (17.2%) from moderate, and 4 (13.9%) from severe level of fasciculation in Group B. severity of succinylcholine-induced fasciculations between the groups was statistically significant ($P< 0.05$). Atracurium is more effective than methocarbamol in decreasing the and severity of succinylcholine-induced fasciculations. (18)

Study conducted in Peoples' Hospital, Yangzhou, China 90 patients scheduled for laparoscopic cholecystectomy were equally randomized into three groups to receive pretreatment of 0.005, 0.01, and 0.02 mg/kg cisatracurium, respectively. After the pretreatments, general anesthesia was induced 3.5 minutes later, Fasciculations were alleviated significantly after the cisatracurium pretreatment of 0.02 mg/kg, more than with the other two doses ($p < 0.01$).incidence of myalgia had no significant changes among the three groups ($p > 0.05$). (23)

In study conducted in Dicle University Hospital, Diyarbakir, Turkey in 90 patients who have

received, Thiopental 5mg/kg, propofol 2mg/kg in and propofol 3.5 mg/kg the result shows that 38%patient was complain mild to moderate pain, (40% patients complain mild and 30 % patients was complain moderate pain) and 20% patients complain mild and 10 % patients was complain moderate pain respectively and none of the group did complain severe myalgia (28)

Study conducted in Chungnam National University, Daejeon, Korea The effect of remifentanil on succinylcholine-induced muscle fasciculations was studied using a double-blind method in 40 adults. After i.v. pretreatment with either remifentanil 1.5μg/kg (remifentanil group, n = 20) or an equivalent volume of i.v. saline (saline group, n = 20).17(85%) in remifentanil and 18(90%) in saline group experience fasciculation .the incidences of muscle fasciculation were similar in the two groups ($p > 0.05$). (16)

Study conducted in Korea University, Seoul, South Korea studied 60 female patients undergoing minor elective surgery, in a prospective double blinded method. Three groups of 20 patients each was pretreated with saline (control group), rocuronium 0.05 mg/kg (rocuronium group) and vecuronium 0.007 mg/kg (vecuronium group), 1.5 mg/kg succinylcholine was injected 3 minute after the pretreatment. The incidence of fasciculations was lowest in the rocuronium group, followed by the vecuronium group, and was highest in the control group. The incidence of myalgia on postoperative day 1 was lower in the rocuronium and vecuronium groups than the control group. Both rocuronium and vecuronium groups were equally effective in preventing myalgia on postoperative day 1. (19)

According to British Journal of Anaesthesia study on Rocuronium pretreatment reduces Suxamethonium-induced myalgia: comparison with vecuronium studied 150 patients, aged 18–60 yr, ASA I or II. All patients were undergoing elective oral surgery under general anaesthesia. induced with fentanyl 1 μg / kg and a sleep dose of propofol. Patients then received vecuronium 1 mg (group V), rocuronium 6 mg (group R) and normal saline (group P). The incidence of succinylcholine induced fasciculation was 42 (84%), 4 (8%), 50 (100%) in vecuronium, rocuronium, and normal saline groups respectively. The incidence of fasciculations in group R was significantly less than that in groups V and P ($P = 0.01$).also Incidence and severity of myalgia was 21 (42%),10 (20%), 35 (70%) in vecronium,rocuronium and normal saline groups respectively. Analysis of the incidence of myalgia revealed significant differences between

groups V and P (P =0.0001) and groups R and P (P= 0.0001). The difference between groups V and R was not significant.(14)

Study conducted in Division of emergency medicine, California university on head trauma patient requiring rapid sequence intubation who met the inclusion criteria received standard rapid sequence intubation maneuvers .patient were randomized to receive either mini dose succinylcholine or pancronium one minute prior to the full paralytic dose of succinylcholine.a fasciculation were recorded using a graded visual scale. of 46 patient, eight of 19(42%) in the pancronium group and six of 27(22%) in the succinylcholine group experienced fasciculation. No statistically difference in fasciculations was detected between the two groups (17)

A Meta-analysis on Prevention of Succinylcholine-induced Fasciculation and Myalgia Fifty-two randomized trials (5,318 patients) were included in this meta-analysis. In controls, the incidence of fasciculation was 95%, and the incidence of myalgia at 24 h was 50%. The average incidence of fasciculation was 95.2% with propofol and 95.0% with thiopentone. The difference was not statistically significant. The average incidence of myalgia at 24 h was 65.4% with propofol and 49.2% with thiopentone. This difference was statistically significant; for prevention of myalgia with thiopentone compared with propofol, A large variety of pretreatments were tested: non depolarizing neuromuscular blockers (atracurium, cisatracurium, *d*-tubocurarine, gallamine,mivacurium, pancronium, rocuronium, vecuronium).Sodium channel blockers (lidocaine), nonsteroidal anti inflammatory drugs (diclofenac, ketorolac, aspirin,) benzodiazepines(midazolam, diazepam), vitamins , magnesium sulfate, calcium chloride, dantrolene, dexamethasone, chlorpromazine, and succinylcholine. The effect of pretreatments on fasciculation was tested in at least three trials each. Nonsteroidal anti inflammatory drugs were not significantly different from placebo; all other pretreatments were significantly decrease incidence and severity of fasciculation and post operative myalgia. (26)

As we had seen from those literature due to unknown pathology of succinylcholine induced myalgia various medications including non-depolarizing muscle relaxant ,magnesium sulphate ,mini dose succinylcholine, propofol , thiopentone , gabapentin , remifentanil , lidocaine, diclofenac and others had been tested with varying degree of success.

