Research Article

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The effect of propofol versus thiopentone sodium as an induction agent on prevention of succinylcholine induced fasciculation and myalgia in adult elective surgical patient in Zewditu memorial hospital, Addis Ababa, Ethiopia. Prospective, Institutional based cohort study:2018

Abstract

Background: Succinylcholine is a commonly used short acting depolarizing muscle relaxant. Even though it is an excellent short acting depolarizing muscle relaxant of choice, still it has inherent side effects. Post-operative myalgia is the most common encountered problem in the first 24hours after succinylcholine administration. The aim of this study is to compare the effect of Propofol versus thiopentone sodium as induction agent on prevention of succinylcholine induced fasciculation and myalgia in adult elective surgical patient

Methods: Prospective, Institutional based cohort study design was conducted on all elective surgical patient who fulfill the inclusion criteria and induced with succinylcholine at Zewditu Memorial Hospital during specified study period. A patient who induced by propofol 3.0mg/kg was taken as Group propofol (n=40) and who induced with Thiopentone sodium 5mg/kg was taken as group thiopentone (n=40). Data was entered in to Epi info version 7 software by investigators and transported to SPSS version 20 statistics window for analysis. Differences of numerical data between groups have been evaluated using independent T-test. Categorical data has been analyzed with the Chi-Square test. A p value of <0.05 was considered as statistically significant.

Results: The demographic data of patients in two groups were comparable. The total incidence of succinylcholine induced fasciculation were 18(45%) and 28(70%) in propofol and thiopentone Groups respectively (P=0.007). The severity of fasciculation was reduced more in propofol group than in group thiopentone group (P=0.044). The total incidence of myalgia was 12(30%) and 21(52.5%) in propofol group and thiopentone group respectively (P=0.048). The severity of myalgia was reduced more in propofol group than thiopentone group (P=0.041).

Conclusion and recommendation:Propofol in comparison with thiopentone sodium is effective in reducing the incidence and severity of fasciculation and myalgia. We recommended to use propofol to reduce succinylcholine induced fasciculation and myalgia which currently suffers our patients.

Keywords: Thiopentone sodium,propofol, prevention of succinylcholine induced fasciculation and myalgia

Volume 12 Issue 2 - 2020

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Received: April 02, 2020 | **Published:** May 04, 2020

Introduction

Succinylcholine 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 and rise in biochemical markers including serum creatine kinase and potassium to increased intra cranial pressure, intra ocular pressure and emesis with aspiration.[1]

Fasciculation may be observed in 95% of patients, but the incidence of myalgia at 24 hours is about 50% following use of succinylcholine.[2]It is generally agreed that post-operative myalgia is un acceptable in modern anesthesia practice.[3]The duration of the discomfort is highly variable. It usually appears on the first day after surgery and lasts for 2 or 3 days but occasionally persists for as long as a week and it is most commonly described as the pain one might suffer after an unaccustomed degree of physical exercise and is usually affecting more than one site of our body that causing disability or limiting activities and difficulty on getting out of bed or turning head which is occur always in the neck, shoulder and upper abdominal muscles.[4]

The pathophysiology of succinylcholine induced myalgia is poorly understood, that is why there is no standard treatment available for this complication. Even though there is no published study and document that explain the experience of our country specifically, the severity and incidence of succinylcholine induced fasciculation and

postoperative myalgia is almost similarly suffers our patient more than surgical site pain as our country is commonly use this drug for induction to facilitate tracheal intubation.

Nondepolarizingagents circumvent most of these problems, but none has the same pharmacokinetic profile as succinylcholine. Rocuronium and rapacuronium come closer, but both have longer lasting effects than succinylcholine and so they could not replace this drug because of their longer lasting effects that delay patient in apnea.[3] Different pretreatment modalities have been advocated to reduce the incidence and severity of fasciculation and myalgia including non-depolarizing neuromuscular blockage[5] intravenous lidocaine[6]non steroidalanti-inflammatory drugs (NSAIDs[7] etc.But all of them come with variable success, except the one pretreatment with small dose of non-deploring neuromuscular blockage which is effective methods, but it is associated with blurred vision, diplopia, and difficulty in breathing and higher doses of succinylcholine is needed to obtain optimal intubating conditions which leads to a longer recovery and apnea period. Cost and availability may also limit its usage especially in developing country. In clinical practice, Propofol has produced conflicting results when administered for the prevention of postoperative myalgia. McClymont[8] found a lower incidence of succinylcholine-induced myalgia in a Propofol group while other study which was done in India in 2014 by using prospective randomized double-blind study stated that a single dose of the drug was not similarly effective.[9] This indicates that even though a lot of researchers try to alleviate this problem they come up with different result and other intolerable side effects, that is why it persist in the world in such a challenging way.

