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ADDIS ABABA, ETHIOPIA

**ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES
DEPARTMENT OF ANESTHESIA
ASSESSMENT ON MAGNITUDE AND ASSOCIATED FACTORS ON
SUXAMETHONIUM INDUCED POST OPERATIVE MYALGIA IN
ADULT ELECTIVE SURGICAL PATIENTS FROM JANUARY 1, 2017 TO
MARCH 1, 2017 AT ZEWUDITU MEMORIAL HOSPITAL, ADDIS
ABABA. CROSS SECTIONAL STUDY.**

BY: - GASHAW ABEBE (MSC STUDENT)

ADVISOR: - MERON ABRAR (BSC, MSC)

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Abstract

Background: - Suxamethonium is a depolarizing muscle relaxant first introduced into clinical practice in 1951, it remains the drug of choice in clinical situations in which rapid paralysis and airway control are priorities. The administrations of succinylcholine may produce post-operative myalgia. Post-operative myalgia is thought to be caused by motor units firing at physiological higher rates following Suxamethonium administration, leading to unsynchronized muscle contractions causing shearing forces of skeletal muscle fibers. The postoperative myalgia is generalized aches and pains that commonly occur 24 to 48 hours after Suxamethonium

Objectives: - To assess the magnitude and associated factors of Suxamethonium induced post-operative myalgia in adult elective surgical procedures that were undergone from January 1, 2017 to March 1, 2017 in Zewuditu Memorial Hospital, Addis Ababa, Ethiopia.

Method:-On 283 eligible patients Hospital based cross sectional study was conducted from January 1, 2017 to March 1, 2017 G.C at Zewuditu Memorial Hospital, using structured questionnaires and checklists and data were collected from all elective surgical patients who fulfill the inclusion criteria during study period and the magnitude of post-operative myalgia was calculated (%), associated factors with myalgia was investigated. Multivariate logistic regression analysis was conducted to identify significant predictors based on p-value less than 0.05 with 95% confidence level.

Results:-Among 160 elective surgical patients the magnitude of Suxamethonium induced post-operative myalgia in the first 24 to 48 hours were in 92(57.5%) and in which at 24 hours the magnitude was about 84(52.5%) whereas at 48 hours 74(46.2). The independent predictors of Suxamethonium induced post-operative myalgia in this study are being female, incidence of fasciculation during induction and analgesia preoperatively.

Conclusion and recommendation:-The magnitude of Suxamethonium induced post-operative myalgia in the first 24-48 hours was higher. To minimize the magnitude of Suxamethonium induced post-operative myalgia and post-operative patient discomfort different prevention techniques should be applied. If possible it is better to avoid the use of Suxamethonium regularly for elective surgical patients.

It is also recommended that premedication of patients with analgesic agent before induction of anesthesia and defasciculation with NDNMBA.

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LISTS OF ACRONYMY AND ABBRAVATION

ASA:-American society of Anesthesiologists

BMI: -body mass index

CCD - chief clinical director

FMOH: -federal ministry of health

HCT: -hematocrit

HGB: -hemoglobin

G.C:- Gregorian calendar

IV:-intra venous

NDNMBA:-non-depolarizing neuromuscular blocking agent

NMBA:-neuromuscular blockade agents

NSAID: -non-steroidal anti-inflammatory drugs

POM: -post-operative myalgia

SCH:-succinylcholine/Suxamethonium

SPSS:-statistical package for social science

CHAPTER ONE INTRODUCTION

1.1 BACK GROUND

Suxamethonium is a depolarizing muscle relaxant first introduced into clinical practice in 1951, it remains the drug of choice in clinical situations in which rapid paralysis and airway control are priorities. The administration of succinylcholine may produce post-operative myalgia ((1-5). That has an overall incidence ranging from 5% to 83%. Post-operative myalgia is thought to be caused by motor units firing at a physiological higher rate following Suxamethonium administration, leading to unsynchronized muscle contractions causing shearing forces of skeletal muscle fibers(5).

The postoperative myalgia are generalized aches and pains that commonly occur 24 to 48 hours after succinylcholine administration that mimic the muscular pains which is usually following violent exercise. It has been postulated that the muscle pain is secondary to the damage produced in the skeletal muscle by the unsynchronized contraction of adjacent muscle fibers just before paralysis occurs (6).

The incidence is variable (20 to 80 percent of patients receiving succinylcholine) and are more common in young, ambulatory patients (7). 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 Suxamethonium may involve calcium-induced phospholipids degradation with release of damaging products of fatty acid metabolism (8).

Despite the recent introduction of short acting non depolarizing neuromuscular blockers, succinylcholine, with its rapid onset of action, short duration of effect, complete and predictable paralysis remains unsurpassed in providing ideal incubating conditions for tracheal intubation (9).

1.2. STATEMENTS OF THE PROBLEM

Suxamethonium since its introduction into clinical practice it has been recognized that fasciculation's, myalgia, and rise in biochemical markers including serum creatine kinase and potassium occurs frequently with its use (10).

Suxamethonium is accepted as the drug of choice for providing ideal intubating conditions and also for rapid sequence induction. However, its usefulness is limited by the frequent occurrence of post-operative myalgia. The reported incidence of Suxamethonium induced myalgia ranges from 1.5 to 89 %(11). The most commonly quoted figure is around 50%. 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.(12)

Several factors have been described as having an influence on this phenomenon. Females are more likely to suffer than males (6).The first attempt to reduce the incidence and severity of muscle pains was pretreatment with gallamine in 1954.Since then; a wide variety of regimens has been tried. The most common practice is to administer a subparalysing dose of a nondepolarising neuromuscular blocker a few minutes before succinylcholine, with the aim of abolishing both the visible fasciculation and the postoperative myalgia. Although much has been written about this technique, controversy exists about the agent of choice for pretreatment, the optimal dose of the agent and the ideal timing interval between pretreatment and Suxamethonium administration(13).

Non depolarizing agents circumvent most of these problems, but none has the same pharmacokinetic profile as succinylcholine. Rocuronium and the newer rapacurium come closer, but both have longer lasting effects than succinylcholine and so they too could not replace it. Several strategies have been advocated to decrease the incidence of these adverse effects, one of the most successful being the administration of small doses of no depolarizing neuromuscular blocking agents before administration of succinylcholine(14).