CHAPTER THREE: OBJECTIVES

3.1. GENERAL OBJECTIVES

- ✓ To assess the effect of mini dose succinylcholine to prevent succinylcholine induced fasciculation and post operative myalgia in comparison with defasciculation dose of pancronium among elective adult surgical patientfrom July 1, to September 1, 2019. In Menelik II Referral Hospital, Addis Ababa, Ethiopia.

3.2. SPECIFIC OBJECTIVES

- ✓ To determine the incidence and severity of fasciculation between groups.
- ✓ To determine the incidence and severity of post operation myalgia between groups.

CHAPTER FOUR: METHODOLOGY

4.1. STUDY AREA AND PERIOD

This study was conducted in menelik II Hospital, the public hospital in Addis Ababa, capital of Ethiopia. Menelik II referral hospital was established in 1910 in Addis Ababa. Since its renovation as referral hospital, it has been serving as referral hospital and giving service in both outpatient and inpatient basis for different department in Ethiopia. Today the hospital is operated by Addis Ababa health bureau.

4.2. STUDY DESIGN

An Institutional based prospective observational cohort study will be conducted from July 1, to September 1, 2019.

4.3. POPULATION

4.3.1. Source population:All adult elective surgical patients who underwent surgical Procedures under general anesthesia with the use of succinylcholine in Menelik II referral Hospital, Addis Ababa Ethiopia,

4.3.1. Study populations: All adult elective surgical patients who underwent surgical Procedures under general anesthesia with the use of succinylcholine during the study Period in Menelik II referral Hospital, Addis Ababa Ethiopia,

4.4. ELIGEBILITY CRITERIA

4.4.1. Inclusion criteria:

a. Patient age between 18−60 years(14)
b. ASA status I and II,
c. BMI below 30kg/m^2(18)

4.4.2. Exclusion criteria:

a. pregnant mother (11)
b. suspected difficult tracheal intubation,
c. Trauma and burn patients
d. Patients with pre-existing musculoskeletal disorders

e. Patients receiving sedatives and treatment with any drug having relaxant.

f. Subjects who had received analgesics within 24 h before schedule procedure.

g. cardiovascular, renal, or hepatic disease

h. Patients who are hypersensitive to any of the drugs in the study

4.5. Sampling technique and sample size determination

4.5.1. Sample size determination

Sample size for study was calculated using double population proportion formula for comparison of two proportions based on the following assumptions: significance level 5%(α=0.05), power of study(1-β) of 80%. In one study done in Pakistan the incidence of fasciculation within pancronium group is 33% and in mini dose succinylcholine group is 15% (20).taking this into consideration , the calculation of sample size has been.

n = (p1q1 +p2q2) (f(a,B)2) / (p1-p2)2 n=(0.33.0.67 +0.15.0.85)(1.96.0.84)2/(0.33-0.15)2=29 in each group .adding of 10% of total sample size as a contingency the sample size in each group will be 32. using two proportion and distributed it for third group so the total sample size will be 96. Where:

n = Sample size in each group

α =significance level (1.96)

1-β=power of study at 80% (0.84)

q1= 1-p1

q2=1-p2

P_1= incidence of fasciculation in mini succinylcholine dose

P_2= incidence of fasciculation in defasciculating dose of pancronium

4.5.2 Sampling technique: systematic random sampling was used to select study participants. The daily operation schedule list was used as a sampling frame. The situational analysis showed that 24 patients who fulfill our inclusion criteria were operated in Menelik referral Hospital per week that got from surgery log book record, according to this data we had 200 patients in our study period, we collected data from 96 patients. So sample interval (k) was calculated as K=200/96,

approximately 2. The first participant was selected randomly using lottery method. Then every two patients were included in this study from the daily operation schedule list until the required sample size was met.