Various drugs have been reported to exhibit some antioxidant activity in vitro[10]whereas Propofol has further been shown to have the ability to form stable radicals and to inhibit the propagation of reactions involving free radicals in experimental animals and man.[11,12]Even though a lot of researchers try to alleviate this problem they come with different result and other intolerable side effects,[8,9] so that is why the researchers were eager to underwent this study to compare the effect of propofol versus thiopentone sodium as an induction agent on prevention of succinylcholine induced fasciculation and myalgia.

Propofol was produce conflicting results when administered for the prevention of postoperative myalgia, most researcher found a lower incidence of succinylcholine-induced myalgia when induced with Propofol while other studies have found that a single dose of the drug was not similarly effective.[8,9]So,the aim of our study is to prove this conflicting result. This study has significance for our anesthetist who used succinylcholine routinely because this study has provided rational and evidence-based case specific practical frame work that reduces the incidence of postoperative myalgia and fasciculation. And will be used as bull's eye in identification of what has been done and what should be corrected to prevent or reduce fasciculation and postoperative myalgia which is taken as source of greater distress to the patient than surgical site wound, therefore conducting such a research make our patient more beneficiary by alleviating postoperative myalgia which suffers them post-operatively and also decrease postoperative analgesic consumption.

Objectives

General objectives

To compare the effect of Propofol versus thiopentone sodium as induction agent on prevention of succinylcholine induced fasciculation and myalgia in adult elective surgical in Zewditu memorial Hospital.

Specific objectives

To determine incidence and severity of fasciculation on patients who underwent elective surgical procedure by using propofol versus thiopentone sodium as an induction agent.

To determine incidence and severity of myalgia on patients who underwent elective surgical procedure by using propofol versus thiopentone sodium as an induction agent.

Materials and methodology

It is Prospective, Institutional based cohort study design and it was conducted from January 1, 2018 to March 20, 2018G.C. This study has been carried out at Zewditu memorial hospital which is located in the capital city of our country 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 five operation theatres two post anesthesia care unit. The study population was including all adult elective surgical patients who underwent surgical procedures under general anesthesia with the use of succinylcholinein in Zewditu memorial Hospital who meet inclusion criteria during the study period. The Inclusion criteriawere patients aged between 18 to 60 years, patients belonging to ASA Class I and Class II and patients with BMI below 35kg/m^{2}and; The exclusion criteria were patients with pre-existing musculoskeletal disorders, patients precurarized with other long acting muscle relaxant,subjects who had received analgesics within 24h before scheduled surgery,patients receiving sedatives other than those determined by the study protocol,patients who are hypersensitive to any of the drugs in the study, pregnant mother,patient with history of drug abuse, Patient with history of burn more than 48hrs and less than six months and massive trauma.

Sample size calculation

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%. The study done in India shows that the incidence of fasciculation with Propofol and thiopentone were 48.48% and 78.79% respectively.[13]Taking this into consideration, the calculation of sample size has been: n (in each region) = (p1q1 + p2q2) (f (α, β))/ ((p1 - p2)^2

n=(0.4848*0.5152+0.7879*0.2121) (1.96*0.84)^2 /0.4848-0.7879)^2 =36 in each group. By adding 10% of total sample size as a contingency thesample size in each group has been (n=40).