Various factors influence the efficacy of pretreatment, including the choice of no depolarizing agent, degree of prejunctional receptor block, interval between administration of pretreatment agent and succinylcholine and speed of onset of no depolarizing agent(15). To avoid unnecessary expense on the patient for post-operative analgesia requirement

1.3 .SIGNIFICANCE OF THE STUDY

Therefore this study is very important to provide rational and evidence based case specific practical frame work on the magnitude of post-operative myalgia, associated factors that increase the magnitude of post-operative myalgia and severity of post-operative myalgia after Suxamethonium.

To provide rational and evidence based case specific practical frame work factors that reduce the incidence of post-operative myalgia.

.It is also important to increase patient's satisfaction by reducing post-operative discomfort.

In my knowledge there is no published study in Ethiopia in my study area so that it can be used as baseline data for further researcher.

CHAPTER TWO

2.1. LITERATURE REVIEW

Randomize placebo control study done in India on 70 patients, Postoperative myalgia (POM), with an incidence rate of ~41%–92%, is one of the most common side effects of this drug and can take several days to cause significant discomfort in patients (16).

According to study conducted in Queen's University of Belfast in 80 adult patient, forty patients were induced with thiopentone 3-5mg/kg and the remaining forty induced with propofol 2-3 mg/kg) and Within each group half the patients (n = 20) were receive Suxamethonium 1 mg.kg in 1sec or at 2 min after the induction agent, 24 hrs after surgery the result showed that the incidence of muscle pains was 35, 60, 35 and 55% in groups PI, PII, TI and TII respectively(17). According to study conducted in America by American society of Anesthesiologists, 2005 for Fifty-two randomized trials (5,318 patients) and the magnitude of myalgia at 24 h was 50%(18).

According to study conducted in University of Pittsburgh, School of Medicine and Magee-Women's Hospital, Pittsburg in 395 healthy outpatients undergoing general anesthesia for ambulatory surgery. Fewer patients were reporting no postoperative pain and more patients reporting moderate-severe pain (19).

Study conducted in Himalayan Institute of Medical Sciences, Dehradun, India; in 61 patients. The overall incidence of muscle fasciculation's was 90%. The severity of myalgia was (5 and 10 of Grade 1 and 2 myalgia respectively). None of the patients complained of myalgia of grade 3 (20).

Rocuronium, in which it has more rapid onset of action compared with other nondepolarising agents, provides well incubating conditions. As the optimum interval for pretreatment with pre-existing is approximately 3 minutes, this property of Rocuronium may be relevant to its use in prophylaxis of muscular side effects after succinylcholine pretreatment on frequency of post-operative muscular effects (21).

Study conducted in India, Institutes of medical Education in 210 patients at three dose levels (1, 1.5 and 2mg/kg) alone as control, or in combination with tubocurarine (0.05 and 0.07mg/kg), gallamine (0.2 and 0.4mg/kg) or pancuronium 0.01 and 0.02mg/kg) the result shows only 10%-30 % patient experience mild to moderate post operative myalgia in tubocurarine, gallamine and pancuronium pretreatment and in the after Suxamethonium 70% of patient was experience post operative myalgia(22).

Study conducted in Liverpool Maternity Hospital and Mill Road Maternity Hospital, Liverpool, England in 130 patient the magnitude of muscle pains in the 41 cases who received gallamine before the Suxamethonium 41.5% complain slight pain where as 17% patient was complain severe pain. The incidence of jaw and neck pains was maximal on the first postoperative day, that of shoulder and limb pain on the second, and that of chest and back pain on the second and third postoperative days(23).

Study conducted North Dakota in fifty patients shows that the magnitude of postoperative myalgia pretreated with saline at the 24-hour were (21%) and (60%) were females where as patients pretreated with atracurium were (12%) and (66%) were females, their locations were neck, shoulder and chest. During the 72-hours, 4% and complained of postoperative myalgia, while in, 8% complained of post operative myalgia (24).

Study report in England shows that premedication with diclofenac was associated with significant reduction in the intensity of myalgia. Among the patients given diclofenac, only 5.9% felt severe and moderate pain 24hr after operation and 35.3% had mild and 52.9% of patients had no pain(25).

According to McLaughlin C, Nesbitt GA, it has been demonstrated that pretreatment with oral aspirin is as effective as pretreatment with a non-depolarizing blocker. Ketorolac, a non-steroidal anti-inflammatory drug (NSAID), would be expected to be as effective as aspirin in the prevention of Suxamethonium myalgia (26).

According to the research conducted in 60 healthy adult patients shows that, Atracurium was associated with a reduced incidence of myalgia (22 %) compared with ketorolac (85 %) and saline .The severity of myalgia after ketorolac was comparable with placebo pretreatment (27).

Study conducted in Royal Victoria hospital in England in 198 healthy adult patients in whom 54 (29%) patients pretreated with other NDNMB had muscle pain and 9 (41%) in Vecroneum pretreated. The frequency of pain on the 2nd day (20% of patients pretreated), in comparison with the 1st day (16% of Patients pretreated). In the vecroneum group the frequency of pain was similar (41%) on both days. The lowest frequency of pain was found in the vecroneum 2-min group (18.5%). All the 1-min pretreatment groups had a frequency of 19-20% except the pancroneum group where the frequency was 25%. The frequencies of pain in the 2-min groups of pancroneum, gallamine and tubocurarine were 28, 30 and 30%, respectively (28).

According to study undertaken in New Delhi India in 60 ,5mg/kg Phenytoin pretreatment significantly reduced myalgia from 45% (nine patients) in the non pretreated to 10% (two patients). Tubocurarine pretreatment (3 mg) resulted in a significant decrease in Fasciculation but myalgia which occurred in five patients remained the same (29).

Study conducted in Iran referral Hospital shows that incidences of myalgia after pretreated with diclofenac at 12, 24 and 48 hours after operation were 23.8%, 19.1%, and 12.7% respectively versus incidences of 52.4%, 47.6%, and 44.4% respectively in placebo pretreated group. The incidence and severity of myalgia were significantly lower in patients receiving diclofenac through three evaluation periods (30).

Study conducted in army medical college in Pakistan in 60 patients result shows pretreated by 0.5mg/ kg Rocuronium18 (60 percent) patients had moderate myalgia and pretreated by 0.1mg/kg Rocuronium and 1.5mg/kg Suxamethoneum the result 16 (53.3 percent) patients had mild myalgia; moderate myalgia was observed in 3(10 percent) patients while no myalgia was observed in 11 (36.7 percent) patients (31).

