

Comparison of Intravenous Paracetamol Prophylaxis versus Placebo for Prevention of Pain with Injection Rocuronium in patients undergoing elective procedures

ANEQUE ALAM KHAN¹, KIRAN MEHWISH², RAVI KUMAR³, PAVAN KUMAR⁴, TAHIR ALI⁵, FAHAD MANSOOR⁶

¹Senior Lecturer, Department of Anaesthesia, Sindh Institute of Urology & Transplantation, Karachi

²Woman Medical Officer, Sindh Govt. Health Department, Karachi

³Assistant Professor, Department of Anaesthesia, Sir Syed College of Medical Sciences for Girls, Karachi

⁴Senior Registrar, Department of Anaesthesia, Al-Tibri Medical College, Karachi

⁵Senior Registrar, Department of Anaesthesia, Jinnah Medical College Hospital, Karachi

⁶Senior Registrar, Department of Anaesthesia, Dow University Hospital/Dow University of Health Sciences, Karachi

Correspondence to Dr Aneque Alam Khan, E-mail: aneque86@gmail.com, Cell: 0334-3659396

ABSTRACT

Aim: To compare the frequency of absence of pain with injection paracetamol versus placebo given before injection rocuronium in patients undergoing elective procedures

Study design: Randomized Controlled Trial

Place and duration of study: Dept of Anaesthesia, Civil Hospital, Karachi from 15th January to 14th July 2017.

Methodology: One hundred and two patients aged 25-75 years of either gender undergoing elective surgery were enrolled. The lottery method was used to divide the patients into two equal groups. Paracetamol (5 mL, 10 mg/mL) or normal saline (5 mL) were used as pretreatment solutions. When the tourniquet was removed after 2 minutes, the rocuronium at 1% concentration was injected throughout the 10 second's period. Patients were then advised and asked to rate their pain on the hand's dorsum using VAS.

Results: Mean age of the patients was 44.11±7.75 years. Mean pain score was 1.49±1.38. Significant difference was observed in the mean pain score in between paracetamol and placebo group (p-value <0.001). Overall absence of pain was found in 49 (40.8%). Absence of pain was found to be higher 34 (69.4%) in paracetamol group as compared to placebo group (p-value <0.001).

Conclusion: Frequency of absence of pain found lower in patients undergoing elective procedures with injection paracetamol versus placebo given before injection rocuronium.

Keywords: Injection rocuronium, Elective procedures, Injection paracetamol, Absence of pain

INTRODUCTION

Fifty to eighty percent of patients felt considerable discomfort and burning pain during the injection of rocuronium (a non-depolarizing neuromuscular blocking medication)¹. In addition to lignocaine, ketamine, thiopentone and ondansetron, tramadol, fentanyl esmolol, dexmedetomidine, acetaminophen, magnesium sulfate, and nitrous oxide, a variety of treatments have been used to alleviate the pain caused by rocuronium with variable success rates²⁻⁶.

For its analgesic and antipyretic properties, paracetamol is widely used around the world. NSAIDs and COX-2 selective inhibitors share a similar spectrum of action. Prostaglandin production and associated components were selectively inhibited by paracetamol. There is a lot of evidence that paracetamol is selective for COX-2. As evidenced by its weak anti-platelet activity and good gastrointestinal tolerability, paracetamol appears to be selective for COX-2⁷.

In one trial, injection paracetamol resulted in 58.3 percent of cases with no pain, while a placebo resulted in just 31.7 percent of cases with no pain. The difference (p=0.002) was found to be significant⁸. Another study found that 22% of patients receiving injection paracetamol had no pain, but only 2% of patients receiving a placebo had no

pain. The difference was found to be significant (p<0.001)¹.

The objective of the study was to compare the frequency of absence of pain with injection paracetamol versus placebo given before injection rocuronium in patients undergoing elective procedures

MATERIALS AND METHODS

This randomized controlled trial study was conducted at Department of Anaesthesia, Civil Hospital, Karachi from 15th January 2017 to 14th July 2017 after approval from ethical committee and comprised 120 patients and was randomly divided in two equal groups. The patients age between 25-75 years old female and male patients having general anaesthesia with ASA I and II were included. Patients underwent elective surgery (hernioplasty, laparotomy, head injury, myomectomy, etc). Patients with chronic pain syndromes with neurological deficits and thrombophlebitis as well as anticipated difficulty with venous access and airway as well as paracetamol and local anaesthetic allergies, as well as analgesic use during the previous 24 hours were excluded. The demographics of the patients (name, age, gender, and the type of surgery) were recorded. A 20-gauge cannula was inserted into the dorsum of the hand and lactated Ringer's infusion was infused. Lactated Ringer's infusion was stopped and the arm with the intravenous line was elevated for 20 seconds for gravity to drain the venous blood. Paracetamol (5mL, 10mg/mL) or normal saline (5 mL) were administered to the