P_1= incidence of fasciculation in Propofol group

P_2= incidence of fasciculation in thiopentone group

$q1= 1-p_1$

$q2=1-p_2$

α =significance level (1.96)

1-β=power of study at 80%(0.84)

Sampling procedures

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 28 patients who fulfill our inclusion criteria were operated in Zewditu Memorial Hospital per week that got from surgery logbook record; according to this data we were had 224 patients in our study period from whom we collected data from only 80 patients. So, sampling interval (k) was calculated as K=N/n=224/80, approximately 3, where N=total study population, n=total sample size. The first participant was selected randomly using lottery method. Then, every three patients were included in this study from the daily operation schedule list until the required sample size was met and groupedafter induction agent given by anesthetist Figure 1.

n=total sample population

N=total study population

K=skip interval

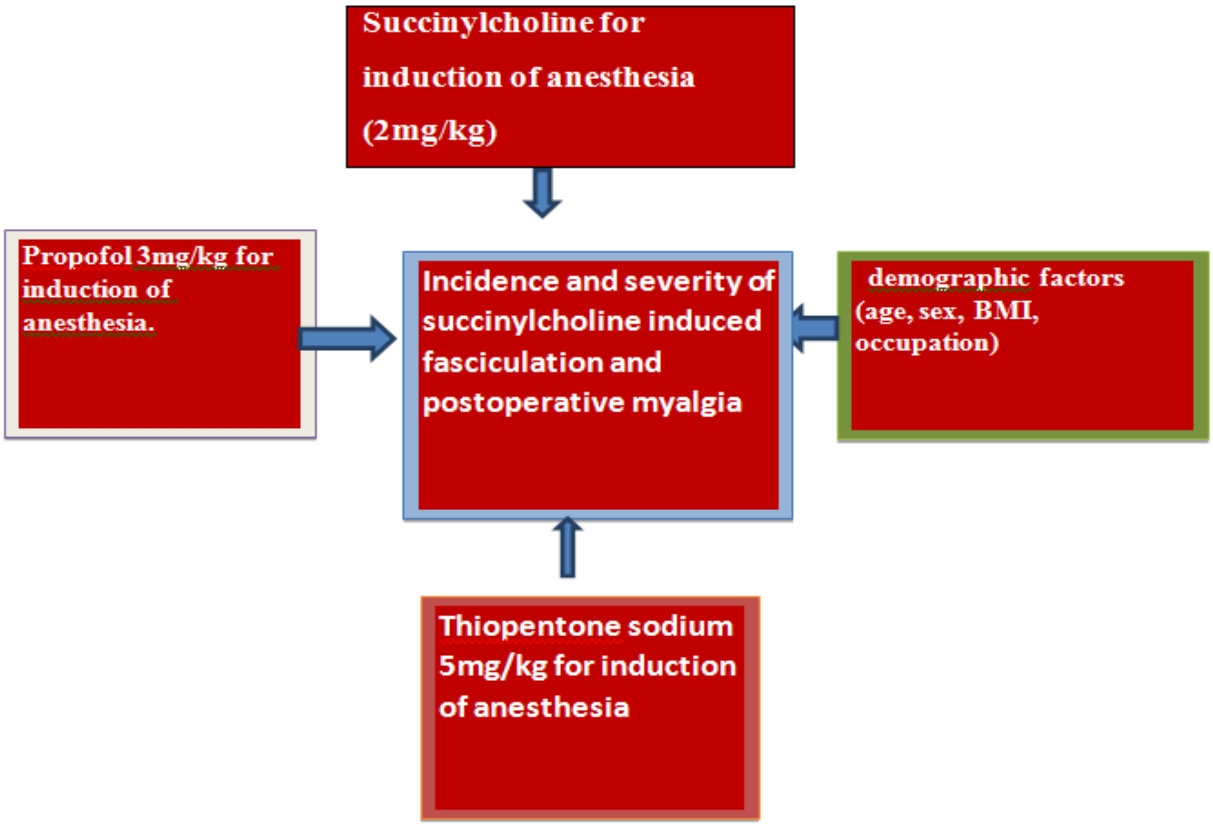

Figure 1 Conceptual frame work. (Adopted from: -22,4 and 6).

Data collection

Questionnaires and Check list were prepared in English and Amharic which includes demographic data, patients ASA class, types of diagnosis, types of procedure, type and doseof induction agent used, type and dose of muscle relaxant used for intubation and maintenance. Our questioner was including incidence and severity of fasciculation andpost-operative myalgia. Data collectors who was trained on how to grade fasciculation and myalgiahas beenobserve 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 nursespost-operatively for myalgia and supervised by principal investigator. Regular supervision and follow up was made. To ensure quality of data, pre-test of the questionnaire have been performed on 5% of study populations who fulfill the inclusion criteria in other hospital which is TikurAnbessa specialized 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 has been assured to improve the quality of data. Data consistency and completeness have been made throughout the data collection, data entry and analysis.

