International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Evaluation of Pain by Using Intravenous Paracetamol as Pre-Emptive Drug in Mandibular 3rd Molar Surgery - An Experimental Study

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Abstract: ***This experimental study aimed to compare and evaluate the efficacy of pre-surgical single dose with post-surgical single dose of intravenous Paracetamol in reducing pain, frequency, and dosages of rescue analgesics in patients undergoing mandibular third molar surgery. The study involved 60 patients, and the efficacy of pre-surgical dose of intravenous Paracetamol in reducing post-operative pain was assessed. The findings suggest that pre-surgical dose of intravenous Paracetamol significantly reduces pain after mandibular third molar surgery. Aim: To compare and evaluate the efficacy of pre-surgical single dose with post-surgical single dose of intravenous Paracetamol in reducing pain, frequency, and dosages of rescue analgesics. Objectives: 1) To evaluate efficacy of pre-surgical dose of intravenous Paracetamol for reduction of pain during mandibular third molar surgery. 2) To evaluate whether intravenous Paracetamol has potent analgesic effect during &/or after mandibular third molar surgery. Methods: An experimental study carried out indepartment of Oral and Maxillofacial Surgery. Total60 patients were selected based on inclusion and exclusion criteria. Informed consent was obtained fromall the patients involved in the study. Patients who will fulfil the study criteria were divided into three equal groups based on preoperative and postoperative dose of Paracetamol and placebo. Conclusion: From our study, we would like to conclude that pre-surgical dose of intravenous Paracetamol significantly reduces pain after mandibular third molar surgery.***

Keywords: Pain, Mandibular Third molar, Paracetamol, Pre-emptive drug

1. Introduction

The chore of medicine is to preserve and restore patient's health and to minimize their suffering.[1] I.V. administration of Paracetamol has been described as the route of choice for rapid analgesia after surgery.[1]

Inadequate acute post-operative pain management is a potent source of complications and a significant cause of decreased quality of life after surgery.[2] Therefore, prophylactic analgesia is a suggested method for treating post-operative pain after third molar extraction.[2]Pre-emptive analgesia, also called pre-operative analgesia, is a way of reducing production of mediators responsible for nerve stimulation. It is characterized as an antinociceptive treatment for the prevention of central changes induced by afferent sensitization due to tissue injuries caused by surgical procedures.[4]Intravenous administration is the route of choice when rapid analgesia is required after surgery. Intravenous propacetamol, administered in a 15-minute infusion, is a fast-acting analgesic agent and is more effective in terms of onset of analgesia than oral paracetamol. In a recent study, Moller et al. have demonstrated that the stable ready to - use paracetamol solution for infusion (intravenous paracetamol) 1 g has a better tolerability profile and efficacy after third molar surgery.[5]

2. Material and Method

The study was carried out for the duration of 18 months from 2021 to 2022 at the Department of Oral and Maxillofacial Surgery for surgical extraction of an impacted mandibular third molar. The study design was an Experimental study. Sampling method was convenience sampling. The patient withdrawal criteria had completed following the Helsinki Ethical Principles for Medical Research Involving Human Subjects.[22]

Inclusion Criteria:

1) Patients who gave written informed consent for being part of the study.
2) Patients of age between 18 to 50 years.
3) Patients who didn't have any uncontrolled systemic diseases.
4) No current medications.
5) No allergies to any of the drugs administered within the study.
6) An absence of local or systemic infection.
7) Impacted mandibular third molars, in the horizontal or mesio-angular position, in accordance with the Winter's classification.

Exclusion Criteria:

1) The Patient who refused to give written informed consent.
2) Patients who were pregnant or breastfeeding mothers.
3) Patients with a history of uncontrolled diabetes and hypertension and any other severe systemic diseases.
4) Patients allergic to Paracetamol or any other NSAIDs.
5) Patients with the suspicion or evidence of narcotics or illicit drug use.
6) Patients with history of hepatic diseases.
7) Patients who had taken self-medication before coming to department.

Subject Withdrawal Criteria: -

1) Patient who wanted to withdraw from the research.
2) Patients who could not follow up for the given period of time.

Armamentarium

1) 5-ml syringe
2) Sterile gloves
3) Scalp van
4) Spirit
5) Sterile cotton swabs
6) IV set
7) Inj. Paracetamol 1gm

3. Method

The patients who had given written informed consent were included in the study. Complete case history for each patient was documented. Clinical findings were identified and documented for each patient. A proper treatment plan was formulated for each individual patient as follows.

