



Original Research Article

To compare the efficacy of oral aspirin vs intravenous diazepam on succinylcholine induced postoperative myalgia

Ramesh R¹, Kantharaja H E^{1,*}, Sushma P², Dayanand V P¹

¹Dept. of Anaesthesiology, BMCRI- Bangalore Medical College and Research Institute, Bengaluru, 560002, Karnataka, India

²Dept. of Anaesthesiology, SHIMOGA Institute of Medical Sciences (SIMS), Shivamogga, Karnataka, India



ARTICLE INFO

Article history:

Received 08-07-2019

Accepted 29-08-2019

Available online 20-11-2019

Keywords:

Aspirin

Diazepam

Myalgia

Succinyl choline

ABSTRACT

Introduction: Succinylcholine is a short acting neuromuscular blocking agent. It has its own side effects which includes dysrhythmias, hyperkalemia, postoperative myalgias, etc. The incidence of muscle pain ranges from 0.2 to 89% and thus the need for the study.

Materials and Methods: 60 adult patients are included in this prospective, randomised, double blind study who are scheduled to undergo elective surgery under general anaesthesia. Two groups were made randomly and Patients received either oral aspirin 600mg one hour before surgery or intravenous diazepam fifteen minutes before induction. Appropriate statistical tests were applied.

Results: Status of muscle pain was recorded at 1st, 6th, 12th and 24th post operative period. Myalgia at 6th, 12th and 24th hour was significantly reduced in aspirin group compared to diazepam group. No difference was seen at one hour.

Conclusion: It was concluded that aspirin prevents succinylcholine induced myalgia more effectively than diazepam in postoperative period.

© 2019 Published by Innovative Publication. This is an open access article under the CC BY-NC-ND license (<https://creativecommons.org/licenses/by/4.0/>)

1. Introduction

Succinylcholine is the only depolarizing neuromuscular blocking agent currently in clinical use. It is characterized by quick onset and short duration of action there by providing excellent intubating conditions. However it has got its own side effects which includes dysrhythmias, hyperkalemia, postoperative myalgias, masseter spasm etc. The incidence of muscle pain ranges from 0.2 to 89%.¹ Muscle pain occurs more commonly after minor surgery, especially in women and in ambulatory patients.² Postoperative skeletal muscle myalgia, which is specially prominent in the muscles of the neck, back and abdomen. Myalgia localized to neck muscles may be perceived as pharyngitis by the patient and attributed to tracheal intubation by the anaesthesiologist. Muscle pain occurs most often in patients undergoing ambulatory surgery.

The theory behind postoperative skeletal muscle myalgia is not fully understood. One theory proposes that myalgia is secondary to muscle damage by succinylcholine induced fasciculations.² This is supported by findings of myoglobinemia and raise in creatine kinase level following succinylcholine administration.³

Another hypothesis suggests a possible role for prostaglandins and cyclooxygenases in Succinylcholine induced myalgia.⁴ Pretreatment with a prostaglandin inhibitor is effective in reducing the incidence of myalgia.⁵ Succinylcholine induced myalgia increases length of stay in hospital thereby increasing the cost of treatment. Therefore prevention of myalgia is very important.

Various agents have been attempted to decrease the postoperative muscle pain namely, Non-depolarising neuromuscular blockers, NSAIDs, benzodiazepines, phenytoin, ketorolac, vitamin E derivatives, local anaesthetics.

Aspirin belongs to NSAID group of drugs, acts by inhibiting the synthesis of prostaglandins and thereby

* Corresponding author.

E-mail address: kanthu.hirenallur@gmail.com (Kantharaja H E).

decreasing the severity of myalgia, if administered preoperatively.

There is inconclusive evidence that benzodiazepines decreases postoperative myalgia. Studies shows that Diazepam has the property to decrease severity of muscle pains.⁶ Hence, we conducted this study to compare the effectiveness of Aspirin and Diazepam on succinylcholine induced myalgia.

2. Aims and Objectives

To study the effect of oral aspirin vs intravenous diazepam in reducing succinylcholine induced myalgia.

To assess severity of fasciculations

To assess severity of myalgia

3. Materials and Methods

After approval from Institutional Ethical Committee, this clinical study was conducted on 60 adult patients based on inclusion and exclusion criteria.

3.1. Inclusion criteria

1. Patient who give written informed consent
2. Patients aged 18-55 yrs.
3. Patients with ASA (American society of anaesthesiologists) grade I & II
4. Patients posted for elective surgery under general anaesthesia.