n=total sample population

N=total study population

K=skip interval

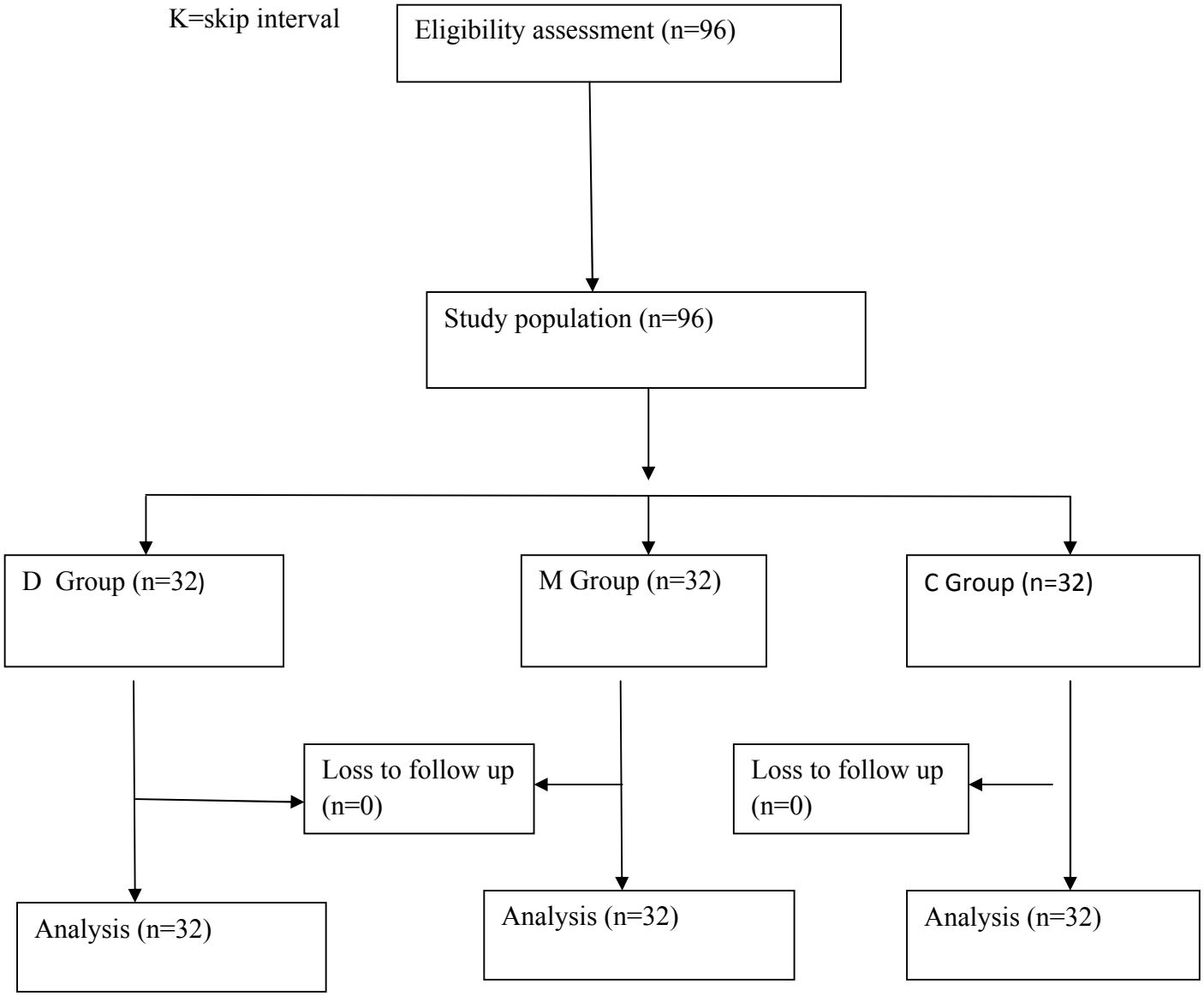

Figure 1: A study flowchart for enrolment of patients who underwent elective surgery under general anesthesia with succinylcholine at menelik referral Hospital.

4.6. Study variables

4.6.1. Dependent Variables: succinylcholine induced fasciculation and post operative myalgia.

4.6.2. Independent Variables:

- Age
- Sex
- BMI
- ASA physical status
- I.V induction agents
- Premedication
- Types of diagnosis
- Types of procedure
- Mini dose of succinylcholine as a pretreatment
- Defasciculating dose of pancronium

4.7 Methods of Data collection:

On arrival of the patients to the operative theater, and after application of the routine hospital monitoring protocol all study patients received standard pre- and intraoperative monitoring general anesthesia was induced with tramadol (100mg), Diclofenac (75mg), Thiopental (3-5mg/kg) and tracheal intubation was facilitated with Suxamethonium (2mg/kg) All patients were artificially ventilated, and the Inhalational anesthetic agent achieved maintenance of anesthesia. Questionnaire and check list were prepared in English and Amharic which includes demographic data, patients ASA class, types of diagnosis, types of procedure, type and dose of induction agent used, type and dose of muscle relaxant used for intubation and maintenance. Our questioner was including incidence and severity of fasciculation and post-operative myalgia. Data collectors who were trained on how to grade fasciculation and myalgia has been observe the fasciculation and interviewed the patients for post-operative myalgia. Data was collected by two BSc anesthetists intra-operatively for fasciculation observation and by two BSc nurses post-operatively for myalgia and supervised by principal investigator. Regular supervision and follow up was made.

4.7.1 Ethical consideration

Ethical clearance was obtained from ethical committee before the start of the study. Official support letter was written to hospital and Addis Ababa health bureau and permission for data collection were sought from the responsible authorities. The purpose and the importance of the study were explained and verbal as well as written informed consent was obtained from each participant. Confidentiality was maintained at all levels of the study by avoiding identifiers and using code to identify patients. The participant involvement in the study and those who wish to quit their participation at any stage were informed and allowed to do so without any restrictions

4.8. Data Quality Control and Assurance.

To ensure quality of data, pre-test of the questionnaire have been performed on 5% of study populations who fulfill the inclusion criteria at Menelik II referral Hospital. The completed questionnaire has been submitted and reviewed daily to avoid loss of data. Close supervision and daily information exchange including by telephone has been used as a means to correct problems during the course of the data collection. Consent for the postoperative survey was obtained and confidentiality have been assured to improve the quality of data. Data consistency and completeness have been made throughout the data collection, data entry and analysis.

