ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 7 | July - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A COMPARATIVE STUDY OF DIAZEPAM AND ASPIRIN FOR RELIEF OF SUCCINYLCHOLINE –INDUCED MYALGIA

Anaesthesiology

Gurumurthy T MD(Anaesthesiology) Associate Professor, Department of Anaesthesiology, Father Muller Medical College, Mangalore

D'Cunha Rithesh* MD(Anaesthesiology)Assistant professor, Department of Anaesthesiology, Father Muller Medical College, Mangalore*Corresponding Author

ABSTRACT

Introduction: Succinylcholine is a short acting depolarizing neuromuscular blocking agent with various side effects which include postoperative myalgias and fasciculations. Our study aims at assessing its incidence and severity and comparing the effects of aspirin and diazepam for relief of succinylcholine induced myalgia.**Materials and Methods:** 100 patients were included in this prospective , randomised , double blind study who were scheduled to undergo elective surgery under general anaesthesia. They were randomly allotted to 3 groups and either received oral aspirin 10mg/kg one hour before induction or intravenous diazepam 0.2mg/kg IV 5 minutes before induction or placebo. Data was analysed using SPSS software and Chi-square test and independent T test was used for statistical analysis. **Results:** The difference in severity of fasciculations between aspirin group and placebo was not statistically significant. The difference in severity of fasciculations between diazepam group and placebo was statistically highly significant. The incidence of myalgia, which was 73.52% in placebo group was reduced to 45.45% , which is statistically highly significant ($p<0.001$) when pretreated with aspirin. The incidence of myalgia , which was 73.52% in placebo group was reduced to 57.58%, which is statistically significant ($p<0.05$) when pretreated with diazepam. **Conclusion:** It was concluded that aspirin prevents succinylcholine induced myalgia more effectively than diazepam in postoperative period.

KEYWORDS

Aspirin, Diazepam, Succinylcholine induced myalgia,

INTRODUCTION:

Succinylcholine is the only depolarizing relaxant in widespread use. In many ways, it is considered a superior muscle relaxant. Its advantages of rapid onset and short duration in the form of quick recovery of muscle power makes it very popular for use in endotracheal intubation especially on a full stomach, orthopaedic manipulation and as a sole relaxant for short procedures.

Its advantages outweigh the disadvantages which include tendency to cause hyperkalemia, rise in intraocular pressure, intracranial pressure, malignant hyperthermia, prolonged apnoea in certain susceptible individuals and postoperative succinylcholine induced myalgia. This generalized myalgia is a frequent and troublesome complication. The incidence is greater after minor procedures and is higher in the age group of 20-50years(1) and ranges from 0.2%-89% (2) .The pain resembles that of pain following violent and prolonged exercise of unaccustomed muscles. The incidence of pain is less in children under 9 years. Women are more susceptible than men.

Degree of fasciculations does not provide a clue to the amount of pain. The time of onset varies from person to person, commonly occuring around 24 hours following administration of succinylcholine.

The etiology of succinylcholine induced myalgia is not fully elucidated , several theories have been postulated and the popular belief is that local trauma produced by the muscle bed due to fasciculations gives rise to pain.(1) Electromyographic evidence suggests that the pain is related to the rate of firing of motor units. This is supported by findings of myoglobinemia and rise in creatine kinase level following succinylcholine administration. (3)

A number of prophylactic measures have been employed to reduce the incidence of succinylcholine myalgia. A common measure is pretreatment with a small dose of a non depolarizing muscle relaxant before induction of anaesthesia(4).Pretreatment with a prostaglandin inhibitor is effective in reducing the incidence of myalgia(5) Other measures include administration of large doses of I.V thiopentone sodium, I.V diazepam, lignocaine , magnesium sulphate, calcium gluconate, lysine acetyl salicylate, oral vitamin C, stretching exercises and volatile anaesthetics.

Each of these measures mentioned have its demerits like increased requirement of succinylcholine and episodes of prolonged apnoea especially for short procedures when treated with a nondepolarising muscle relaxant. Hemodynamic instability is associated with incremental use of thiopentone and volatile anaesthetics.

Aspirin belongs to NSAID group of drugs, acts by inhibiting the synthesis of prostaglandins and thereby decreasing the severity of myalgia, if administered preoperatively. There is inconclusive evidence that benzodiazepines decrease postoperative myalgia. Studies show that Diazepam has the property to decrease severity of muscle pains.(6)

By this study an attempt has been made to resort to safe, simpler and effective methods of overcoming the issue of succinylcholine induced myalgia by using more freely available nonsteroidal anti inflammatory drugs and its efficacy is assessed when pretreated orally for patients receiving succinylcholine. In this study, we have compared the efficacy of 2 different classes of drugs; aspirin and benzodiazepine(diazepam) in preventing succinylcholine induced post operative myalgia.