Research conducted in Castle Hill Hospital, Cottingham, and Yorkshire, England in 236 patients shows that patients received 50mg Suxamethoneum(1sec),50mg Suxamethoneum(10sec), 5mg gallamine followed 50mg Suxamethoneum(1min) and 5mg gallamine followed 50mg Suxamethoneum (2 min) the result shows that patients the incidence

of pains was 13.8%, in groups 2 was 15.67% ,in group 3 was 11.44%and in group 4 was 7.6.where as 79.1% was men and the remaining 20.9% was women patients respectively (32).

In one 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 non of the group did complain severe myalgia (33).

According to study conducted in Chungnam National University, Daejeon, Korea in forty patients result shows that the incidence of Mild myalgia after ramifentanl pretreatment were occurred in 1 patient (5%) where as in non treatment patient were in 2 patients (10%)(34).

According to study Dayanand Medical College and Hospital, Ludhiana, Punjab, India in Ninety adult patients who received one dose of propofol, repeat dose of 0.5 mg/kg propofol , and repeat dose of 1.0 mg/kg propofol the result shows that 56.67% of patients had no (grade I) myalgia and 3.33% patients had severe grade IV myalgia, there was no postoperative myalgia (grade I) in 80% of patients and no patient had grade IV (severe) myalgia and 93.33% did not have myalgia (grade I) and none of the patients ever had grade III (moderate) or IV (severe) myalgia respectively(35).

According to in Kurdistan University of Medical Sciences, Santander in Iran randomized double-blind study in 143 patients, who were received 0.5 mg/kg of ketamine and the same volume (5ml) of normal saline). Overall, the incidence of POM in Group K was significantly less, when compared with Group N ($P<0.05$), but both groups were comparable based on the grade 2 of POM. Result shows (18.1%) of patients in ketamine group had myalgia, whereas in non pretreated group (50%) of patients had myalgia. Grade 1 POM was lower in Group K when compared with Group N (nine in Group K versus 33 in Group N, whereas the incidence of grade 2 POM was comparable among patients of the two groups (36).

According to the study conducted in Hanyang University School of Medicine, Seoul, Korea to determine optimal dose of Rocuronium to prevent succinylcholine-induced fasciculation and myalgia on one hundred patients by dividing into five groups. Twenty patients were allocated

randomly to each pretreatment group: 0.02 mg/kg Rocuronium (Group 0.02), 0.03 mg/kg Rocuronium (Group 0.03), 0.04 mg/kg Rocuronium (Group 0.04), 0.05 mg/kg Rocuronium (Group 0.05) and 0.06 mg/kg Rocuronium (Group 0.06). On postoperative day 1, the incidence and severity of myalgia were Group 0.02 (n = 20) ,9 (45) ,Group 0.03 (n = 20), 7 (35) ,Group 0.04 (n = 20), 4 (20) ,Group 0.05 (n =20) 4 (20) , Group 0.06 (n = 20) ,2(10)respectively(37).

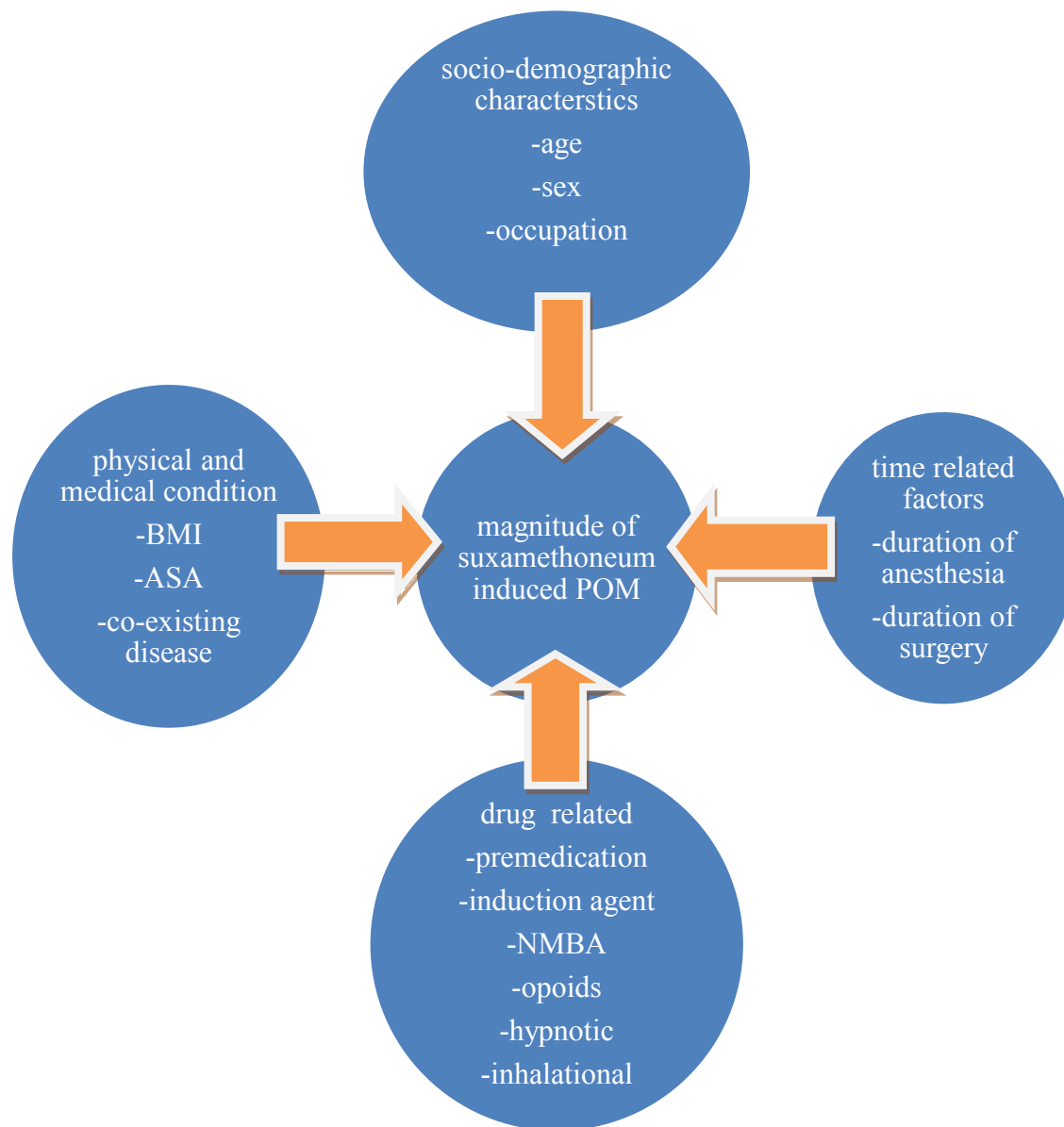
According to the study done in GTB Hospital, Shahdara, and Delhi, India on 60 adult patients to evaluate the effectiveness of magnesium sulfate with propofol induction of Anesthesia induction on succinylcholine induced fasciculation and myalgia.MG groups were pretreated with magnesium sulfate 40 mg/kg body weight in 10 ml volume, while patients of NS group were given isotonic saline 0.9% in the same volume (10ml) intravenously slowly over a period of 10 min..After 24 h of surgery, no patient of MG group and 30% patients of NS group had myalgia with a significant difference ($P < 0.002$)(38).