Patients were injected with pre-operative medicines according to their groups, i.e.

Group 1 patients were administered with 1gm of IV Paracetamol 60 minutes before surgery and IV placebo (100 mL of saline) after surgery.

Group 2 patients were administered with IV placebo (100 mL of saline) 60 minutes before surgery and 1gm of IV Paracetamol 60 minutes after surgery.

Group 3 patients were administered with IV placebo (100 mL of saline) 60 minutes before and after surgery.

In accordance with the protocol for preoperative antisepsis, local anesthesia was performed by blocking the inferior alveolar and lingual, buccal nerves with a maximum of 2 doses of 2 mL of lignocaine hydrochloride (40 mg), with epinephrine (1:200, 000) using a plastic disposable injection syringe. 10 minutes after anesthesia administration, a horizontal and sulcular incision was performed, and a mucoperiosteal envelope flap was elevated. The bone covering the impacted third molar tooth was removed with the use of a surgical handpiece and rotary instrument. During the operation, saline water was to protect the bone from developing a high temperature. After extraction of the third molar, the cavity was treated with curettage, lavage with saline, and sutured. At 60 minutes after the operation, the patient received the postoperative allotted drug. In addition, Aceclofenac 100 mg was prescribed as a rescue medication for each patient, in case the study medication won't provide sufficient pain relief. Subsequently, all the patients recorded their pain intensity using a 10-point graduated visual analogue scale (VAS), on which the endpoints were defined as 0 (no pain at all) and 10 (worst pain one can imagine) (Fig. 2) Postoperative pain was recorded on the VAS at 0, 4, 8, 24 hours after completion of the procedure by contacting the patient on phone. Also, the patients were asked for their total aceclofenac intake during the first 24 hours (at 0, 4, 8 and 24 hours) after completion of the procedure.

4. Result

The data obtained from the study was entered in to excel sheet to prepare a master chart (Annexure-III) and this data was statistically analyzed using the ANOVA test, One-way ANOVA test, Post hoc Bonferroni test, Post hoc Tukey test and Chi-square test on IBM SPSS 21.0 version (2015) software.

Amongst all total (N=60) number of participants, the maximum age was 45 years old and the minimum age was 18 years old. The mean age in group A, group B and group C was 26.65 years, 29.30 years and 30.10 years respectively (Table 1, Graph 1). The maximum number of females were observed (n=33) in which, group A had 10 males and 10 females, group B had 9 males and 11 females and 8 males and 12 females were in group C. (Table 2, Graph 2).

On the Comparison of change in VAS score in each group, immediately after surgery the mean VAS score in group A, group Band group C was 1.20, 2.75& 2.65respectively. After 4 hours in group A, it was 1.90, in group B was 2.65 and in group C was 3.35.After 8 hours of surgery in group A means value was 1.55, in group B 1.70 and in group C 2.05. After 24 hours in group A- 1.15, in group B-1.25 and in group C-1.00.The result was statistically significant $p \leq 0.05$. (Table 3, Graph 3)

In group A, there was a significant increase in VAS score after surgery till 4 hours (0.002) and significant decrease till 8 hours (1.000) and 12 hours (0.342).In group C, there was a significant increase in VAS score after surgery till 4 hours (0.211) and significant decrease till 8 hours (<0.001) and 12 hours (<0.001). This showed significant difference at $p \leq 0.05$. (Table 4)

After surgery, group A showed significantly lower VAS score than group B (<0.001) and group C (<0.001) and there was no difference between group B & group C(0.945). After 4 hrs, group A showed significantly lower VAS score than group C (0.002) and almost similar VAS score as that of group B (0.154). There was no difference between group B & group C after 4 hrs (0.195). After 8 hrs and 24 hrs, there was no difference in VAS score among three groups. There was significant at p≤0.005 by Post hoc Tukey test. (Table 5)

There was a significant difference in number of patients with rescue analgesia required with group C (100%) showing significantly maximum number of patients requiring rescue analgesia than group A (20%) and group B (30%). (Table 6, Graph 4).71.7% of total population did not have any complications. In group A, 5% suffered from pain, 10% had trismus and 5% had swelling. In group B, 15% had pain, 10% had trismus and 5% had paresthesia. In group C, 10% had pain, 10% had trismus, 5% had swelling and 10% had more than one expected complication. (Table 7, Graph 5)

The significance of this study lies in assessing the efficacy of pre-surgical dose of intravenous Paracetamol in reducing pain and the need for rescue analgesics in patients undergoing mandibular third molar surgery. Understanding the effectiveness of this analgesic approach can contribute to improved pain management in dental surgical procedures.