3.2. Exclusion criteria

1. Patient refusal.
2. Patients undergoing major surgeries.
3. Pregnancy, burns, infection, emergency surgical procedures.
4. H/O allergy to drugs
5. Coagulation disorders
6. Previous history of pain, trauma, neuromuscular disorders, musculoskeletal and endocrine disorders.

3.3. Sample size

To detect a difference of 20% myalgia between 2 groups, keeping the power at 80% and alpha error at 0.05, a minimum of 60 patients were required, presuming a success rate of 95%.

Patients were randomized to one of the two groups using computer generated random allocation chart.

Group 1: Aspirin group (30 patients)

Group 2: Diazepam group (30 patients)

After preanaesthetic examination, patients were explained about the procedure. Baseline serum potassium concentrations were noted. An intravenous access was secured in non-dominant limb. In the recovery room, either

aspirin or diazepam was given to the study patients by nurses who were not related to the study.

Aspirin 600mg was given orally one hour prior to surgery and diazepam 0.05mg/kg intravenously was given 15 minutes before induction. Timing of the drugs given was based on the pharmacokinetic principles of the drug.

Premedication Inj. Ranitidine 50 mg and Inj. Ondansetron 4 mg IV was given. In the operating room, monitors connected and preoperative vital parameters were recorded. Anaesthesiologist unaware of the study drug given to patients administered general anaesthesia and monitored the patient subsequently.

All patients were preoxygenated with 100% oxygen. Induction with thiopentone 3-5mg/kg IV and paralysed with succinylcholine 1.5mg/kg IV

Presence and degree of fasciculations were assessed on a four point scale :⁷

Grade 1: No fasciculations

Grade 2: Mild, fine fasciculations at the eyes, neck, face or fingers without limb movement

Grade 3: Moderate fasciculations occurring bilaterally or obvious limb movement

Grade 4: Severe when widespread, sustained fasciculation.

Tracheal intubation done with appropriate size endotracheal tube and maintained with air and sevoflurane supplementation with controlled ventilation. After the patient had spontaneous efforts, vecuronium was given. After completion of surgery reversal given and patient extubated.

Postoperatively all the patients were assessed for myalgia. Myalgia was defined as "muscle pain not related to surgical intervention". Following are the grades of myalgia.⁸

Grade 1: Absence of muscle pain

Grade 2: Stiffness limited to one area only

Grade 3: Muscle pain or stiffness noticed spontaneously by the patient, which may require analgesic therapy

Grade 4: Generalized, severe or incapacitating discomfort.

The incidence and severity of myalgia was recorded by a blinded observer after 1 hour, 6 hours, 12 hours and 24 hours after extubation.

3.4. Statistical analysis

Data was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Independent t- test was used as test of significance to identify the mean difference between two quantitative variables. P value (Probability that the result is true) <0.05 was taken as statistically significant.

Table 1: Demographic data

	Group Diazepam Mean±SD	Aspirin Mean±SD	P value
Age	37.0±6.6	37.3±11.2	0.919
Weight	55.1±7.4	48.7±3.9	<0.001*
Duration of surgery	64.5±9.9	67.8±9.3	0.241

4. Results

The demographic data were comparable between the groups in terms of Age, weight, ASA grade, and duration of surgery. In terms of Fasciculations there was no statistically significant difference between two groups. There was a statistically significant difference in Median and Mean scores of myalgia which was observed between two groups at 6 hour, 12 hour and 24 hours. No difference was observed at 1 hour. Higher myalgia was seen in diazepam group compared to Aspirin group. Mean potassium levels between two groups were comparable at pre operative period, 1 hour and 24 hours.

5. Discussion

Succinylcholine (SCh) is the only clinically available depolarizing neuromuscular blocker. It was introduced by Thesleff and Foldes and associates in 1952, drastically changed anaesthetic practice because of its quick onset and ultrashort duration of action allowed for both rapid endotracheal intubation and rapid recovery of neuromuscular strength.⁹ Succinylcholine is made up of two molecules of Acetylcholine (ACh) which binds to ACh receptors present on the postjunctional area of muscle end plate, thereby generating action potential. succinylcholine is not metabolized by acetylcholinesterase which is present on the postjunctional area leading to sustained depolarization of muscle end plate resulting in fasciculations. However, because the opening of perijunctional sodium channel is time limited, this Continuous and sustained depolarization ends up in muscle relaxation. SCh even though it is not metabolized by acetylcholinesterase, but it is rapidly gets hydrolysed by plasma cholin esterase, also called as pseudocholinesterase. This explains its ultrashort duration of action.