Data processes sing and analysis

The data was entered on epi info version 7 and was exported to SPSS version 20 statistics software for analysis. The principal investigator wasperformed data entry and cleaning. Normality of the distribution of data was tested by using the Shapiro-wilk test ($p>0.05$ considered as normally distributed).Descriptive statistics was used to summarize data, tables and figures for display results. We summarized data as mean±SD or Number (percentage).Equality of variances was checked by using Levene's F test (sig value >0.05 considered

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as equal variance assumed). Differences of numerical data between groups have been evaluated using independent T-test. Categorical data have beenanalyzed with the Chi-Square test.A p value of <0.05 has beenconsidered as statistically significant Figure 2.

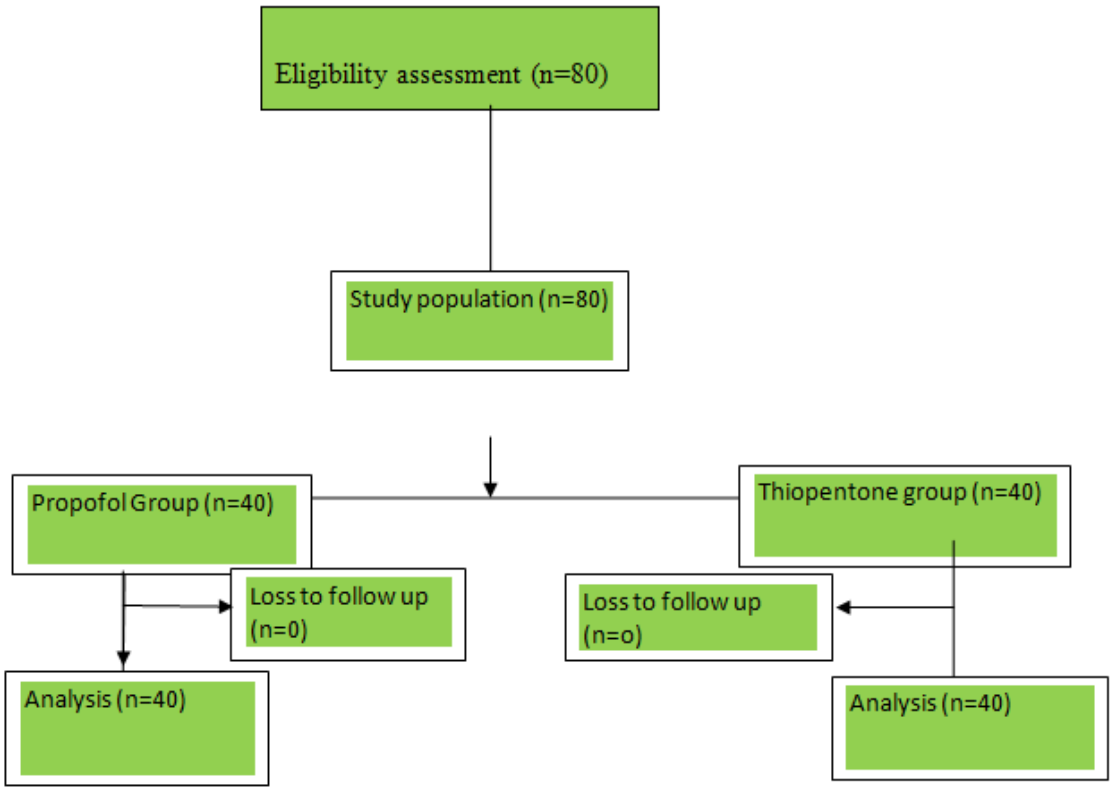

Figure 2 A study flowchart for enrolment of patients who underwent elective surgery under general anesthesia with succinylcholine at Zewditu Memorial Hospital, from january1, to March 20,2018.

Result

Demographic characteristics of the patients

Total 80 adult elective surgical patients were involved in this research and the mean age of the patients was 42.8±10.52 and 42.05±11.195 in "P" and" T" groups respectively. Among the participant 31(38.8%) and 17(21.3%) were labor workers and civil servant in 'P' and 'T' groups respectively. The majority of diagnosis was cholelithiasis that account 35(43.8%) of all diagnosis that followed by goiter. From the participant 12(30%) was males and 28(70%) were females in P group and 10(25%) was males and 30(75%) was females in T groups (p=0.617). Among the participant 34(85%) was ASAI and 6(15%) was ASAII in P group and 31(77.5%) was ASAI and 9(22.5%) was ASAII in T group (p=0.393 Table 1.