5. Discussion

Pain is a subjective experience with two complementary aspects: one is a localized sensation in a particular body part; the other is an unpleasant quality of varying severity commonly associated with behaviours directed at relieving or terminating the experience[24].

Impaction of the third molar teeth is a common disorder which often necessitates their removal. After third molar surgery, the common postoperative sequelae are pain, trismus and buccal swelling. It is well documented that pain after removal of impacted third molars is of short duration and reaches its maximum intensity in the early postoperative period.[25] Most severe pain occurs followed by third molar surgery in first 12 hours and reaches maximum intensity 6-8 hours post operatively[23]. The removal of the impacted third molar and the resultant tissue and cellular destruction brings about the release and production of several biochemical mediators involved in the pain process, in particular, histamine, bradykinin and the prostaglandins. Meechan and Seymour in 1993 said, the pain experience is especially useful for evaluating the efficacy of single doses of analgesics.[25] Single dose studies also facilitate investigations between pharmacokinetic variables of the drug and efficacy. So, in my study, I have used single dose of paracetamol to evaluate its efficacy. The time course of action for IV paracetamol is quick: it usually reaches peak concentration as soon as infusion is complete (about 15 min). According to the product information, the analgesic effect of paracetamol starts within 5 min, peaks at 1 h and lasts 4–6 h.[3]

I.V. administration of Paracetamol was selected to be route of administration because I.V. administration achieves rapid, reliable serum paracetamol level within therapeutic analgesic range and I.V. route has 100% bioavailability.[27] Weil et al. studied paracetamol for pain relief after surgical removal of lower wisdom teeth. They concluded that paracetamol is a safe, effective drug for the treatment of postoperative pain following the surgical removal of lower wisdom teeth[26].

In 2001, Norman et al also used ketorolac as pre-emptive drug in ankle surgery and concluded that a single 30-mg dose of ketorolac administered intravenously before tourniquet inflation appears to have pre-emptive analgesic effects in subjects having open reduction and internal fixation of unilateral ankle fractures.[7]In 2018, Vinishdharma Thenarasu et al. evaluated the comparative effects of Diclofenac and Paracetamol and concluded that Diclofenac is more effective than Paracetamol as a pre-emptive analgesia.[4]

Several studies state that the use of pre-operative analgesics in adults before dental extraction of third molars cause significant decrease in post-operative pain scores when pre-emptive analgesia was performed.All these studies have supported the idea of using pre-emptive analgesia before surgery but few studies have chosen other NSAID over paracetamol as it has a weak anti-inflammatory property.

In 2020, Pablo Santos and colleaguesconcluded that, the pre-emptive administration of analgesics did not significantly reduce trans- and post-operative pain in children after primary molars extraction.[20]This study doesn't support our study.

The limitations of this study are -1.The study is non randomised. 2.The parameter taken was VAS scale, the intensity and tolerance to the pain varies person to person. 3.The effect of I.V. paracetamol was very good in the patient, that patient didn't require any analgesic even after 24 hours. But ended up with swelling and trismus which subsided after 8days.

6. Conclusion

Based on the results of this experimental study, it can be concluded that a pre-surgical dose of intravenous Paracetamol significantly reduces pain after mandibular third molar surgery. This finding highlights the potential of pre-emptive analgesia using intravenous Paracetamol as an effective approach to manage post-operative pain in dental surgical procedures.

Funding
No funding to declare.

Acknowledgement
Authors declare no conflicts of interest with respect to authorship and publication of this article.

Author contributions
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Dr Samruddhi Danave, Dr Rahul Laturiya, Dr Sheeraz Badal and Dr Punam Nagargoje. The first draft of the manuscript was written by Dr Samruddhi, Dr Minal and

Dr Varsha. All authors read and approved the final manuscript.

Ethical approval- The study was performed in line with the principles of the Declaration of Helsinki Approval was granted by the Ethics Committee of University named MIDSR Dental College, Latur Institutional ethical committee **(**Date-14/01/2021/ MIDSR/STU/PG/560/34/2021**).**

Consent to participate- Informed consent was obtained from all individual participants included in the study. Written informed consent was obtained from the patients.

Consent to publish- Not required.