Received on 13-03-2021

Accepted on 27-07-2021

patient after the arm was lowered. When the tourniquet was removed after 2 minutes, the rocuronium at 1 percent concentration was injected throughout a 10 second period. When rocuronium was injected into the patient's hand, he was counselled and asked if he felt any pain on the hand's dorsum and the absence of pain was described as such Propofol and fentanyl were administered as soon as the pain was assessed. The attending anaesthesiologist determined the appropriate technique to continue the anaesthetic.

SPSS-21 was used for data entry and analysis. Both groups were compared using the chi-square test. A P-value of less than 0.05 was judged significant in the study.

RESULTS

In paracetamol group, there were 15(25%) patients with ≤ 45 years of age whereas 45(75%) patients with >45 years of age. In placebo group, 25(41.7%) patients were presented with ≤ 45 years of age whereas 35(58.3%) patients with >45 years of age. In paracetamol group, there were 18(30%) males whereas 42(70%) females. In placebo group, 39(65%) were males whereas 21(35%) were females. Frequency of laparotomy was found to be higher in both group, i.e. 26(43.3%) and 19(31.7%) respectively (Table 1).

Mean pain score was 1.49 ± 1.38 . Significant difference was observed in the mean pain score in between paracetamol and placebo group (p -value < 0.001) (Table 2).

Absence of pain was found to be higher 34(69.4%) in paracetamol group as compared to placebo group (p -value < 0.001) (Table 3).

Table 1: Demographic information of the patients in both groups (n=120)

Variable	Paracetamol group		Placebo group	
	No.	%	No.	%
Age (years)				
≤ 45	15	25.0	25	41.7
> 45	45	75.0	35	58.3
Gender				
Male	18	30.0	39	65.0
Female	42	70.0	21	35.0
Type of surgery				
Hernioplasty	18	30.0	10	16.6
Laparotomy	26	43.3	19	31.6
Hysterectomy	9	15.0	13	21.7
Head Injury	4	6.7	13	21.7
Myomectomy	3	5.0	5	8.4

Table 2: Comparison of pain score according to groups (n=120)

Pain score	Paracetamol	Placebo	P value
		1.01 ± 1.24	1.96 ± 1.36

Table 3: Relationship of absence of pain with group (n=120)

Absence of pain	Paracetamol	Placebo	P value
Yes	34 (69.4)	15 (30.6)	< 0.001
No	26 (36.6)	45 (63.4)	

DISCUSSION

Paracetamol's analgesic impact is thought to be the result of both central and peripheral actions⁹. Paracetamol selectively suppresses peripheral PGE2 release and

increases cyclooxygenase-2 (COX-2) gene expression¹⁰. Paracetamol also inhibits COX-2 activity in human blood cells, and PGE2 production in human blood monocytes according to Hintz et al¹¹. Canbay et al¹² found that paracetamol pre-treatment reduced propofol-induced injection discomfort. In control, acetaminophen and lidocaine groups, the total incidence of propofol-induced injection pain was 64 percent, 22 percent, and 8 percent respectively. They also hypothesized that paracetamol's analgesic effects might be related to its effects on COX-2 and PGE2.

There were 1.49 ± 1.38 mean pain scores in the present study. The significant difference ($P < 0.001$) in the mean pain score between the paracetamol and placebo groups was observed. Overall 49 peoples (40.8%) have no pain. As compared to the placebo group, the paracetamol group had a higher rate of 69.4% pain relief.

Overall the incidence of rocuronium-induced injection was found as 74.4% 35% and 30.8% in control, paracetamol and lidocaine groups as reported by Jeon et al.¹³ They found that pretreatment with 50 mg of paracetamol was as effective as 40 mg of lidocaine on the control of rocuronium-induced withdrawal movement. Koppert et al¹⁴ used the tourniquet technique to explore medicines' peripheral effects without causing a central reaction comparable to a Bier block.

According to some previous studies, rocuronium-induced injection, pain was more common in women than men¹⁵⁻¹⁷. Lidocaine reversibly blocks peripheral pathways by blocking excitable membrane and its effect on rocuronium-induced injection pain has been demonstrated to be dose dependent¹⁸.