AIM:

To assess the incidence and severity of post succinylcholine fasciculations and myalgia and compare the effects of aspirin and diazepam for relief of succinylcholine-induced myalgia

METHODOLOGY:

The study was conducted on 100 patients between the age group 15 and 60 years, ASA grade 1 and 2 undergoing various elective surgical procedures of 30 to 60 minutes duration, after obtaining ethical clearance.

The patients were allocated randomly into 3 groups:

Group 1(aspirin group) : 33 patients who received aspirin 10mg/kg orally dissolved in 30ml of water given 1 hour before induction of anaesthesia.

Group 2(diazepam group): 33 patients who received diazepam 0.2mg/kg IV 5 minutes before induction of anaesthesia.
Group 3(placebo group): 34 patients who received normal saline 10ml IV before induction of anaesthesia.

Exclusion criteria:

1. Patients undergoing major surgeries or emergency surgery
2. Pregnancy, burns, infection.
3. History of myalgia, peptic ulceration, anticoagulant therapy
4. Known sensitivity to aspirin and its derivatives

All patients were assessed preoperatively with routine preanaethetic examination and investigations. Patient anxiety was allayed by counseling and informed consent obtained. No sedation was given the

previous night and patient was kept NPO for 8-10 hours. No premedication was given on the morning of the surgery. Preoperatively pulse and blood pressure was recorded.

Each patient was administered aspirin or diazepam or normal saline based on the group allocated. An IV line with ringer lactate was started and 0.6mg atropine was administered. In all the groups induction was done with thiopentone sodium 5mg/kg IV followed by IV succinylcholine 2mg/kg and orotracheal intubation.

The presence and absence of visible fasciculations was recorded following administration of succinylcholine and graded as follows(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.

In all the groups, anaesthesia was maintained intraoperatively with 67% nitrous oxide and 33% oxygen and 0.5-1% halothane and pancuronium 0.8mg/kg. At the end of the surgery, all patients were reversed with neostigmine 0.05mg/kg and atropine 0.02 mg/kg. Patients were extubated with adequate recovery.

Intraoperative monitoring using cardiocap II was done. The patient was observed for 24hours postoperatively by monitoring vitals and assessing Myalgia.

Myalgia was assessed at 6hours, 18hours and 24 hours with the following questions:

1. Were you able to move about after recovery from anaesthesia? If not,why?

2. Did you have any pain and weakness in your muscles:? If so, details

If the answer to question 2 was 'yes' the patients were asked these additional questions:

1. When did the first pain occur?
2. Where did you first notice it?
3. Is it similar to any other pain experienced?
4. Were there any aggravating or relieving factors?

Myalgia was defined as "muscle pain not related to surgical intervention" and graded as (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.

STASTICALANALYSIS:
Data was analyzed using SPSS software. Chi-square test and Independent t- test were used as test of significance. P value (Probability that the result is true) <0.05 was taken as statistically significant.

RESULTS:
The incidence and severity of fasciculations and postoperative muscle pain was studied in all 3 groups and compared.

To establish statistical relationship relating to fasciculations among different groups, moderate and severe fasciculations were combined to make DF=1. Relating to muscle pain, moderate and severe pains were combined to make DF=1. On computation of data the Chi-square value shows statistically significant difference between 2 groups.

Table 1: Incidence and severity of fasciculations

Grading	Group 1 (Aspirin)		Group 2(Diazepam)		Group 3(Placebo)	
	No. of cases	%	No. of cases	%	No.of cases	%
No	3	9.10	17	51.51	2	5.88
Mild	11	33.33	11	33.33	10	29.41
Moderate	14*	42.42	5**	15.16	15*	44.12
Severe	5	15.15	0	0	7	20.59
Total	33	100	33	100	34	100

*p>0.05, Not significant
**p<0.001, Highly significant

In group 1 (Aspirin), there were no visible fasciculations in 3 cases(9.1%) and in the remaining 30 patients(90.9%) visible fasciculations were present. Out of the 30 patients, fasciculations were mild in 11 patients(33.33%), moderate in 14 patients(42.42%) and severe in 5 patients (15.15%).

In group 2 (Diazepam), there were no visible fasciculations in 17 cases(51.51%) and in the remaining 16 patients(48.49%) visible fasciculations were present. Out of the 16 patients, fasciculations were mild in 11 patients(33.33%), moderate in 5 patients(15.16%). There were no severe fasciculations seen in this group.

In group 3 (Placebo), there were no visible fasciculations in 2 cases(5.88%) and in the remaining 32 patients(94.11%) visible fasciculations were present. Out of the 32 patients, fasciculations were mild in 10 patients(29.41%), moderate in 15 patients(44.12%) and severe in 7 patients (20.59%).

The difference in severity of fasciculations between group 1 and 3 was not statistically significant.

The difference in severity of fasciculations between group 2 and 3 was statistically highly significant.