4.9. Data processing and analysis.

The data was entered in to epi info version 7 and transported to SPSS version 22 statistics software for analysis. The data were tested for normality using histogram and Shapiro-wilk normality test and homogeneity of variance by Levene's test for normally distributed .Normally distributed and continuous data were analyzed using one way analysis of variance (ANOVA) with post hoc analysis for multiple test and non-normally distributed data analyzed using kuruska-walih H rank test.

The comparison of categorical variable analyzed using Pearson chi-square test or fisher's exact test with post hoc as required. Data were presented as mean$\pm$ SD for normally distribution, median$\pm$ IQR for non normally distributed and categorical data were presented as frequency (percentages).p-values <0.05 will be considered statistically significant.

4.10. Dissemination plan.

The research will be presented for the entire department staff. it will also be presented at the annual research conference. The research will be submitted to journals for publication.

4.12. Operational definitions.

ASA status: is surgical risk stratification validated by American Society of Anesthesiologist

ASA I: a healthy patient with no organic/physiological/ psychiatric problems

ASA II: controlled medical conditions with mild systemic effect and no limitation of functional ability

Defasciculating dose of pancronium: administration 0.01mg/kg of a small dose of a non-depolarizing neuromuscular blocking agent (NDMBA) one minute before induction of anesthesia.

Mini dose succinylcholine: administration of 0.2mg/kg succinylcholine as a pretreatment one minutes before induction of anesthesia.

Grade 0 = no fasciculations;

Grade 1(mild) = fine fasciculations of the eyes, neck, face or fingers, without limb movement.

Grade 2(moderate) = fasciculations occurring at more than two sites, or obvious limb movement.

Grade 3(severe) = sustained and widespread fasciculations in the trunk and limbs.

POM: generalized aches and pains that commonly occur until 24 hours after succinylcholine administration.

Nil: - No muscle pain or stiffness

Mild myalgia: -muscle pain or muscle stiffness at one site but not causing disability or limiting activities.

Moderate myalgia: -muscle pain or muscle stiffness at more than one site but not causing disability or limiting activities.

Severe myalgia: -muscle pain or stiffness at one or more site and causing disabilities or limiting activity

Incidence and severity of succinylcholine induced fasciculation and post operative myalgia was adopted from (15)

CHAPTER FIVE: RESULT

5.1 Demographic and perioperative characteristics of the patients

During the study period, a total of 96 patients were included for final analysis based on whether they received mini-dose succinylcholine or defasciculating dose of pancronium as a pretreatment for prevention of succinylcholine induced fasciculation and myalgia and those without of pretreatment as unexposed group.

The demographic patient characteristic data collected, including age, gender. weight, height, BMI,ASA status, were comparable for all three groups. Majority of the study participant were female with cholelithiasis but there is no statistical difference between three groups.

Table 1: Socio demographic and perioperative characteristic of patient who underwent elective surgical procedure in menelik II referral Hospital, Addis Ababa, 2019.

Variables	Defasciculating dose of pancronium (n=32)	Mini dose of succinylcholine (n=32)	Control (n=32)	P- value
Age(years)	46±8.24	46.4±10.1	45.9±7.8	0.97
Weight(kg)	62.9±4.9	62.6±5.2	63.1±4.7	0.93
Height(cm)	165(10)	166(10)	165(7)	0.43
BMI	24.6±1.7	24.6±2.3	25.9±2.6	0.09
Sex(M/F)				0.94
Male	9(9.3%)	8(8.3%)	9(9.3%)	
Female	23(23.9%)	24(25%)	23(23.9%)	
ASA status				0.44
ASA 1(n,%)	26(27%)	28(29.1%)	24(25%)	
ASA 2(n,%)	6(6.2%)	4(4.1%)	8(8.3%)	
Induction agent				
Thiopental	33.3%	33.3%	33.3%	
Analgesia during induction (mg)				
Tramadol IV	100(0)	100(0)	100(0)	
Diclofenac IM	75(0)	75(0)	75(0)	

Value are presented as: Mean±SD, Median (IQR),one way ANOVA test, Kuruska-Walih H rank test, chi-square test and $p<0.05$ is statistically significant.

5.2. Comparisons of the incidence and severity of fasciculation.

In control group , 2(6.3%) of the patients showed no fasciculations, while 12 (37.5%),13 (40.6%) and 5(15.6%) of the patients had mild, moderate and vigorous fasciculations, respectively. Fasciculations were absent in 24(75%) of patients in mini dose succinylcholine group, while the remainder 8 (25%) had mild fasciculations only after succinylcholine pretreatment. In defasciculating dose of pancronium , 15 (46.9%) of the patients had no fasciculations, while 13 (40.6%), 4 (12.5%) of the patients had mild, moderate fasciculations, respectively, after pancronium pretreatment

The severity of fasciculations was significantly lower with mini dose succinylcholine pretreatment compared with NS and pancronium pretreatment (p=0.000 and p=0.012 respectively).Furthermore, in Group C, almost all patients had fasciculations, whereas fasciculations were absent in 75% of patients in Group M and 46.9% of patients in Group D. Therefore, succinylcholine pretreatment significantly decreased the incidence of fasciculations as compared with control group and pancronium (p =0.000 and p = 0.013 respectively); but also pretreatment with defasciculating dose of pancronium significantly decreased the incidence of fasciculations as compared with control group (p=0.000). Among those 55(57.2%) patient who had fasciculation 43(61.4%) was female and 12(46.2%) was male. The incidence of succinylcholine induced fasciculation has a difference between female and male (p=0.179). Among those participants who had succinylcholine induced fasciculation 45(57.7%) was ASA I and 10(55.6%) was ASA II, the incidence of succinylcholine induced fasciculation has a difference between ASA II and ASA I (0.869).of the participants who developed succinylcholine induced fasciculation 43(53.8%) were in normal weight range and 12(75%) were overweight in their BMI (0.595) (for detail see table3)