Study conducted on sixty patients undergoing direct laryngoscope at Hacettepe University, Ankara, Turkey between January and March 2010 to assess Effects of dexmedetomidine on succinylcholine-induced myalgia in the early postoperative period result showed in group D, only one patient suffered from mild myalgia, and 29 patients had no myalgia. In group C, 10 patients suffered from mild myalgia, and 20 patients had no myalgia. The incidence and severity of myalgia were significantly higher in group C ($p=0.014$)(39).

According to A randomized double blind case control study conducted on sixty adults ASA I or II patients on in Department of Anaesthesia and Surgical Intensive Care Unit, Liaquat National Hospital, Karachi result showed that fasciculations were noticed in group "A" as 100 % (mild to severe) and in group "B" 13.3% (mild). Postoperative myalgias at 6 and 12 hours after surgery were 76.66 % in group "A" and 16.66 in groups "B". After 24hours in group "A' post operative myalgias were 93.33% and group "B" 23.33 %(40).

The consumption of fentanyl in the first 24 h was significantly less in the group P compared to the group C (674.03 ± 137.84 mcg vs. 1002.67 ± 214.43 mcg).Sedation score was significantly higher in group p(41).

2.2 conceptual frameworks



CHAPTER THREE- OBJECTIVE

3.1 GENERAL OBJECTIVE

- ✓ To assess the magnitude and associated factors of Suxamethonium induced post-operative myalgia in adult elective surgical patients from January 1, 2017 to March 1, 2017G.C in Zewuditu memorial Hospital, Addis Ababa Ethiopia.

3.2 SPECIFIC OBJECTIVES

- ✓ To assess the magnitude of Suxamethonium induced post-operative myalgia in adult elective surgical patients.
- ✓ To identify factors associated with Suxamethonium induced post-operative myalgia in adult elective surgical patients.

CHAPTER FOUR METHODS AND MATERIAL

4.1 Study Area and period

This study was carried out at Zewuditu memorial hospital which is located in the capital city of Addis Ababa, Ethiopia .The hospital is one of the governmental Hospitals in Addis Ababa city administration, and gives services for specialty of gynecology and obstetrics, neurosurgery, general surgery, internal medicine and pediatrics. It has four operation theatres two post anesthesia care unit and the study was carried out from January 1, 2017 to March 1, 2017G.C.

4.2 Study design

Hospital based cross sectional study design was employed.

4.3 population

4.3.1 Source Population

All adult elective surgical patients who were underwent surgical procedures in Zewuditu memorial Hospital, Addis Ababa Ethiopia, 2017 G.C.

4.3.2 Study population

All adult elective surgical patients who were under went surgical procedures under general anesthesia in Zewuditu memorial Hospital from January 1, 2017 to March 1, 2017G.C.

4.4 Eligibility criteria

4.4.1 Inclusion criteria

-ASA status I and II

-BMI below 35kg/m²

-Patients age 18-65 years of old

4.4.2 Exclusion criteria

-All patients who were undergone surgery in regional anesthesia.

-All patients who were undergone surgery under GA without relaxation

-patients who were admitted to ICU

-patients with neuromuscular disorder

4.5. Sampling Technique and Sample Size Determination

4.5. 1. Sample size determination

The sample size was calculated using the single population proportion formula

$$n = \frac{(Z_{\alpha/2})^2 \times (p) \times (q)}{d^2}$$
$$= \frac{((1.96)^2 \times (0.5) \times (0.5))}{(.05)^2} = 384$$

Where n=number of sample size

Z=desired 95% confidence level=1.96

P=0.5 maximum population proportion, since no previous studies found.

$$q=1-p=1-0.5=0.5$$

d= is margin of sampling error tolerated (5%) of sample size.

By using correction formula for finite population since source population are less than 10,000.

$n = n \div (1 + n \div N)$ where

n=the sample size 384

N= total number of patients who were undergone elective operation, in two months 283

$$= 384 \div (1 + 384 \div 283)$$

$$= 160$$

Mean of midyear population is used to get total number of elective patients who were undergone operation in two months duration. The midyear population from situational analysis is 851.so, the size of population in two month is divided by 3 gives 283 .from this final sample size is 160.

4.5.2. Sampling techniques

Systematic random sampling techniques was used to select study participants by using skip interval $k = N/n$, $k = 283/160 = 2$ starting from 1st patient from schedule list.

n=total sample population

N=total study population

K=skip interval

4.6 Study variables

4.6.1 Independent Variables

Socio-demographic

- Age
- Sex
- Ethnicity
- occupation

Physical and medical condition

- BMI
- ASA physical status
- premedication drug used

Drugs and surgery related

- Induction drug used
- NMBD used
- Dose of drugs used
- Duration of anesthesia
- Type and Duration of surgery
- Incidence fasciculation

4.6.2. Dependent Variables

Suxamethonium induced post-operative myalgia

4.7 Plan of Data Collection

Check list was prepared in English which includes socio demographic data, physical characteristics of the patient, patients ASA class, medical co-morbidities, diagnosis, premedication drug used, types of procedure, type and dose induction used, the time gap between pretreatment and Suxamethonium, type and dose analgesic agent used, type and dose of muscle relaxant used for intubation and maintenance, duration of anesthesia and type, durations of surgery. Questionnaires were prepared in English which includes POM intensity assessment methods and onset of POM and the patients were interviewed by data collector. The data collection was under taken by MSC anesthesia students in the OR and nurses by reviewing patients chart and interviewing patients and the principal investigator was supervised the completeness of the data daily.

