International Journal of Anesthesiology & Research (IJAR)
ISSN 2332-2780

Incidence And Severity Of Suxamethonium Induced Fasciculation And Post-Operative Myalgia, And Their Association With Different Iv Induction Agents Among Adult Patients Underwent Elective Surgery At Jimma Medical Center, A Prospective Cohort Study

Research Article

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Abstract

Background: Suxamethonium induced fasciculation (SIF) and post-operative myalgia (POM) is one the side effects occurred following administration of suxamethonium.
Objective: The present study aimed to assess the incidence and severity of SIF and POM, and their association with different IV induction agents among adult patients underwent elective surgery at Jimma medical center (JMC).
Methods: Prospective cohort study design was employed among a sampled 140 patients whoinduced by four IV induction agents (propofol, thiopentone, ketamine and ketofol) where in each group 35 patients were equally distributed. SIF and POM were assessed by separated structured grading and scoring toolsintraoperatively and post-operatively (respectively) after exposing patients toalready mentioned four induction agents. Data was entered into Epidata version 4.3.1 and finally exported to SPSS version 20 for further analysis. Cross tabulation/chi square and binary logistic regression were applied to determine their association. P-value < 0.05 was declared as statistically significant.
Results: The incidence of SIF was 94.3% and differs among induction agents (non-statistically significant difference) (propofol 32(22.9%), thiopentone 34(24.3%), ketamine 33(23.6%) and ketofol 33(23.6%) (P-value=0.204). The incidence of POM was 29.3% and highest among ketamine group 15(10.7%) and also varies among groups (propofol 6(4.3%), thiopentone and ketofol (each10(7.1%)) (P-value=0.255). The likelihood of POM occurrence was more likely among patients induced by ketamine [OR 1.8(0.7-5.1), p=0.215)] and thiopentone [OR 1.1(0.3-2.8), p=0.999)] but less likely among patients induced by propofol [OR 0.5(0.1-1.6), p=0.259)] by taking patients induced by ketofol as reference. The likelihood of SIF occurrence was also varies among IV induction agent(about two fold among thiopentone groups [OR 2.1(1.2-23), p=0.563]), but not showed statistically significant difference among groups.
Conclusion and Recommendation: Even though, the incidence of both SIF and POM were profound and no statistically significant safe IV inductions that mitigate this adverse effect(fasciculation and POM) following administration of suxamethonium, other option of muscle relaxant was warranted.

Keywords: Suxamethonium Induced Fasciculation; Post-Operative Myalgia; Incidence, Severity; IV Induction Agents; JMC, Ethiopia.

Introduction

Despite suxamethonium started to be used as one of the anesthetic drugs for muscle relaxation with extra short onset of action and brief duration of action since 1949, it was also accompanied with different side effects [1, 2]. One of the profound side effect is neuromuscular effects and muscle pain that patients experienced at post-operative period probably due to intraoperative fasciculation discerned or secondary to damage produced in the muscle during fasciculation [3-6]. The possible mechanism of SIF is due to prejunctional depolarizing action of succinylcholine, resulting in repetitive firing of the motor nerve terminals and antidromic

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Received: October 09, 2020
Accepted: April 03, 2021
Published: April 30, 2021

Citation: Mebratu Tila, Zemenu Muluken, Negashu Dadi, Mesfin Zewude, Elias Habtu, Getahun Dendir, WonduReta Demissie. Incidence And Severity Of Suxamethonium Induced Fasciculation And Post-Operative Myalgia, And Their Association With Different Iv Induction Agents Among Adult Patients Underwent Elective Surgery At Jimma Medical Center, A Prospective Cohort Study. *Int J Anesth Res.* 2021;09(03):624-629. **doi:** http://dx.doi.org/10.19070/2332-2780-21000124

discharges that manifest as uncoordinated muscle contractions [7]. The phenomenon of POM was first noted in 1952 by Churchill-Davidson following injections of succinylcholine due to diffuse uncoordinated contractions of muscle bundles [8]. POM refers to occasional vigor of muscle contractionsthat may give rise to a feeling of muscular stiffness/ pain of (facial, jaw, neck, shoulder, chest, back, trunk, limb/extremities)after consciousness has been regained. It commonly manifested as the pain one might suffer after strenuous physical exercise and usually affecting more than one site that causing disability or limiting activities and difficulty on getting out of bed or turning head postoperatively [9, 10]. It is postulated due to increased intracellular calcium concentrations, membrane phospholipid degradation, and release of free fatty acids or free radicals, which lead to increased membrane permeability [11-13].