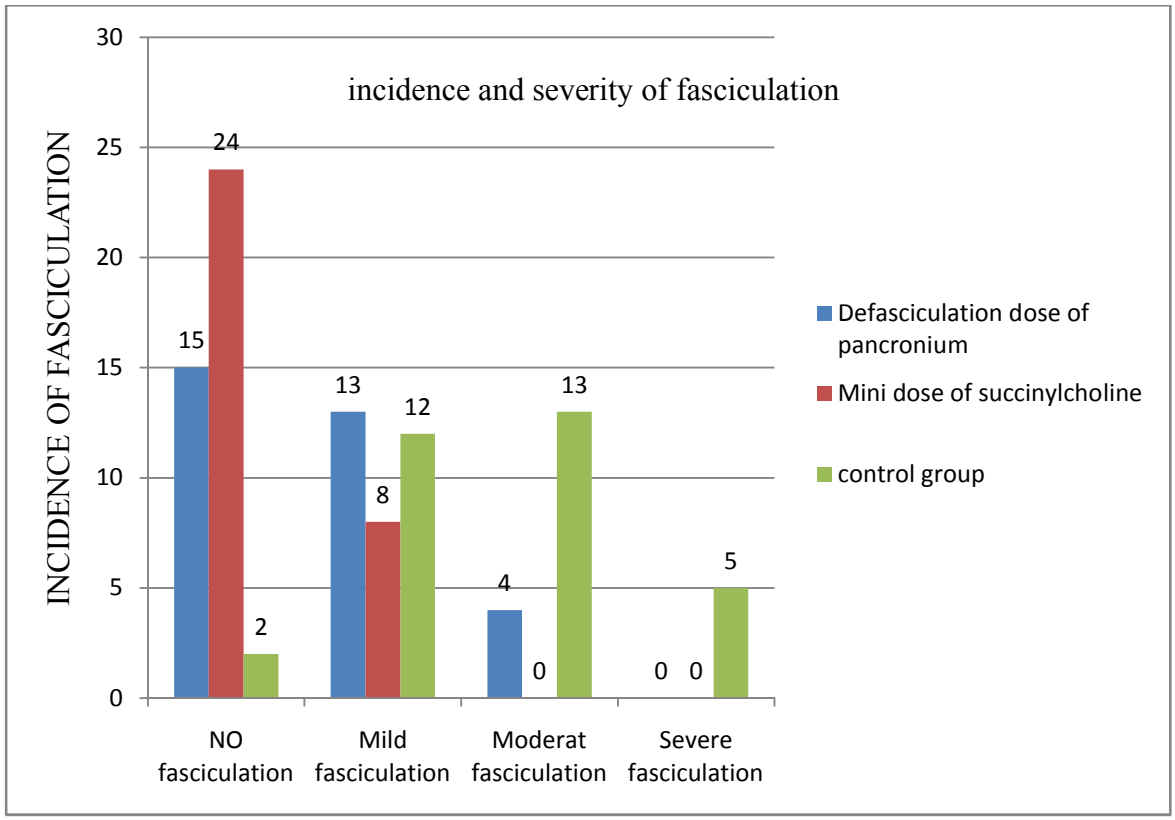

Figure 2: distribution of succinylcholine induced fasciculation in patient who underwent elective surgery under general anesthesia patient at menelik II referral hospital.

5.2 comparisons of the incidence and severity of Post-operative myalgia

Among the participant 18 (18.8%) had post operative myalgia. 6 (18.8 %) experience mild post operative myalgia and there were no moderate and severe post operative myalgia in “D” group, 3 (9.4%) experience mild post operative myalgia and there were no moderate and severe post operative myalgia in “M” group and 9 (28.1%) experience mild post operative myalgia and there were no moderate and severe post operative myalgia in “C” group. There was no difference in the presence or severity of myalgia between the three groups, irrespective of the pretreatment used. Among those participant who had post operative myalgia 11(61.1%) complain neck pain and 7(38.8%) complain shoulder pain. from those none of seek analgesia. Among the participant who feel post operative myalgia 4 (22.2%) feel pain after six hours, 14 (77.8%) were feel after twelve hours post operatively. From those participants who developed POM 3(11.5%) was male

and 15(21.4%) were female (p=0.270). Although there was no significant correlation between fasciculation and POM (Spearman rho =0.199). (for detail see figure and table below)