Table 1 Distribution of demographic characteristics of patients who were underwent elective surgical procedures from january1,2018 to march 20,2018 G.Cin Zewditu memorial Hospital

Variables	Propofol group (n=40) (Mean ± SD)	Thiopentone group (n=40) (Mean ±SD)	p-value
Age	42.8±10.52	42.05±11.195	0.758
Weight	61.25±8.962	61.9±11.21	0.734
Height	1.675±0.0579	1.675±0.0543	0.953
BMI	21.788±3.180	22.08±3.979	0.712

Notes: *Data are presented as mean and standard deviation by using independent t-test*

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Intra operative data

Among those 13(32.5%) experience mild fasciculation, five (12.5%) experience moderate fasciculation and there was no severe fasciculation experienced in 'P' Group and 15(37.5%) experience mild fasciculation, 10(25%) experience moderate fasciculation and three (7.5%) experience severe fasciculation in "T" Group. The severity of fasciculation has difference between propofol group and thiopentone group(P=0.007). Among those 46(57.7%) patient who experienced fasciculation 15(68%) was male and 31(53%) was female. The incidence of succinylcholine induced fasciculation has a difference between female and male (P=0.053). Among those participants who developed fasciculation 31(67.39%) and six (13%) were labor workers and civil servant respectively. Revealed that the incidence of succinylcholine induced fasciculation has a difference among those (P=0.138). Among those participants who developed succinylcholine induced fasciculation 35(53.85) and 11(73.33%) were ASAI and ASAII respectively. The incidence of succinylcholine induced fasciculation has a difference between ASAII and ASAI (P=0.071). Of the participants who developed succinylcholine induced fasciculation eight (72.72%) were under weight, 32(57.14%) were in normal range and six (54.54%) were overweight in their BMI respectively(p=0.055).

Post-operative data

Generally, 33(41.25%) of participant develops post-operative myalgia. Among those participants who developed POM 20(25%), 10(12.5%) and 3(3.75%) were experienced mild, moderate and severe post-operative myalgia respectively. Incidence and severity of POM indicated that seven (17.5%) was mild and five (12.5%) was moderate in "P" Group and 13(32.5%) was mild, five (12.5%)was moderate and three (7.5%) was severe myalgia in "T" Group. The incidence and severity of myalgia has a difference between propofol group and thiopentone group (P=0.048). Among those participants who experienced myalgia post-operatively 12(36.36%) complain shoulder pain which is followed by abdomen, arm, and throat pain; from those 15(45.45%) seek analgesia and 14(42.42%) of them were treated by diclofenac. Among those participants who feel post-operative myalgia 4(12.12%) feel at the first hour post-operatively, 18(54.54%) were feel after six hours post operatively; eight (24.24%) were feel after twelve hours post operatively and only three (9.09%) of the participant were feel muscle pain after 24 hours. From those participants who developed POM 27(46.55%) were females and the remaining 6(27.27%) were males (P=0.187). There was no correlation between succinylcholine induced fasciculation and post-operative myalgia (Spearman rho=-0.144).

Table 2 Incidence and severity of succinylcholine induced fasciculation and myalgia in patient who induced by propofol versus thiopentone sodium in Zewditu memorial Hospital; From January 1,2018- March 20, 2018

Parameter		Propofol group (n=40) (%)	Thiopentone group (n=40) (%)	p-value
Fasciculation	Incidence	18(45%)	28(70%)	0.044
	Nil	22(55%)	12(30%)	
	Mild	13(32.5%)	15(37.5%)	0.007
	Moderate	5(12.5%)	10(25%)	
	Severe	0(0%)	3(7.5%)	
Myalgia	Incidence	12(30%)	21(52.5%)	0.041
	Nil	28(70%)	19(47.5%)	
	Mild	7(17.5%)	13(32.5%)	0.048
	Moderate	5(12.5%)	5(12.5%)	
	Severe	0(0%)	3(7.5%)	

Notes: Nil: - No fasciculation/myalgia; chi-square test was used for analyze

Table 3 Incidence and severity of succinylcholine induced fasciculation among patients with different body mass index(BMI) who underwent elective surgical procedure at Zewditu Memorial Hospital, Addis Ababa, Ethiopia, 2018.