CONCLUSION

Frequency of absence of pain found lower in patients undergoing elective procedures with injection paracetamol versus placebo given before injection rocuronium.

Conflict of interest: Nil

REFERENCES

- Uzun S, Erden IA, Canbay O, Aypar U. The effect of intravenous paracetamol for the prevention of rocuronium injection pain. *Kaohsiung J Med Sci* 2014;30(11):566-9.
- Yavascaoglu B, Kaya FN, Ozcan B. Esmolol pretreatment reduces the frequency and severity of pain on injection of rocuronium. *J Clin Anesth* 2007;19(6):413-7.
- Ayoglu H, Altunkaya H, Ozer Y, Yapakci O, Cukdar G, Ozkoeak I. Does dexmedetomidine reduce the injection pain due to propofol and rocuronium? *Eur J Anaesthesiol* 2007; 24(06): 541-5.
- Jeon Y, Back S-U, Park SS, Kim SO, Back W-Y, Yeo J-S. Effect of pretreatment with acetaminophen on withdrawal movements associated with injection of rocuronium: a prospective, randomized, double-blind, placebo controlled study. *Korean J Anesthesiol* 2010; 59(1):13-6.
- Shin YH, Choi SJ, Jeong HY, Kim MH. Evaluation of dose effects of magnesium sulfate on rocuronium injection pain and hemodynamic changes by laryngoscopy and endotracheal intubation. *Korean J Anesthesiol* 2011;60(5):329-33.
- Kwak H-J, Chae YJ, Lee SY, Kim YJ, Kim J-Y. Combination of nitrous oxide and lidocaine to prevent withdrawal after

- rocuronium in children. *Korean J Anesthesiol* 2010;58(5):446-9.
7. Graham GG, Davies MJ, Day RO, Mohamudally A, Scott KF. The modern pharmacology of paracetamol: therapeutic actions, mechanism of action, metabolism, toxicity and recent pharmacological findings. *Inflammopharmacology* 2013;21(3):201-32.
 8. Ates G, Kose EA, Oz G, Apan A. Effect of paracetamol pretreatment on rocuronium-induced injection pain: a randomized, double-blind, placebo-controlled comparison with lidocaine. *J Clin Anal Med* 2014;5(6):507-10.
 9. Abbott FV, Hellemans KG. Phenacetin, acetaminophen and dipyron: analgesic and rewarding effects. *Behav Brain Res* 2000; 112(1-2):177-86.
 10. Lee YS, Kim H, Brahim JS, Rowan J, Lee G, Dionne RA. Acetaminophen selectively suppresses peripheral prostaglandin E2 release and increases COX-2 gene expression in a clinical model of acute inflammation. *Pain* 2007;129(3):279-86.
 11. Hinz B, Cheremina O, Brune K. Acetaminophen (paracetamol) is a selective COX-2 inhibitor in man. *FASEB J* 2008;22(2): 383-90.
 12. Canbay O, Celebi N, Arun O, Karagoz AH, Saricaoglu F, Ozgen S. Efficacy of intravenous acetaminophen and lidocaine on propofol injection pain. *Br J Anaesth* 2008;100(1):95-8.
 13. Jeon Y, Baek S, Park SS, Kim SO, Baek W, Yeo J, Effect of pretreatment with acetaminophen on withdrawal movements associated with injection of rocuronium: a prospective, randomized, double-blind, placebo controlled study, *Korean J Anesthesiol* 2010; 59(1):13-6.
 14. Koppert W, Sittl R, Schmelz M. The Bier block as an experimental tool to differentiate peripheral and central effects of analgesics on people. *Schmerz* 2000;14(2):69-76.
 15. Mencke T, Beerhalter U, Fuchs-Buder T. Spontaneous movements, local reactions and pain on injection of rocuronium: A comparison between female and male patients. *Acta Anaesthesiol Scand* 2001;45(8):1002-5.
 16. Mencke T, Schreiber JU, Knoll H, Stracke C, Kleinschmidt S, Rensing H, Silomon M. Women report more pain on injection of a precurarization dose of rocuronium: A randomized, prospective, placebo-controlled trial. *Acta Anaesthesiol Scand* 2004;48(10): 1245-8.
 17. Chirella AB, Jolly DT, Huston CM, Clanachan AS. Comparison of four strategies to reduce the pain associate with intravenous administration of rocuronium. *Br J Anaesth* 2003;90(3):377-9.
 18. Cheong KF, Wong WH. Pain on injection of rocuronium: influence of two doses of lidocaine pretreatment. *Br J Anaesth* 2000;84(1):106-7.