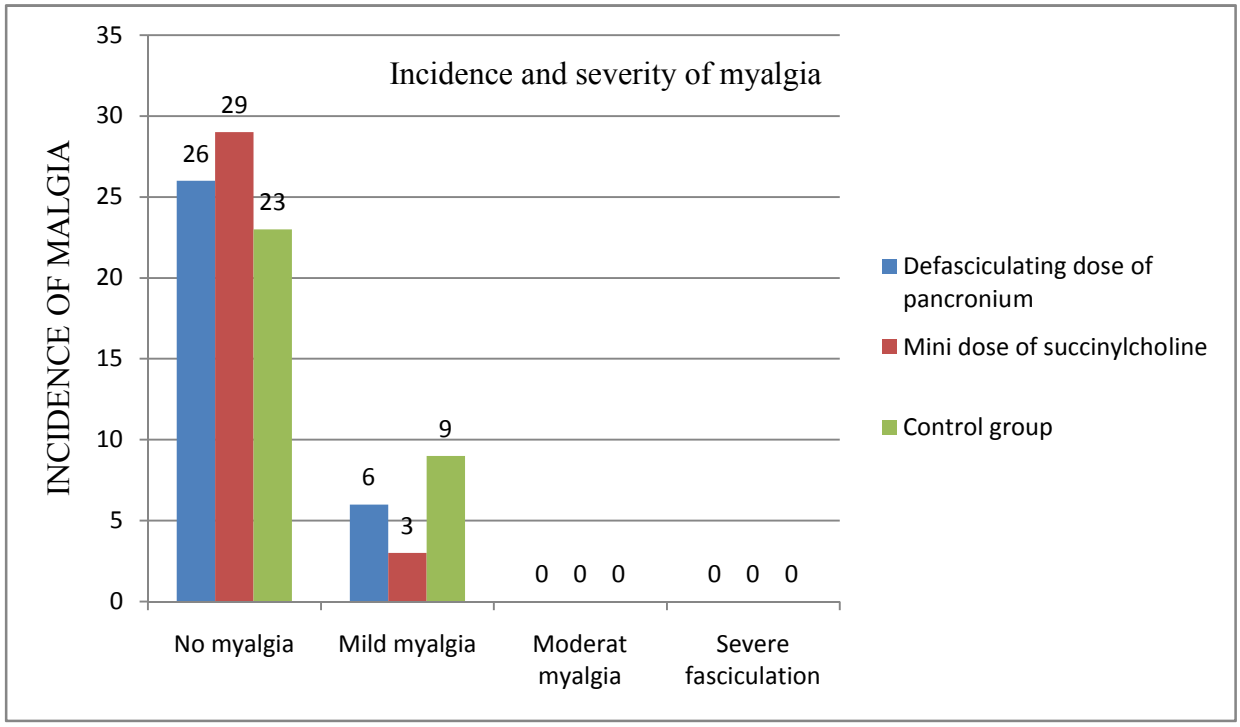

Figure 3: distribution of succinylcholine induced fasciculation in patient who underwent elective surgery under general anesthesia patient at menelik II referral hospital.

Table 2: Incidence and severity of succinylcholine induced fasciculation and myalgia in patient who underwent elective surgery under general anesthesia patient at menelik II referral hospital.

parameter		"D" group (n=32)	"M" group (n=32)	"C" group (n=32)	p-value
Fasciculation	Incidence	17(53.1%)	8(25%)	30(93.8%)	0.000
	Nil	15(46.9%)	24(75%)	2(6.3%)	0.000
	Mild	13(40.6%)	8(25%)	12(37.5%)	
	Moderate	4(12.5%)	0(0%)	13(40.6%)	
	Severe	0(0%)	0(0%)	5(15.6%)	
Myalgia	Incidence	6(18.8%)	3(9.4%)	9(28.1%)	0.158
	Nil	26(81.3%)	29(90.6%)	23(71.9%)	0.161
	Mild	6(18.8%)	3(9.4%)	9(28.1%)	
	Moderate	0(0%)	0(0%)	0(0%)	
	Severe	0(0%)	0(0%)	0(0%)	

Notes: Nil = No fasciculation /myalgia; chi-square test was used for analyze to identify differences in the incidence, Difference in the severity was compared by using kruskal-Wallis test.

Table 3:- Incidence and severity of succinylcholine induced fasciculation and post operative myalgia among patients with different BMI

Variable		Frequency (%)		
BMI		Normal weight (18.5-24.9)	Over weight (25-29.9)	p- value
Fasciculation	Nil	37(46.3%)	4(25%)	0.026
	Mild	28(35%)	5(31.3%)	
	Moderate	13(16.3%)	4(25%)	
	Severe	2(2.5%)	3(18.8%)	
Myalgia	Nil	64(80%)	14(87.5%)	0.485
	Mild	16(20%)	2(12.5%)	
	Moderate	0(0%)	0(0%)	
	Severe	0(0%)	0(0%)	

Notes: Nil = No fasciculation /myalgia Difference in the severity was compared by using Mann Whitney

CHAPTER SIX: DISCUSSION

Succinylcholine is the best drug for rapidly providing ideal conditions for short procedures requiring endotracheal intubation. Unfortunately, its use is associated with muscular fasciculation and postoperative myalgia. The effectiveness of mini doses of succinylcholine and NDMB drugs in reducing the incidence of fasciculations or preventing them has been shown to be drug-specific and is dependent on the interval between pretreatment and the administration of the main dose of succinylcholine.(29) The interval needed for pancronium to prevent succinylcholine induced muscle fasciculations in 90% of patients is 5.26 minutes (15).However, applying this interval for succinylcholine pretreatment would result in significant hydrolysis of the drug by plasma cholinesterase. Based on this concept, we used a 1.5-minuteinterval in this study, to ensure the mini-dose succinylcholine elicited its peak effect before its hydrolysis(29). However, we also know that pancronium does not reach its peak effect in this interval, but double-blind comparisons of mini-dose succinylcholine with NDMB drugs for the prevention of succinylcholine-induced muscle fasciculations should include standardized intervals for all drugs, beginning at 90 seconds, to accurately evaluate the efficacy of these approaches.(30)