Variables		Frequency (%)				P-value
BMI		Under weight(<18.5)	Normal range (18.5-24.9)	Over weight (25-29.9)	Stage I obese (30-34.9)	-
Fasciculation	Nil	3(27.3%)	24(42.9%)	5(45.5%)	2(100%)	0.055
	Mild	4(36.4%)	19(33.9%)	5(45.5%)	0(0%)	
	Moderate	3(27.3%)	11(19.6%)	1(9.1%)	0(0%)	
	Severe	1(9.1%)	2(3.6%)	0(0%)	0(0%)	
Myalgia	Nil	7(63.6%)	32(57.1%)	7(63.6%)	1(50%)	0.949
	Mild	2(18.2%)	15(26.8%)	2(18.2%)	1(50%)	
	Moderate	2(18.2%)	6(10.7%)	2(18.2%)	0(0%)	
	Severe	0(0%)	3(5.6%)	0(0%)	0(0%)	

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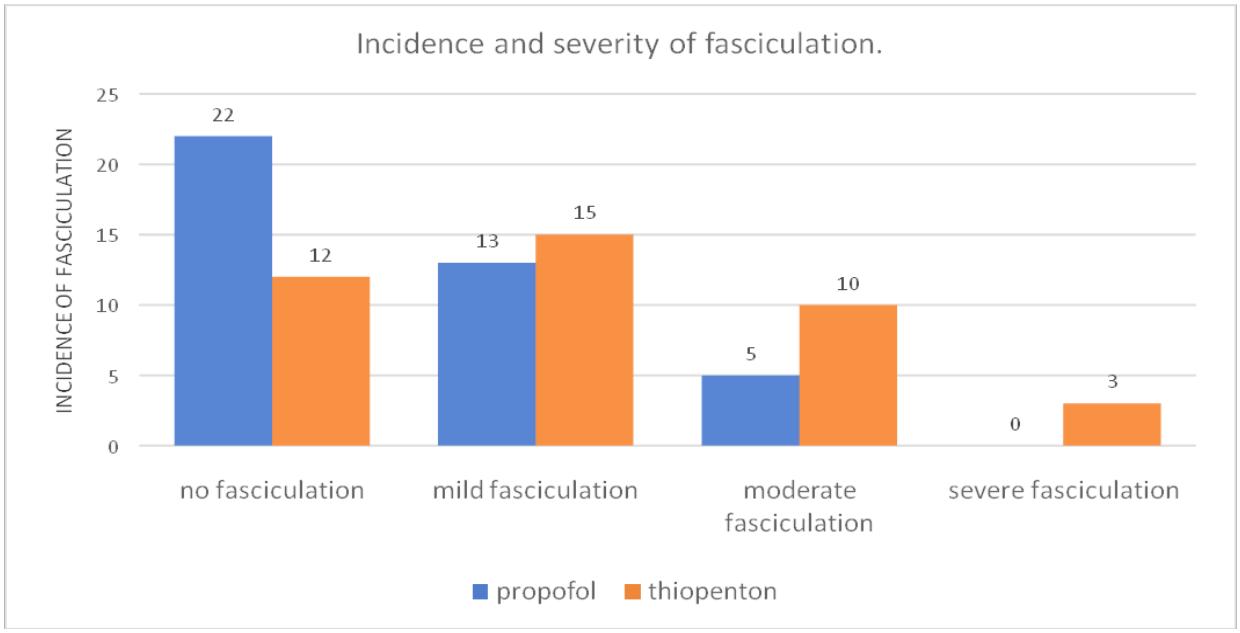

Figure 3 Distribution of succinylcholine induced fasciculation in patient who underwent elective surgical patient at Zewditu Memorial Hospital from January1,2018 to March20,2018 G.C.