The incidence of POM is significant and varies among patients underwent surgery with succinylcholine. The duration of discomfort is also highly variable among patients but, it usually appears on the first day after surgery and lasts for 2 or 3 days, occasionally persists for as long as a week [14-16]. POM is revealed as source of distress to patients than surgical site wound for its unpleasant consequences to patients' quality of life (delayshospital admission period, expose to unplanned expenses, prolongs time to return to daily activity and influence individual's productivity) [17, 18]. The incidence of POM also varies among IV induction agents (minimal among propofol [19, 20]) and interventional studies reported that its incidence was minimized by pretreatment of atracurium [21], rocuronium [22], vecuronium [23] diclofenac [24], ketorolac [25],phenytoin [26], lidocaine [27], benzodiazepines [28], calcium gluconate [29] and magnesium sulfate [30].

Despite, the applicability of ideal muscle relaxants that used instead of suxamethonium in developed countries for their minimal side effects; it is the only available and utilized short acting muscle relaxant in the setting and considering that the incidence of fasciculation and POM are inevitable. Thus, the present study was aimed to sort/opt for the possible IV induction agent/s that has/have minor side effects (SIF and POM) because it is the standard to prevent/reduce fasciculation and POM.

Materials and Methods

The study was conducted among a total of 140 patients underwent elective surgeryby four IV induction agents (propofol, thiopentone, ketamine and ketofol) from August 1-September 30, 2019 at JMC. JMC islocated at Jimma zone, Oromia region at distance of 350 km to southwest from the capital of Ethiopia, Addis Ababa.Itis one of the pioneer teaching referral hospitals of the country serving millions of population in the catchment area.

A prospective cohort study design was employed to assess POM and SIF after all patients were equally exposed to different four induction agents (propofol, thiopentone, ketamine and ketofol) 35 patients in each groupaimed to sort for the possible induction agent/s that has/have minor side effects.

SIF was assessed intraoperatively following sux administration by structured questionnaire for grading and scoring of fasciculation [31, 32] and operationalized as:

- Fasciculation: refers to any involuntary contraction/tremor of skeletal muscles discerned immediately following administration of sux.
- Grade 0 fasciculation (Nil): No visible fasciculation
- Grade 1(mild): Fine fasciculation of the eyes, face, neck, fingers without movement of limbs
- Grade 2(moderate): Fasciculation of greater intensity at more than two sites or movement of
- Limbs (fasciculation involving limbs and/or trunk).
- Grade 3(severe): Vigorous sustained and widespread fasciculation or fasciculations with movement of one or more limbs and/or movements requiring forceful retention.

POM was assessed postoperatively at 24hrs by structured tools (Postoperative Myalgia Survey (PMS) with 14-item and Postoperative Myalgia Evaluation Scale (PMES which is a modification of the Visual Analog Pain Scale (VAPS) with 4-Likert scale /0-3) [33,34]and operationalized as:

- POM: refers generalized aches/sores/stiffness/pains of muscles that commonly occur within 24 hours after surgery.
- Nil: No muscle pain or stiffness
- Mild myalgia: Slight pain at one site but not causing disability.
- Moderate myalgia: Pain at more than one site but not causing disability
- Severe myalgia: Pain at more than one site, causing disability in turning head and standing-up.

The data was entered into Epidata version 4.3.1 and finally exported to SPSS version 20 for further analysis. Both descriptive statistics and analytical statistics were applied and the finding was reported bytables/figures and narration.Binary logistic regression was usedto assess the association ofoutcome variable (POM) with fasciculation and IV induction agents. P value < 0.05 was considered as statistically significant. The study was approved by ethical review board of Jimma University and letter of permission/cooperation was collected from school anesthesia and the hospital. After the purposes of the study was explained to patients who underwent elective surgery, both verbal and written consent were taken from volunteer participants.Informationgathered from respondents waskept confidential.

Results

Baseline characteristics of patients underwent elective surgery

A total of 140 participants were enrolled to the study with the mean age of 36.5 +10.5 that ranged from 18-60 years, with male to female ratio of 1:2.18. Respondents were exposed to four IV inductions agents (each 35) intraoperatively and all relaxed by suxamethoniumas detailed in Table 1.

Incidence of sux induced fasciculation and its severity

The incidence of fasciculation at intraoperative period following the administration of sux was 94.3% in general where it varies among induction agents (higher among patients induced with thiopentone34 (24.3%)and lower among propofol group 32 (22.9%). As severity of SIF was assessed by grading and scoring tool of fasciculation, majority of them were allocated to moder-

ate 54(38.3%) scale. Among total of 41 patients with mild fasciculation, majority was seen among patients induced by ketamine 15(10.7%) where the rest mild SIF was observed among thiopentone 11(7.9%), ketofol 8(5.7%) and propofol 7(5.0%). Moderate SIF was also dominantly observed among patients induced by propofol and ketamine (each 15(10.7%)). But, severe scale of SIF was higher among patients induced by thiopentone 13(9.3%) followed by ketofol 11(7.9%), propofol 10(7.1%) and ketamine 3(2.1%) as seen on (Table 2).