4.8 Data Processing and Analysis

The data was entered on epi info version 7 and was exported to SPSS version 20 computer program for analysis. Descriptive statistics was used to summarize data, tables and figures for display results. Bivariable and multivariable logistic regression analysis was used to see the effect of independent variable on magnitude of Suxamethonium induced myalgia. Those variables which were significant on bivariate analysis at p-value less than 0.2 were taken to multivariate analysis. In multivariate analysis value of less than 0.05 was used as a cut of point for presence of association. Strength of association was measured by 95% confidence interval and/ Odd ratio.

4.9 Data Quality Control and Assurance

A data collector was trained by principal Investigators. Pretest was done for 5% of sample population at each operation theatre and ward of Tikur Anbessa Specialization Hospital. During data collection; regular supervision and follow up was made. Principal Investigator was cross check for completeness and consistency of data every day. All materials used for data collection was arranged sequentially and data was stored in safe and secure place.

4.10 Dissemination plan

Copies of the research will be disseminated to college of health science, school of medicine/department of anesthesia, Zewuditu memorial Hospital, Addis Ababa University student research office, Ethiopian Association of Anesthetists, Ethiopian ministry of health. Finally it will send to national and international journal publishers for publication.

4.11 Operational definitions

Bolus dose:-administration of all calculated dose of a given drug at once.

Fasciculation:-diffuse uncoordinated muscle contractions seen after intravenous administration Suxamethonium.

Induction agent:-the first anesthetic agent that result loss of consciousness.

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

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

Myalgia: -generalized aches and pains that commonly occur 24 to 48 hours after succinylcholine administration.

Precurarization: -administration of a small dose of a non-depolarizing neuromuscular blocking agent (NDMBA) a few minutes before SCH.

Pretreatment: -administration of any drugs that will be reduce the magnitude of POM

Repeated dose:-administration of a given drug more than two times

Self-timing:-the time gap between pretreatment dose and intubation dose of Suxamethonium

Severe pain:-muscle pain or stiffness at one or more site and causing disabilities or limiting activity and requiring analgesic therapy.

4.12 Ethical Consideration

Prior to data collection, this proposal was reviewed by the ethical committee of college of health science school of medicine department of anesthesia. Then, after that official letter for permission was requested from department of anesthesia, which has given to Zewuditu memorial hospital clinical director office. Moreover, the objective of the study was explained to both hospital administration and the patients who were included in the study. Verbal consent from the patients was asked and Confidentiality of the information was assured by using code numbers than personal identification names and keeping questionnaires locked.

CHAPTER FIVE

RESULTS

Socio-demographic characteristics of the patients

Total 160 adult elective surgical patients were involved in this research and the mean age of the patients was 39.11 ± 11.35 . The mean BMI was 23.43 ± 3.94 , of them 66(41.3%), were with $18-24.9 \text{ kg/m}^2$, 54(33.8%) were $25-29.9 \text{ kg/m}^2$ and 11(6.9%) patients' BMI was greater than $30-34.9 \text{ kg/m}^2$. 51(31.9%) of the participants were Amhara and 40(25%) were Oromo in ethnicity and majority of participants were civil servant in occupation. Only ASA I and ASA I were included in the study and majority of participants were American society of anesthesiology physical status one (ASA I). The majority of diagnosis was general surgery cases account about 132(82.5%).

Table 1:- Distribution of socio-demographic characteristics of patients who were under gone elective surgical procedures from January 1,2017to march 1, 2017 in Zewuditu memorial Hospital.

| variables | | Frequency (%) | Mean±SD |
|------------|----------------------------|---------------|--------------|
| Age | 18-29 | 38(23.8) | 39.21±11.350 |
| | 30-41 | 59(36.9) | |
| | 42-53 | 41(25.6) | |
| | 53-65 | 22(13.8) | |
| Sex | male | 76(46.5) | |
| | female | 84(52.5) | |
| BMI | Bellow 18 kg/m^2 | 29(18.1) | 23.43±3.942 |
| | $18-24.9 \text{ kg/m}^2$ | 66(41.3) | |
| | $25-29.9 \text{ kg/m}^2$ | 54(33.8) | |
| | $30-34.9 \text{ kg/m}^2$ | 11(6.9) | |
| occupation | Civil servant | 94(58.75) | |
| | merchant | 22(13.75) | |
| | farmer | 15(9.37) | |
| | Labor worker | 20(12.5) | |
| | others | 8(5) | |
| ASA | I | 129(80.4%) | |
| | II | 31(19.6) | |

Intra operative data

106(66.3%) patients were induced with thiopental, 51(31.9%) patients were induced by propofol and only three patients were induced with ketamine. Almost all of patients were maintained with 0.75%-2.5% MAC of halothane. The majority of procedures were general surgery account about 132(82.5%) of patients. The mean duration of anesthesia and surgery was 2.63 ± 0.724 and 2.29 ± 0.608 hr respectively

Table 2: distribution of intraoperative factors for patients who were underwent elective surgical procedure from January 1, 2017 to March 1, 2017 in Zewuditu memorial Hospital.

| Drugs type | | Frequency (%) |
|---------------------------------|------------------------|---------------|
| Premedication(mg) | Diazepam | 2(1.3) |
| | Dexamethasone | 3(1.9) |
| | Phenytoin | |
| Analgesia preoperatively | tramadol | 35(26.71) |
| | diclofenac | 24(18.32) |
| | Tramadol, diclofenac | 71(44.4) |
| | phetidine | 1(0.6) |
| | No analgesia | 29(18.1) |
| Induction dose of Suxamethoneum | ≤ 100 mg | 109(68.1) |
| | 101-120mg | 35(25.9) |
| | >120 mg | 16(10) |
| Analgesic intra operatively | Diclofenac. Tramadol | 20(12.5) |
| | diclofenac | 7(4.4) |
| | tramadol | 7(4.4) |
| | Peripheral nerve block | 15(9) |
| NMBA | Suxamethoneum | 6(3.8) |
| | vecroneum | 94(58.8) |
| | pancroneum | 37(21.9) |
| | atracuroneum | 23(14.4) |