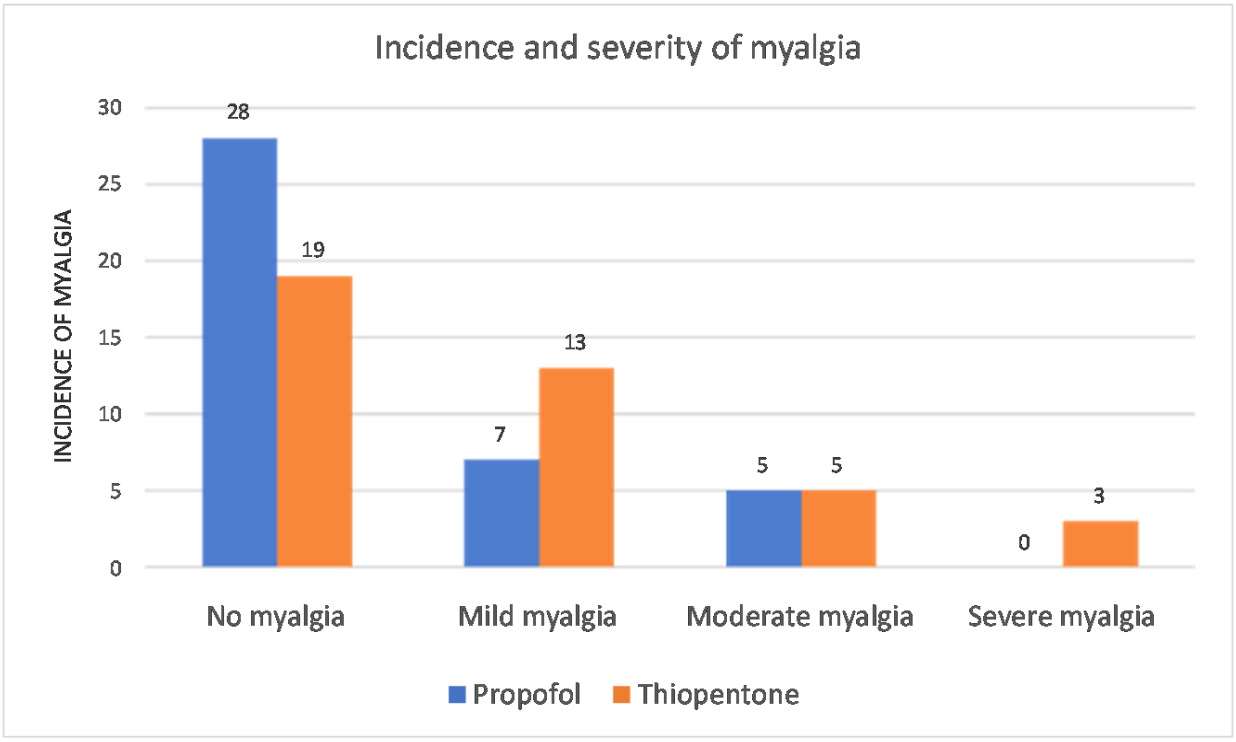

Figure 4 Distribution of succinylcholine induced myalgia in patient who underwent elective surgical patient at Zewditu Memorial Hospital from January1,2018 to March 20,2018 G.C.

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Discussion

In our study 18(45%) and 28(70%) were experienced fasciculation in propofol group and Thiopentone sodium group respectively. Incidence and severity of fasciculation has a difference between 'p' group and 'T' group significantly (P=0.007). In comparison with this study the study results reported from Gujarat, India on 99 patients who allocated randomly into three equal groups by using prospective, randomized, controlled clinical study stated that the total incidence of fasciculations were 25(75.76%,16(48.48%)& 26(78.79%) in group p1, p2&T respectively (p<0.001). Severity of fasciculation was reduced more in group" p2" than the two.[13]In our study 12(30%) and 21(52.5%) were complained post-operative myalgia in "P" Group and "T" Group respectively. Incidence and severity of myalgia has a difference between propofol group and thiopentone group significantly (P=0.048). In the study conduct in Gujarat, India on 99 patients in 2013 into three groups by using prospective randomized study compared to this study stated that the total incidence of myalgia was 19(57.57%),10(30.3%)&23(69.7%) in group p1, p2&T respectively (p<0.001).[13]In our study 28(70%) of the patient in thiopentone sodium group developed mild to severe succinylcholine induced fasciculation. In contrast to this study, the study done in Iran farabi eye hospital stated that 47.4% to 59.3% was developed moderate to severe succinylcholine induced fasciculation.[14] The difference may arise from different dose of succinylcholine that was used in ours and their study.In line with our study,study conducted Shoroghi, Mehrdad who try to investigate on effect of thiopentone on severity and duration of succinylcholine induced fasciculation on 300 patients ASA I&II to two groups who received intravenous succinylcholine immediately and 30 seconds after thiopental injection respectively. Moderate to severe fasciculation was found more in the group using succinylcholine 30 seconds after thiopentone injection(p=0.038).[15]

In study conducted at Diyarbakir, Turkey in 2003 by using 90 patients in three groups in which group-p1 took 2.5mg/kg propofol, group-T took 5mg/kg thiopentone and group-p2 took 3.5mg/kg propofol stated that the severity of fasciculation was significantly reduced in group-p2(P=0.01);[4]which is in line with our study.