Furthermore, we must also consider that the incidence and severity of fasciculations were significantly lower in patients pretreated with pancronium than in those pretreated with succinylcholine. Interms of the dosing interval of 5.26 minutes for pancronium, it may be that this time interval may further decrease the incidence of fasciculations (15)

There are several advantages to succinylcholine pretreatment. First, pretreatment with NDMBs can attenuate the effect of succinylcholine and consequent deterioration during intubation. However, problem can be overcome by increasing the dose of succinylcholin.(17)

This study revealed that the incidence and severity of fasciculations were significantly decreased with mini dose succinylcholine pretreatment, compared with defasciculation dose of pancronium ($p=0.012$).In line with our study, the study results reported from Pakistan on 70 patients who allocated randomly into equal two groups by using prospective, randomized, controlled clinical study stated that the total incidence of fasciculation were significantly decreased with mini dose succinylcholine pretreatment, compared with defasciculation dose of pancronium ($p=0.01$).(20)

In our study 8(25%) had mild fasciculation, and there was no moderate and sever fasciculation in “M” Group. In contrast to this study, the study done in Tehran, Iran. Stated that 23.1% patients had no fasciculations,while 42.3%, 30.8% and 3.8% of the patients showed mild, moderate and vigorous fasciculations, respectively, with succinylcholine pretreatment and 3.8% of the patients showed no fasciculations, while 30.8% had mild, 53.8% had moderate and 11.5% had vigorous fasciculations in NS groups. Results showed that the incidence and severity of fasciculations were significantly decreased by pancronium pretreatment compare with pretreatment with succinylcholine ($p< 0.0001$) or NS group ($p=0.0003$) (15) difference may arise from different dose of succinylcholine used as a pretreatment in ours and their study.

Our study show that 8 (25%) had mild fasciculations and there is no moderate or severe fasciculation in Group "M". In contrast to our study. Study reported from Indian in a patient received 0.01 mg/kg pancronium group ,Fasciculations were absent in 90% and mild in 10% of patients and in a patient received 0.03mg/kg SCH pretreatment group, 10% had mild, 40% had moderate, and 20% had vigorous fasciculations. Pretreatment with pancronium decreased the incidence and severity of fasciculations significantly ($P < 0.0001$) compared with and mini-dose SCH. (25).the presence or severity of fasciculations in patients who received either NS or mini dose SCH did not differ significantly. difference may arise from different dose of succinylcholine used as a pretreatment in ours and their study or because application of the 3.5-min interval to SCH pretreatment would allow for significant hydrolysis of the drug by plasma cholinesterase.

In our study 6 (18.8%) ,3 (9.4%) and 9 (28.1%)were complained post operative myalgia in “D”, “M” and “C” Group respectively. all groups did not show statistically significant difference regarding the post operative myalgia ($p=0.158$). In line with our study the study conducted from Pakistan on 70 patients who allocated into equal two groups by using prospective, randomized, controlled clinical study stated that the total incidence of post operative myalgia was 7 (10%) in defasciculating dose of pancronium and 4 (5.7%) were in mini dose of succinylcholine ($p >0.10$).(20)

In our study 6 (18.8 %),3 (9.4%) and 9 (28.1%) experience mild post operative myalgia in “D” “M” and “C” Group respectively, there were no moderate and severe post operative myalgia in

all group. which is comparable with study done in Iran . 2 (7.4%), 2 (7.7%) and 3(11.5%) had experience mild post operative myalgia in pancronium, mini-dose succinylcholine and NS group respectively. and there were no moderate and severe post operative myalgia in all group.(15)

This study revealed that there is no correlation between succinylcholine induced fasciculation and post-operative myalgia (Spearman rho=0.199). It was comparable with study conducted in University of Tehran, Iran79 patients were randomly assigned to three groups by using prospective, randomized, controlled clinical study concluded that there is no correlation between fasciculation and myalgia (Spearman rho=0.137)(15).

6.1 Strength of the study

Study participant were homogenous between groups.

6.2 Limitation of the study

Lack of prior study on this and related title in our country.

Most studies we used for comparison were randomized control trial.

CHAPTER SEVEN: CONCLUSION AND RECOMMENDATION

7.1. Conclusion

Pretreatment with 0.2mg/kg mini dose of succinylcholine before 90 seconds of induction agent is effectively reduced the incidence and severity fasciculation in comparison with 0.01mg/kg defasciculating dose of pancronium. But there is no significant difference on the incidence and severity of post operative myalgia between groups. .

7.2 Recommendation

According to this study we recommended anesthesia professional to use mini dose of succinylcholine which significantly reduce incidence and severity of fasciculation. We recommend researcher to undergo further study on adverse effect of those drugs between groups.

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ANNEX III. INFORMATION AND CONSENT FORM.