The popularity of SCh has been decreased because of its adverse effects which includes dysrhythmias, postoperative myalgia, hyperkalemia, etc. Postoperative skeletal muscle myalgia is one of the most commonly encountered adverse effect of SCh. Its incidence widely ranges between 0.2 to 89%.¹ One theory explains the reason behind myalgia is due to the initial unsynchronized and sustained contractions of adjacent muscle fibers just before it ends up in muscle relaxation.² This theory has been substantiated by finding myoglobinemia and there is increase in serum creatine kinase levels following administration of SCh. This

unsynchronised and sustained contraction might produce damage to the muscle fibers, thereby causing postoperative muscle pain.¹⁰ Prevention of SCh induced myalgia is at most important in the postoperative period. This uneasiness in terms of myalgia adds to the delayed recovery of the patients, increases the length of stay in the hospital and thereby increases the cost of treatment.

The first and foremost attempt to decrease the incidence and severity of postoperative skeletal muscle myalgia was pretreatment with gallamine in 1954.¹¹ Preoperative administration of various agents have been tried to reduce postoperative myalgia. Prior administration of a small dose of a nondepolarizing muscle relaxant is not always effective in preventing succinylcholine induced postoperative skeletal muscle pain.¹² Prostaglandins and cyclooxygenases plays an important role in the development of postoperative myalgia. Prostaglandins can cause further tissue damage and increases the pain. So to reduce the incidence and severity of myalgia, this prostaglandin mediated destructive cycle should be stopped. Pretreatment with nonsteroidal anti inflammatory agent like aspirin, a prostaglandin synthesis inhibitor has been shown to be effective in reducing the incidence as well as severity of skeletal muscle pain following succinyl choline administration.

Diazepam is one of the several agents that has been tried in reducing the incidence and severity of myalgia after succinylcholine administration. Diazepam has been shown to be effective in decreasing the incidence and severity of postoperative skeletal muscle pain following administration of succinylcholine.^{13–16}

McLoughlin C, Nesbitt GA, Howe JP¹⁷ conducted a study on the effect of pre-operative administration of oral aspirin on Suxamethonium induced myalgia showed the use of NSAIDs especially aspirin 600mg given 1 hour prior to surgery causes a significant reduction in post operative myalgia. In our study there is a significant reduction in the postoperative myalgia at 6, 12, 24 hrs. in aspirin group compared to diazepam group.

Fahmy NR, Malek NS, Lappas DG¹⁸ conducted a study on effects of diazepam and d-tubocurarine on Neuromuscular, circulatory and adverse effects of intravenous succinylcholine (SCh). They observed pretreatment with Diazepam prevented Postoperative myalgia associated with SCh administration.

Jan-Uwe Schreiber, Christopher Lysakowski, Thomas Fuchs-Buder, Martin R. Trame¹⁹ conducted meta analysis

Table 2: ASA Grade

ASA		Group Diazepam		Aspirin		P value
		Count	%	Count	%	
1	1	22	91.7%	23	88.5%	0.706
	2	2	8.3%	3	11.5%	

Table 3: Fasciculations

Fasciculations	Grade	Group Diazepam		Aspirin		P value
		Count	%	Count	%	
1	1	7	29.2%	8	30.8%	0.210
	2	17	70.8%	15	57.7%	
	3	0	0.0%	3	11.5%	

Table 4: Myalgia

	Group Diazepam Mean±SD	Aspirin Mean±SD	P value
Myalgia 1hr	2.0±0.6	1.7±0.7	0.059
Myalgia 6hr	1.8±0.6	1.0±0.4	<0.001*
Myalgia 12hr	1.8±0.5	1.0±0.4	<0.001*
Myalgia 24hr	1.3±0.5	0.7±0.6	<0.001*

Table 5: Preop and Postop Potassium levels

	Group Diazepam Mean±SD	Aspirin Mean±SD	P Value
Preop	4.2±0.6	4.3±0.7	0.601
1 Hour	4.4±0.6	4.6±0.6	0.618
24 Hours	4.4±0.7	4.2±0.5	0.284

on Prevention of succinylcholine induced fasciculation and myalgia. In the above meta-analysis best efficacy was found with nonsteroidal anti-inflammatory drugs (two trials tested aspirin). Benzodiazepines had a weak but statistically significant effect on myalgia. In our study aspirin group had statistically significant reduction in postoperative myalgia compared to diazepam group and also there was no significant difference in Mean potassium levels between two groups at pre operative period, 1 hour and 24 hours.