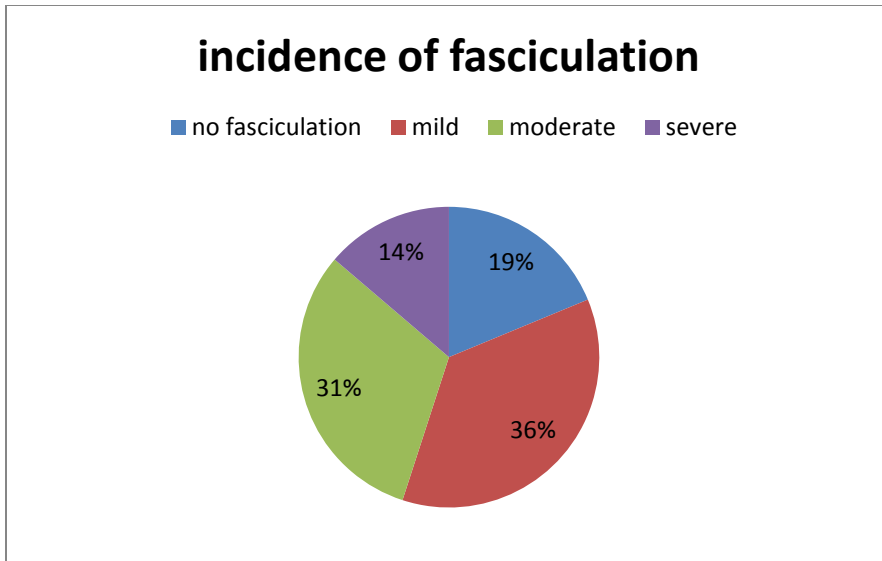


Figure 1: Distribution of severity of fasciculation in patients who were under went elective surgical procedure from January 1, 2017 to March 1, 2017 in Zewuditu memorial Hospital.

Post operative data

31(33.69%) were experience mild POM 12(13.04%) were male and 19(20.65%) females, 35(38.04%) had moderate POM 13(14.13%) were males and 22(23.91%) were female and out of 26(28.25%) who had severe pain 7(7.6%) were males and 19(20.65%) were females. 145(90.6%) patients had treated with diclofenac and tramadol post operatively for myalgia, 7(4.4%) patients got combined Diclofenac, tramadol and peripheral nerve block and 5(3.1%) patients did not get any analgesia for post operative pain management.

Table 3: Distribution of Suxamethonium induced post operative myalgia in patients who were under went elective surgical procedure from January 1, 2017 to March 1, 2017 in Zewuditu memorial Hospital.

| Variable | | Frequency (%) |
|-------------------|---------------|---------------|
| Myalgia | Yes | 92(57.5) |
| | no | 68(42.5) |
| Myalgia at 24hr | yes | 84(52.5) |
| | no | 76(47.5) |
| Myalgia at 48hr | yes | 74(46.2) |
| | no | 86(53.8) |
| Myalgia in female | yes | 61(67.31) |
| | no | 23(30.26) |
| Myalgia in male | yes | 31 (33.7) |
| | no | 45(69.73) |
| Site of myalgia | One | 31(19.4) |
| | two | 45(28.1) |
| | More than two | 16(10) |

Table 4: Distribution of the relationship between induction agent and Suxamethonium induced post operative myalgia from January 1, 2017 to March 1, 2017 in Zewuditu memorial Hospital.

| | | Induction agent | | | total |
|---------|-----|-----------------|-----------|----------|-------|
| | | thiopentone | propofol | ketamine | |
| myalgia | Yes | 62(58.49%) | 28(54.9%) | 2(66.6%) | 92 |
| | No | 44 | 23 | 1 | |
| total | | 106 | 51 | 3 | 160 |

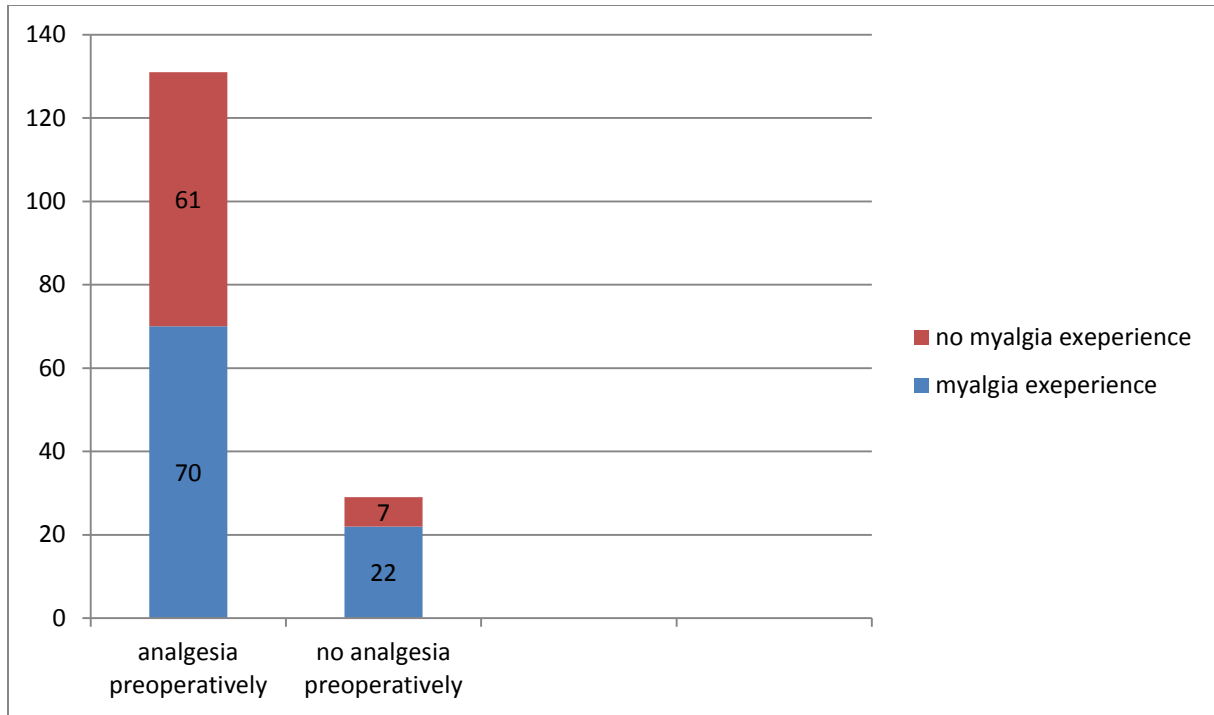


Fig: 2 the relationship between preoperative analgesia and Suxamethonium induced post operative myalgia.....21

Factors associated with post operative Suxamethonium induced myalgia

In multivariable analysis when 95% confidence interval for adjusted odds ratios were calculated among these variables post operative Suxamethonium induced myalgia of patient showed statistically significant associated with sex of patients ($p=0.000$, analgesia preoperatively ($p=0.016$) and incidence of fasciculation ($p=0.001$), the odd of post operative Suxamethonium induced myalgia were four times more likely than being female as compared to odd of being male (AOR=4.015, 95%CI 1.959, 8.228), odd of post operative Suxamethonium induced myalgia were 0.265times less likely had analgesia preoperatively than odd of as compared had not analgesia preoperatively (AOR=0.265, 95%CI 0.090, 0.780) and the odd of post operative Suxamethonium induced myalgia five times higher likely had fasciculation during induction to as compared than odd of had not fasciculation during induction (AOR=5.095, 95%CI 1.938, 13.497).