Hello, my name is _____ from Addis Ababa University, college of health science, Post graduate studies. I will be going to conduct study on reduction of fasciculation and Post operative myalgia which resulted by succinylcholine. So, you are kindly requested to be included in this study, which will have importance in reduction of postoperative myalgia & increase patient satisfaction. The interview will take about 5 minutes, your information will never have passed from individual to individual or from institution to institution without your agreement. Your participation is voluntarily & you have a right to not participate fully or partially. If you agree to be part of this study, I will start my question by asking general identification points. Only honest answer would contribute for improvement of our health service. The study has approval from AAU. May I continue?

YES NO

If you say "yes" for the above question here there is a consent form that you will going to sign to be part of the study.

I have been briefly informed about the study and I clearly understood the objective of the study, since it does not affect my personal life, I do not need any remedy. Consequently, I here to approve my consent to take part in the study as interview with my signature.

Signature_____ Date_____

ሰላም፣ስመ_____ ይባላለሁኝ የአአዩ ጠ/ሳ/ኮ ድህረምረቃ ፕሮግራም ተማሪ ስሆኝ ፣አንድ አንድ የኢኒስተዝያመዳኒቶችየሚያመጡትየጡንቻመርገብገብእናከሆፕራስሆንበኋላየጡንቻህመምለመቀነስጥናትላይስሆንየእርሶበበጎ ፍቃደኝነትመሳተፍአስፈላጊመሆኑንእየገለፅኩጥያቀውከ5 ደቂቃበላይአንደማይወስድላረጋግጥሎት እወዳለው፤በተጨማርምየእርሶማረጃከሰውወደሰውወይምከተቋምወደተቋምያለእርሶፍቃድእንደማይተላለፍቃል እየገባው፣የእርሶተሳታፍነትበሙሉፍቃደኝነቶብቻየምረጋገጥመሆኑንእያረጋግጥሎት፤በመጨረሻምየጥናቱተሳታፊ መሆንከፈለጉከዚበታችየተገለፀውንየስምምነትወረቀትአምብቦእንድፈርሙልኝበትህትናእጠቃለው፤

የጥናቱይዘትበትክክልየተገለፀልኝስሆንአላማውንምተረድቻለው፣በመሆኑምያለምንምማመንታትየጥናቱአካልመሆነን በፍርማየአረጋግጣለው፤

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ANNEX II. QUESTIONNAIRES

Addis Ababa University College of public Health and Medical Science school of Medicine, department of Anesthesia.

A data collection format, for patients who will be undergo elective surgical procedures from January 20, 2019 to march 30, 2018 in Menelik II referral Hospital, Addis Ababa, Ethiopia. The purpose of this study to compare the effect of defasciculating dose pancronium versus mini dose of succinylcholine as a pretreatment modality on prevention of succinylcholine induced fasciculation and myalgia.

First of all, I would like to acknowledge for your willingness to participate in this study and also, I would like to assure I will keep the confidentiality of this record in case that you may not want to be public

Instructions:

A. Fill the blank space provided.

B. Encircle the alternatives when necessary.

C. Check the questions for completeness.

Part 1. Identification:

1.1. Patient MRN_____1.2. Age (in year) _____ 1.3. Sex: A. Male B. Female

1.4.Weight_____kg

1.5.Height_____cm

1.6. BMI_____ Kg/m2 and

Part 2 Preoperative evaluation

2.1. Diagnosis _____2.2. procedure_____

2.3. ASA A) I B) II

2.4. Induction agent used (dose in mg/kg)

A. Propofol_____mg/kg B. Thiopental_____mg/kg

C. ketamine_____mg/kg

2.5.Analgesia during induction

A.tramadol ___mg/kg B.Diclofenac____mg/kg C.otherspecify_____mg/kg

Part 4: Incidence and severity of fasciculation

A. No fasciculation

B. Mild fasciculation (involves eyes, face, neck, fingers without movement of limbs)

C. Moderate fasciculation (Fasciculation of greater intensity at more than two sites or movement of limbs)

D. Severe fasciculation (Vigorous sustained and widespread Fasciculation)

Part 5: patients compliant post-operative muscle pain

5.1. Do you have any pains and aches or stiffness in your muscles other than the operation site?

A . Yes B. No

5.2. If you answer yes for Que.8.1 in which part of your body feel this pain?

A Neck, B. Shoulder, B. Arm, C. Throat, D. Abdomen, and F. Buttocks.

5.3. Did you take any medication for the pain? A. Yes B. No

5.4 If you answer yes for Que.8.3 what are this medication you have taken?

A. NSAID_____ B. Opioids_____

5.5. Does this pain restrict your normal activity? A. yes B. No

A. Can you get out of bed? C. Can you able to turn your head? C. Can you cough without distress or pain?

5.6 When did you start feeling this pain?

A. After first1hr of pop time B. After 6hrs of pop time C. After 12 hrs of POP time

D. After 24hrs of POP time

6. Incidence and severity of myalgia. A. Nil myalgia

B. Mild myalgia (muscle pain or muscle stiffness at one site but not causing disability or limiting activities).

C. Moderate myalgia (muscle pain or muscle stiffness at more than one site but not causing disability or limiting activities).

D. Severe myalgia (muscle pain or stiffness at one or more site and causing disabilities or limiting activity).

Name of data collector_____ Status/profession _____ Signature_____

Thank you!!!