Table 2: Incidence and severity of muscle pains postoperatively

Degree of pain	Group 1 (Aspirin)		Group 2(Diazepam)		Group 3(Placebo)	
	No. of cases	%	No. of cases	%	No.of cases	%
Nil	18	54.54	14	42.42	9	26.47
Slight	9	27.27	9	27.27	5	14.71
Moderate	5**	15.15	8*	24.24	16	47.06
Severe	1	3.04	2	6.07	4	11.76
Total	33	100	33	100	34	100

*p<0.05,Significant
**p<0.001, Highly significant

In group 1(Aspirin), there were no pains in 18 patients(54.54%) and in the remaining 15 patients(45.45%), pain was present. Out of the 15 patients, pain was slight in 9 patients(27.27%), moderate in 5 patients (15.15%) and severe in 1 patient(3.04%).

In group 2(Diazepam), there were no pains in 14 patients(42.42%) and in the remaining 19 patients(57.58%), pain was present. Out of the 19 patients, pain was slight in 9 patients(27.27%), moderate in 8 patients (24.24%) and severe in 2 patient(6.07%).

In group 3 (Placebo), there were no pains in 9 patients(26.47%) and in the remaining 25 patients(73.52%), pain was present. Out of the 25 patients, pain was slight in 5 patients(14.71%), moderate in 16 patients (47.66%) and severe in 4 patient(11.76%).

The incidence of myalgia, which was 73.52% in placebo group was reduced to 45.45% , which is statistically highly significant (p<0.001) when pretreated with aspirin.

The incidence of myalgia , which was 73.52% in placebo group was reduced to 57.58%, which is statistically significant (p<0.05) when pretreated with diazepam.

DISCUSSION:
Postoperative myalgia associated with administration of succinylcholine is a common problem.

Prostaglandins and cyclooxygenases play an important role in the development of postoperative myalgia. Prostaglandins cause further tissue damage and increase the pain leading to increase in post

operative morbidity thereby prolonging hospital stay, especially following day care surgeries. This may last 2-6 days and vary in intensity from mild malaise and tenderness to generalized and severe pain. Neck, shoulders ,pectoral muscles, ribcage and upper abdomen are frequently affected.

Many techniques have been employed in an attempt to reduce its incidence. The most common and successfully proven technique is pre treatment with a small dose of nondepolarising muscle relaxant before induction. The nondepolarising neuromuscular blocker can affect the desired neuromuscular effects of succinylcholine causing resistance to subsequently administered succinylcholine. The mechanism is not entirely clear, but the common theory is that the defasciculating dose binds to a number of cholinergic receptors, thereby preventing succinylcholine from gaining access to them. Thus, this method is not free from problems, creating an inadequate condition for tracheal intubation, which may be hazardous during a rapid sequence induction. Thus,a higher dose of succinylcholine is commonly recommended after pretreatment an d prior administration of a small dose of a nondepolarizing muscle relaxant is not always effective in preventing succinylcholine induced postoperative skeletal muscle pain. (9)

Non steroidal anti-inflammatory drugs and benzodiazepines have been widely used in anaesthesia in order to achieve postoperative pain relief and as a sedative ,respectively, and to decrease opiate requirements.

The present study was designed to evaluate the efficacy of orally administered NSAID's viz Aspirin and Benzodiazepine viz. Diazepam to prevent succinylcholine induced myalgia.

The variables in the study have been reduced to a minimum by standardizing the age, sex distribution, usage of similar premedication, standard anaesthetic techniques and assessment of patients for 24 hours at 6-hour intervals postoperatively.

In a study conducted by McLoughlin C et al (10) on the effect of pre-operative administration of oral aspirin on Suxamethonium induced myalgia , the use of NSAIDs especially aspirin 600mg given 1 hour prior to surgery showed a significant reduction in post operative myalgia. In a recent study by Ramesh R et al there is a significant reduction in the postoperative myalgia at 6, 12, 24 hrs. in aspirin group compared to diazepam group.(11)

Fahmy NR et al(12) 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 et al (13) conducted a meta analysis on Prevention of succinylcholine induced fasciculation and myalgia. In the 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 the study by Ramesh et al (11), aspirin group had statistically significant reduction in postoperative myalgia compared to diazepam group

CONCLUSION:

It would appear from the results that pretreatment with aspirin could be effective to prevent succinylcholine induced myalgia. Diazepam is also effective, however, not to the extent of aspirin,in preventing postoperative myalgia.

REFERENCES:

1. Waters DJ, Mapleson WW. Suxamethonium pains: hypothesis and observation. Anaesth. 1971;26:127–141.
2. Brodsky JB, Brock-Utne JG, Aamuels SI. Pancuronium pretreatment and post succinylcholine myalgias. Anaesthesiol. 1979;51:259–261
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. Ebeling BJ, Keienburg T, Hausmann D, Apfelstaedt C: Das Wirkungsprofil von Succinylcholin nach Präkurarisierung mit Atracurium, Vecuronium oder Pancuronium. Anasthesiol Intensivmed Notfallmed Schmerzth 1996; 31:304–8
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.
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. 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.
10. 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.
11. 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
12. Fahmy NR, Malek NS, Lappas DG. Diazepam prevents some adverse effects of succinylcholine. Clin Pharmacol Ther. 1979;26(3):395– 403.
13. 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.