Incidence of POM and its severity

The incidence of POM at 24 hours of post-operative period was 29.3% that complained for muscle pain/stiffness among 41 patients where the higher magnitude screened among patients induced by ketamine 15(10.7%), followed by thiopentone and ketofol (each 10 (7.1%)) while minimal among propofol group 6(4.3%. POM was also further allocated to mild 30(21.4%), moderate 10(7.1%) and severe scale 1(0.7%). Severe scale of POM was only observed among patients induced by thiopentone (Table 3).

Association of POM with IV induction agents

The association of POM with IV induction agents was performed by logistic regression. Despite, non-statistically significant difference, the occurrence of POM was varied among IV induction agents. The likelihood of POM occurrence was more likely among patients induced by ketamine [OR 1.8(0.7-5.1), p=0.215)]

Table 1. Baseline characteristics of patient underwent elective surgery with sux and four IV induction agents at JMC, 2019.

Variables	Categories	Frequency	Percentage (%)
Age in years	18-30	51	36.4
	31-40	50	35.4
	41-50	23	16.4
	51-60	16	11.4
	Total	140	100
Sex	Male	44	31.4
	Female	96	68.6
	Total	140	100
BMI	<18	11	7.9
	18-24	96	68.6
	>24	33	23.6
	Total	140	100
Residency	Rural	78	55.7
	Urban	62	44.3
	Total	140	100
Educational status	No formal education	58	48.6
	Primary school	43	30.7
	Secondary school	20	14.3
	College and above	9	6.4
	Total	140	100
Occupational status	Farmer	22	15.7
	Merchant	68	48.6
	Labor worker	4	2.9
	Gov't employee	16	11.4
	Others	30	21.4
	Total	140	100
IV induction	Propofol	35	25
	Thiopentone	35	25
	Ketamine	35	25
	Ketofol	35	25
	Total	140	100
ASA status	1	128	90
	2	14	10
	Total	140	100
Type of surgery	Gynecological	37	26.4
	Surgical	72	51.4
	Plastic	12	8.5
	Ortho	3	2.1
	Maxillofacial	16	11.4
	Total	140	100

Table 2. Incidence and severity of fasciculation among different induction agents, 2019.

Variables	Categories	IV induction agent				Total	P-value
		Propofol	Thiopentone	Ketamine	Ketofol		
Fasciculation status	No	3 (2.1%)	1 (0.7%)	2 (1.4%)	2 (1.4%)	8 (5.7%)	0.204
	Yes	32 (22.9%)	34 (24.3%)	33 (23.6%)	33 (23.6%)	132 (94.3%)	
	Mild	7 (5.0%)	11 (7.9%)	15 (10.7%)	8 (5.7%)	41 (29.3%)	
	Moderate	15 (10.7%)	10 (7.1%)	15 (10.7%)	14 (10.0%)	54 (38.6%)	
	Severe	10 (7.1%)	13 (9.3%)	3 (2.1%)	11 (7.9%)	37 (26.4%)	
	Total	35 (25.0%)	35 (25.0%)	35(25.0%)	35 (25.0%)	140 (100.0%)	

Table 3. Incidence and severity of POM among different induction agents, 2019.

Variables	Categories	IV induction agent				Total	P-value
		Propofol	Thiopentone	Ketamine	Ketofol		
POM status	No	29 (20.7%)	25 (17.9%)	20 (14.3%)	25 (17.9%)	99 (70.7%)	0.255
	Yes	6 (4.3%)	10 (7.1%)	15 (10.7%)	10 (7.1%)	41 (29.3%)	
	Mild	4 (2.9%)	6 (4.3%)	12 (8.6%)	8 (5.7%)	30 (21.4%)	
	Moderate	2 (1.4%)	4 (2.9%)	3 (2.1%)	1 (0.7%)	10 (7.1%)	
	Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	
	Total	35 (25.0%)	35 (25.0%)	35(25.0%)	35 (25.0%)	140 (100.0%)	

Table 4. Association of POM with IV induction agents among patient underwent elective surgery at JMC, 2019.