6. Conclusion

Prevention of succinylcholine induced myalgia is most important and various methods have been used to prevent the same. Our study shows that oral aspirin prevents succinylcholine induced myalgia more effectively than intravenous diazepam.

7. Source of Funding

None.

8. Conflict of Interest

None.

References

1. Brodsky JB, Brock-Utne JG, Aamuels SI. Pancuronium pretreatment and post succinylcholine myalgias. *Anaesthesiol.* 1979;51:259–261.
2. Waters DJ, Mapleson WW. Suxamethonium pains: hypothesis and observation. *Anaesth.* 1971;26:127–141.
3. Maddineni VR, Mirakhur RK, Cooper AR. Myalgia and biochemical changes following suxamethonium after induction of anaesthesia with thiopentone or propofol. *Anaesth.* 1993;48:626–628.
4. Jackson MJ, Wagenmakers AJM, Edwards RHT. The effect of inhibitors of arachidonic acid metabolism on efflux of intracellular enzymes from skeletal muscle following experimental damage. *Biochem J.* 1987;241:403–407.
5. Naguib M, Farag H, Magbagbeola JA. Effect of pretreatment with lysine acetyl salicylate on suxamethonium induced myalgia. *Br J Anaesth.* 1987;59:606–610.
6. Wong FS, Chung F. Succinylcholine-associated postoperative myalgia. *Anaesth.* 2000;55:144–152.
7. Kararmaz A, Kaya S, Turhanoglu S, Ozyilmaz MA. Effects of high dose propofol on succinylcholine induced fasciculations and myalgia. *Acta Anaesthesiol Scand.* 2003;47:180–184.

8. Nimmo SM, Mccann N, Broome IJ, Robb HM. Effectiveness and sequelae of very low dose suxamethonium for nasal intubation. *Br J Anaesth.* 1995;74:31–34.
9. Miller's Anaesthesia. vol. 1. Elsevier saunders ; 2015., p. 958–959.
10. Paton WDM. The effects of muscle relaxants other than muscular relaxation. *Anaesth.* 1959;20:453–463.
11. Churchill-Davidson H. Suxamethonium (succinylcholine) chloride and muscle pains. *Br Med J.* 1954;1:74–75.
12. Dermers-Pelletier J, Drolet P, Girard M. Comparison of rocuronium and d-tubacurarine for prevention of succinylcholine induced fasciculations and myalgia. *Can J Anaesth.* 1997;44:1144–1147.
13. Baker AB. Induction of anaesthesia with diazepam. *Anaesth.* 1969;24:388–394.
14. Eisenberg ME, Balsley S, Katz RL. Effects of diazepam on succinylcholine-induced myalgia, potassium increase, creatine phosphokinase elevation, and relaxation. *Anesth Anal.* 1979;58:314–317.
15. Fahmy NR, Malek NS, Lappas DG. Diazepam prevents some adverse effects of succinylcholine. *Clin Pharmacol Ther.* 1979;26:395–398.
16. Davis AO. Oral diazepam premedication reduces the incidence of post-succinylcholine muscle pains. *Can J Anaesth.* 1983;30:603–606.
17. McLoughlin C, Nesbitt GA, Howe JP. Suxamethonium induced myalgia and the effect of pre-operative administration of oral aspirin. A comparison with a standard treatment and an untreated group. *Anaesth.* 1988;43(7):565–567.
18. Fahmy NR, Malek NS, Lappas DG. Diazepam prevents some adverse effects of succinylcholine. *Clin Pharmacol Ther.* 1979;26(3):395–403.
19. Schreiber J, Lysakowski C, Fuchs-Buder T, Trame MR. Prevention of succinylcholine induced fasciculation and myalgia. A meta-analysis of randomized trials. *Anaesth.* 2005;103:877–884.

Author biography

Ramesh R Associate Professor

Kantharaja H E Assistant Professor

Sushma P Senior Resident

Dayanand V P Associate Professor

Cite this article: Ramesh R , Kantharaja H E , Sushma P , Dayanand V P . To compare the efficacy of oral aspirin vs intravenous diazepam on succinylcholine induced postoperative myalgia. *Indian J Clin Anaesth* 2019;6(4):508-512.