Our study showed that 13(32.5%) experienced mild, five (12.5%) experienced moderate and three (7.5%) experienced severe myalgia in Thiopentone group and seven (17.5%) experienced mild five (12.5%) experienced moderate myalgia in "P" group. There was no severe myalgia in Propofol group which is comparable with study done in Turkey on 90 patients in three groups who have received G-1 thiopentone 5mg/kg, Group-2 propofol 2mg/kg and group-3 propofol 3.5mg/kg stated that 38% patient was complain mild to moderate pain, and 20% patients complain mild and 10 % patients was complain moderate pain respectively and none of the group did complain severe myalgia.[12]In contrast to our study, a meta-analysis reported from American society of Anesthesiologist stated that, the average incidence of myalgia in the first 24 hours with thiopental was 49.2% and with propofol was 65.4%.[16] The difference may arise from the different dose of propofol used in meta-analysis.

Our study also revealed that 13(32.5%) and five (12.5%) experienced mild and moderate fasciculation in Propofol group respectively;15(37.5%), 10(25%) and three (7.5%) experienced mild, moderate and severe fasciculation in Thiopentone group respectively. In contrast to our study, study reported from India on repeated bolus dose of propofol in three groups stated that 66.7% patients in group 3(who received repeated bolus dose of 1gm Propofol) was showed 0 grade fasciculation's.[17]

In comparison with this study the study conducted in Queens's University of Belfast in 80 adult patients, 40 patients were induced with thiopentone 3-5mg/kg and the remaining 40 induced with propofol 2-3 mg/kg) and Within each group half the patients (n = 20) were receive Succinylcholine 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.[9]

This study revealed that there is no correlation between succinylcholine induced fasciculation and post-operative myalgia (Spearman rho=-0.144). It was comparable with study conducted in Gujarat, India on 99 patients who allocated randomly into three equal groups by using prospective, randomized, controlled clinical study concluded that there is no correlation between fasciculation and myalgia (Pearson's r correlation r=-0.139).[6]

Conclusion

Propofol in comparison with thiopentone sodium is effective in reducing the incidence and severity of succinylcholine induced fasciculation and myalgia. Reduction of post-operative succinylcholine induced myalgia result in reduction of post-operative analgesic requirement.

Limitations

Lack of prior study on this and related tittles in Ethiopia was one of the limitation to lay a foundation for understanding the problem. the other one is most studies we used for comparison were randomized control trial.

Acronmy and abbravation

ASA, American society of Anesthesiologists; BMI, body mass index; BSc, Bachelor of science; FMOH, federal ministry of health;GA, General anesthesia; HGB, hemoglobin; IM, Intra muscular;IV, intra venous; NDNMBA, non-depolarizing neuromuscular blocking agent; NDA, Non-depolarizing agent; NMBA, neuromuscular blockade agents; NSAID, non-steroidal anti-inflammatory drugs;POM, post-operative myalgia; P, Propofol; T,Thiopentone; RSI, Rapid sequence induction; SCH, succinylcholine/Suxamethoneum

Declarations

Ethics approval and consent to participate

The study conducted after obtaining approval from IRB of Addis Ababa University health science college, school of medicine, department of Anesthesia. A legal letter submitted to Zewditu memorial hospital, Addis Ababa, Ethiopia where the study conducted.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Citation: Hika A, Akalu L, Melese, et al. The effect of propofol versus thiopentone sodium as an induction agent on prevention of succinylcholine induced fasciculation and myalgia in adult elective surgical patient in Zewditu memorial hospital, Addis Ababa, Ethiopia. Prospective, Institutional based cohort study:2018. *J Anesth Crit Care Open Access.* 2020;12(2):79–86. DOI: 10.15406/jaccoa.2020.12.00436