Variables	Category	Myalgia status			Estimation	
		Yes; No(%)	No; No(%)	Total; No(%)	OR(95% CI)	P-value
IV induction agents	Propofol	6 (4.3)	29 (20.7)	35(25.0)	0.5(0.1-1.6)	0.259
	Thiopentone	10 (7.1)	25 (17.9)	35(25.0)	1.1(0.3-2.8)	0.999
	Ketamine	15 (10.7)	20 (14.3)	35(25.0)	1.8(0.7-5.1)	0.215
	Ketofol	10 (7.1)	25 (17.9)	35(25.0)	1	
	Total	41(29.3)	99(70.7)	140(100.0)		

Table 5. Association of SIF with IV induction agents among patient underwent elective surgery at JMC, 2019.

Variables	Category	Fasciculation status			Estimation	
		Yes; No(%)	No; No(%)	Total; No(%)	OR (95% CI)	P-value
IV induction agents	Propofol	32 (22.9)	3 (2.1)	35(25.0)	0.6(0.1- 4.1)	0.645
	Thiopentone	34 (24.3)	1 (0.7)	35(25.0)	2.1(1.2-23)	0.563
	Ketamine	33 (23.6)	2 (1.4)	35(25.0)	1.1(0.1-7.5)	0.999
	Ketofol	33 (23.6)	2 (1.4)	35(25.0)	1	
	Total	132 (94.3)	8 (5.7)	140(100.0)		

and thiopentone [OR 1.1(0.3-2.8), p=0.999)] but less likely among patients induced by propofol [OR 0.5(0.1-1.6), p=0.259)] by taking patients induced by ketofol as referenceas detailed in Table 4.

Association of SIF with IV induction agents

The likelihood of SIF occurrence was also varies among IV induction agent(about two fold among thiopentone groups [OR 2.1(1.2-23), p=0.563]), but not showed statistically significant difference among groups (Table 5).

Discussions

A total of 140 respondents wereenrolled to the study with the mean age of 36.5+10.5 that ranged from 18– 60 years who equally exposed to four IV inductions agents(each 35) intra-operatively and intended to assess POM within 24 hours of post-operative period by applying prospective cohort study design.

The incidence of fasciculation at intraoperative period following the administration of sux was 94.3% and it varies among induction agents (higher among patients induced with thiopentone 34

(24.3%) and lowest among propofol group 32 (22.9%) probably due to propofol effect of antioxidant like a-tocopherol and it accumulates in the biomembranes with an ability to form stable radicals and inhibits propagation of reactions involving free radicals to attenuate postoperative myalgia caused by succinylcholine [13, 35, 36]. This finding was in harmony with studiesconducted previously [5, 13, 37, 38].

Severity of fasciculation was identified and allocated as mild 41(29.3%), moderate 54(38.6%) and severe 37(26.4%) also differs among groups: mild fasciculation was more observed among ketamine group 15(10.7%) and lessseen among propofol group 7(5.0%). Moderate SIF was also dominantly observed among patients induced by propofol and ketamine (each 15(10.7%)). But, severe scale of SIF was higher among patients induced by thiopentone 13(9.3%) followed by ketofol 11(7.9%), propofol 10(7.1%) and ketamine 3(2.1%). This pattern was also supported by previous studies [39, 40]. Among total of 41 patients with mild fasciculation, majority was seen among patients induced by ketamine 15(10.7%) where the rest mild SIF was observed among thiopentone 11(7.9%), ketofol 8(5.7%) and propofol 7(5.0%).

The incidence of POM was 29.3% in general and varies among IV induction agents (highest ketamine 15(10.7%), followed by thiopentone and ketofol (each 10 (7.1%)) while minimal among propofol group 6(4.3%.This finding was also supported by other studies [13, 37-40].

In comparable with present finding, the study conducted by McClymont to compare POM among thiopentone and propofol reported that the propofol group had a significantly lower incidenceof suxamethonium myalgia (19%) compared with the thiopentone group (63%) (P<O.05) [41].

Even though, there is no statistically significant difference in the occurrence of POM, the present study revealed dominance of POM among ketamine group. But, Previous studies reported less incidence among ketamine due to ketamine effects of both antinociceptive and pronociceptive actions via NMDA receptor and aminergic (serotonergic and noradrenergic) receptors and possible interferes with nicotinic, muscarinic, monoaminergic and opioid receptors in abolishing pain [42]. The study conducted by Nasseri and Arvien that compared ketofol and propofolwas also reported high incidence of POM among propofol group than ketofol group against our finding [43]. Thus, further studies with large sample and strong design will be inspired to mediate the existing findings.

Conclusion

Even though, the incidence of both SIF and POM were profound and there is no statistically significant safe IV inductions that mitigate this adverse effect (fasciculation and POM) following administration of suxamethonium, other option of muscle relaxant was warranted/inspired at the setting and the country at all.

Acknowledgments

We would like to thank Jimma University for providing financial support and also extend our heartfelt gratitude to patients involved in the study.

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