Table 5: Distribution of peri-operative factors associated with Suxamethonium induced post operative myalgia who were under went elective surgical procedure from January 1, 2017 to March 1, 2017 in Zewuditu memorial Hospital.

| Variables | | Patients with myalgia | | Odds Ratio | | P-Value |
|--------------------------|-------------|-----------------------|----|---------------------|---------------------|---------|
| | | Yes | No | Crude (95%CI) | Adjusted (95%CI) | |
| sex | female | 61 | 23 | 3.85(1.984,7.47) | 4.015(1.959,8.228) | <0.001* |
| | male | 31 | 45 | 1 | 1 | |
| Analgesia preoperatively | yes | 70 | 22 | 0.308(0.117,808) | 0.265(0.090,0.780) | 0.016* |
| | No | 61 | 29 | 1 | 1 | |
| fasciculation | yes | 84 | 46 | 5.807(2.072,12.173) | 5.095(1.938,13.497) | 0.001* |
| | No | 8 | 22 | 1 | 1 | |

Bold= reference

CHAPETR -SIX

6.1 DISCUSSIONS

Suxamethonium since its introduction into clinical practice it has been recognized that fasciculation's, myalgia, and rise in biochemical markers including serum creatine kinase and potassium occurs frequently with its use. post-operative myalgia is thought to be caused by motor units firing at physiological higher rate following Suxamethonium administration ,leading to unsynchronized muscle contractions causing shearing forces of skeletal muscle fibers(5).

In this study a total of 92(57.5%) of patients who underwent general anesthesia had post Suxamethonium induced myalgia with in the first 24 to 48hr of post operative day. The rate of myalgia in patients 24hr was relatively higher than in the 48hr of post operative day.

In comparison with this study the study results reported from America and a Meta analysis study done in Canada, in America by American society of Anesthesiologists, in Pakistan and Iran the magnitude of succinylcholine-induced myalgia were ranges from 5%to 83%, (1.5 to 89% but the most commonly quoted figure is around 50%), 41%–92%, 50 percent, respectively.

Study conducted in army medical college in Pakistan (60 percent) patients had moderate myalgia and pretreated by 0.1mg/kg Rocuronium and 1.5mg/kg Suxamethonium the result was 16 (53.3 percent) patients had mild myalgia; moderate myalgia was observed in 3(10 percent) patients while no myalgia was observed in 11 (36.7 percent) patients. The variation may be from all previous Meta analysis because of different setup in different hospitals and countries but in this was single centered study.

In contrast to our study the study done in GTB Hospital, Shahdara, and Delhi, India was lower magnitude of Suxamethonium induced post operative myalgia after 24h of surgery it was about 30% of patients had myalgia with a significant difference and study conducted at Hacettepe University, Ankara, Turkey 33.33% patients suffered from mild myalgia, and 67.67patients had no myalgia. Whereas in other Study conducted in India, Instutes of medical Education in 210 patients at three dose levels (1, 1.5and 2mg/kg) after Suxamethonium 70% of patient was experience post operative myalgia(22).It was higher than in our study result.

Our study revealed that the regardless to the induction and dose agent the severity of post operative Suxamethonium induced the severity of pain is the same 31(33.69%) were experience mild POM, 35(38.04%) had moderate POM and 26(28.26%). Study in Turkey in contrast to our study at higher dose of propofol the magnitude of POM was higher. 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 non of the group did complain severe myalgia respectively(33).

This study revealed that being female was strongly associated with post operative Suxamethonium induced myalgia. Out of 92 patients who have pain experienced post operative Suxamethonium induced myalgia 31 (33.7%) were male and 61(67.3%) were females. developed severe pain out of these 19.77 were males and 36.04% of pain was mild pain and greater in female patients it was comparable to study conducted by Vinit K, etal females are more likely to suffer than males (6) and also Study conducted North Dakota in fifty patients shows that the magnitude of postoperative myalgia at the 24-hour were (60%) were females it much to our result. The reason may be due to female's hormones play roles in having more pain sensitivity, females have greater nerve density, psychological experience of pain differs from males they worry about pain and feel more helpless about it.

According to this study the result showed that the most site of pain were shoulder in 39 patients, neck in 26 patients, arm in 17 patients and 8 patients on throat and 45(28.1%) patients experienced two site pain and 31(19.4%) had one site pain and only 16(10%) patients had more than two site pain and in comparable to this study according to the Study conducted in Liverpool Maternity Hospital and Mill Road Maternity Hospital, Liverpool, England the site of pain the incidence of jaw and neck pains was maximal on the first postoperative day, that of shoulder and limb pain on the second, and that of chest and back pain on the second and third postoperative day(23).Study conducted North Dakota in fifty patients to assess the magnitude and site of Suxamethonium induced myalgia of postoperative myalgia at the 24-hour the result showed that the most locations were neck, shoulder, and chest.

This study revealed that the incidence of fasciculation significantly associated with the magnitude post operative myalgia that of 81.25% patients had experienced fasciculation ($p=0.001$). From those patient had fasciculation 84(64.61%) were had POM and 46(35.39%) patients were did not have POM. And also the study conducted in Himalayan Institute of Medical Sciences, Dehradun, India the overall incidence of muscle fasciculation's was 83.9%in (20)

A study conducted in Department of Anaesthesia and Surgical Intensive Care Unit, Liaquat National Hospital, Karachi result showed that fasciculations were noticed 100 % (mild to severe) and 6 and 12 hours after surgery the incidence of POM were 76.66 % and after 24hours post operative myalgias were 93.33% (40).fasciculation was significantly associated with myalgia.

The reason may be due to fasciculation involves vigorous contraction by muscle bundles with no possibility of shortening and without synchronous activity in adjacent bundles. This might produce fiber rupture or damage, thus causing pain.

71(54.19%) of the patients were received combined tramadol and diclofenac and 35(26.71%), 24(18.32%) participant were received tramadol and diclofenac alone during pre operatively as analgesia. Study conducted in Iran referral Hospital shows that magnitude of myalgia after pretreated with diclofenac at 12, 24 and 48 hours after operation were 23.8%, 19.1%, and 12.7% respectively versus incidences of 52.4%, 47.6%, and 44.4% respectively in placebo pretreated group. The incidence and severity of myalgia were significantly lower in patients receiving diclofenac through three evaluation periods.

Conducted in England shows that premedication with diclofenac was associated with significant reduction in the intensity of myalgia. Among the patients given diclofenac, only 5.9% felt severe and moderate pain 24hr after operation and 35.3% had mild and 52.9% of patients had no pain(25) comparable to these result our study showed that less magnitude of post operative myalgia in patients had received analgesia at induction the reason may in our study most Anesthetist used diclofenac as analgesic agent preoperatively. It has been suggested that the underlying mechanism of muscle damage associated with administration of Suxamethonium may involve calcium-induced phospholipids degradation with release of damaging products of fatty acid metabolism. The reason may be NSAID may be interrupt prostaglandin mediated destructive cycle.

According to study conducted in Queens's University of Belfast with thiopentone 3-5mg/kg and with propofol 2-3 mg/kg) and) were receive Suxamethonium 1 mg.kg for intubation 24 hrs after surgery the result showed that the incidence of muscle pains was 60, and 55% in groups Propofol, and thiopentone respectively (33).In comparable to above study this study showed that with standard dose of thiopentone and propofol the incidence of POM in patients induced with thiopentone were 62(58.49%) and from those patients induced with propofol were 28(54.9%) and from those patients induced with ketamine were 2(60%)

6.2 Strength of the Study

To my knowledge this is the first study in my study area in Ethiopia to assess the magnitude of Suxamethonium induced post operative myalgia and to determine predictors of myalgia in elective surgical patients; so it can be used as a baseline data for researchers and policy makers.

6.3 Limitation of the Study

It is a single center study, therefore, our results cannot be generalized to other centers that follow different pretreatment options, intra-operative and post operative analgesia and anesthetic techniques in different Hospitals.

CHAPTER SEVEN

CONCLUSION AND RECOMMENDATION

7.1. Conclusion

In our study the magnitude of Suxamethonium induced post operative myalgia in the first 24 to 48hrs. The independent predictors of Suxamethonium induced post operative myalgia in this study were being female, fasciculation during induction and analgesia at induction.

7.2 Recommendation

To minimize the magnitude of Suxamethonium induced post operative myalgia and post operative patient discomfort different prevention techniques should be applied.

If possible it better to avoid the use of Suxamethonium regularly for elective patients.

It is recommended that premedication of patients with analgesic agent before induction anesthesia especially with NSIDA.

It is also recommended that pretreatment of patients with NDNMBD before Suxamethonium.

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ANNEX-I- 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 underwent elective surgical procedures from November 14, 2016 to February 13, 2017 in Zewuditu memorial Hospital, Addis Ababa, Ethiopia. . The purpose of this study to assess the magnitude and risk factors Suxamethonium induced post-operative myalgia in elective surgical procedures.

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. BMI _____ Kg/m² and 1.5. Occupation A. farmer B. merchant C. labor D .civil servant F. other

1.6. Ethnic group A. Oromo B.Amhara. C.Tigrie D.Gurage F. Wolayita F.other specify_____

Part 2 Preoperative evaluation

2.1. Diagnosis _____ 2.2.procedure_____

2.3ASA I _____ II _____ III _____ IV _____

Part

. Pretreatment dose in mg

A. diazepam _____

B. Ketorolac _____

C. Aspirin _____

D. Diclofenac _____

E. phentoin _____

F. Lidocaine(IV) _____

G. other _____

+Part 4. Induction agent used (dose in mg)

A. propofol _____

B. Thiopental _____

C. Ketamine _____

D. opiant used at induction _____

E. no opioid at induction _____

F. Inhalation agent _____

Part 5. precurarization drugs used before Suxamethonium dose in mg

A. suxamethonium _____

B. vecuronium _____

C. Atracurium _____

D. Pancuronium _____

E. Rocuronium _____

Part 6. The time gap between precurarization and Suxamethonium administration

A. after one min _____

B. after two min _____

C. after three min _____

D. after four min _____

E. after five min _____

Part 7. muscle relaxant used for intubation dose in mg

A. suxamethonium _____

B. vecuronium _____

C. Atracurium _____

D. Pancuronium _____

E. Rocuronium _____

Part 8. anesthetic agent used for intra operative maintenance

A. propofol infusion (rate/min) _____

B. Halothane (MAC) _____

C. Isoflurane (MAC) _____

D. Sevoflurane (MAC) _____

E. Desflurane (MAC) _____

F. Analgesic agent _____

G. Ketamine _____

Part 9. muscle relaxant used for intra operative maintenance dose in mg

A. suxamethonium _____

B. vecuronium _____

C. Atracurium _____

D. Pancuronium _____

E. Rocuronium _____

Part 10. patients compliant post-operative muscle pain

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

A. Yes B. No

10.2. If you answer yes for Que.10.1 in which part of your body feel this pain?

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

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

10.4 If you answer yes for Que.10.3 what are this medication you have taken?

A. NSAID _____

B. Opioid _____

10.5. 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?

10.6 When did you start feeling this pain?

A.After 6hr of pop time

B.After 12hrs of pop time

C.After 24 hrs of POP time

D.After 48hrs of POP time

F.After 72 hrs of POP time

Name of data collector_____

Status/profession _____ Signature_____

Thank you!!!

ANNEX –II ASSURANCE OF PRINCIPAL INVESTIGATOR

The under signed agrees to accept responsibility for the scientific ethical and technical
Conduct of the research project and for provision of required progress reports as
Per terms and conditions of the Research Publications Office in effect at the time of
Grant is forwarded as the result of this application

Name of the student: _____

Date. _____ Signature _____

Approval of the primary Advisor

Name of the primary advisor: _____

Date. _____ Signature _____