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Tables

Table 1: Distribution of study participants according to their age

Group	Mean	SD	Minimum	Maximum
Gr A	26.65	5.967	18	37
Gr B	29.30	6.199	19	41
Gr C	30.10	6.172	23	45

Table 2: Distribution of study participants according to their sex

Group	Male	Female
Gr A	10 (50%)	10 (50%)
Gr B	9 (45%)	11 (55%)
Gr C	8 (40%)	12 (60%)

Table 3: Comparison of change in VAS score in each group

Groups	After surgery		4 hours		8 hours		24 hours		p value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Gr A	1.20	0.89	1.90	1.07	1.55	0.95	1.15	1.39	0.013*
Gr B	2.75	0.97	2.65	1.42	1.70	1.03	1.25	0.79	<0.001*
Gr C	2.65	1.09	3.35	1.27	2.05	1.32	1.00	0.92	<0.001*

Repeated measures ANOVA test; * indicates significant difference at p≤0.05

Table 4: Pairwise comparison of change in VAS score in each group

Group	AS vs 4	AS vs 8	AS vs 24	4 vs 8	4 vs 12	8 vs 12
Gr A	0.002*	1.000	1.000	1.000	0.107	0.342
Gr B	1.000	0.002*	<0.001*	0.009*	<0.001*	0.278
Gr C	0.211	0.372	<0.001*	<0.001*	<0.001*	<0.001*

AS: After surgery; Post hoc Bonferroni test; * indicates significant difference at p≤0.05.

Table 5. Pairwise comparison of VAS score among three groups

Interval	Gr A vs Gr B	Gr A vs Gr C	Gr B vs Gr C
After surgery	<0.001*	<0.001*	0.945
@4hours	0.154	0.002*	0.195
@8hours	0.904	0.335	0.581
@24hours	0.952	0.896	0.738

Post hoc Tukey test; * indicates significant difference at p≤0.05

Table 6: Comparison of no of patients with rescue analgesia required

Group	n	%	p value	Pairwise comparison
Gr A	4	20%	<0.001*	Gr A vs Gr B: 0.716
Gr B	6	30%		Gr A vs Gr C: <0.001*
Gr C	20	100%		Gr B vs Gr C: <0.001*

Chi-square test; * indicates significant difference at p≤0.05

Table 7. Evaluation of complications

	Gr A		Gr B		Gr C		Total	
	n	%	n	%	n	%	n	%
No	16	80	14	70	13	65	43	71.7
Pain	1	5	3	15	2	10	6	10
Pain & Trismus	0	0	0	0	1	5	1	1.7
Paresthesia	0	0	1	5	0	0	1	1.7
Swelling	0	0	0	0	1	5	1	1.7
Trismus	2	10	2	10	2	10	6	10
Trismus & Swelling	1	5	0	0	1	5	2	3.3
Total	20	100	20	100	20	100	60	100

Figures

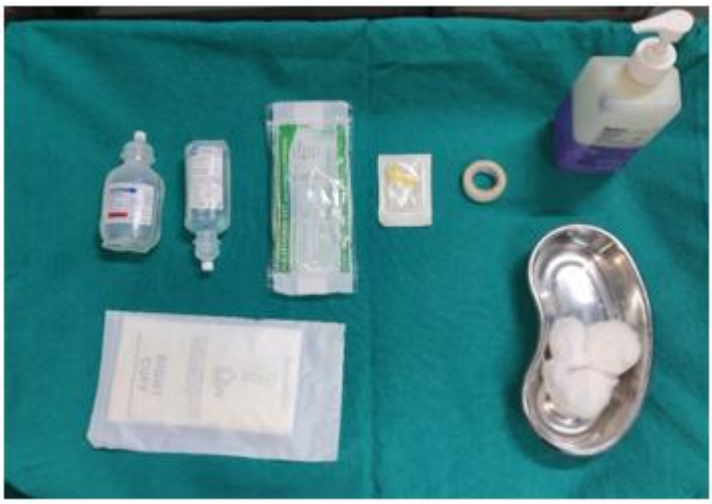


Figure 1: Armamentarium

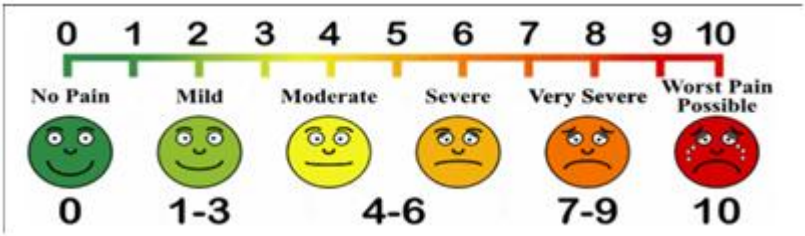
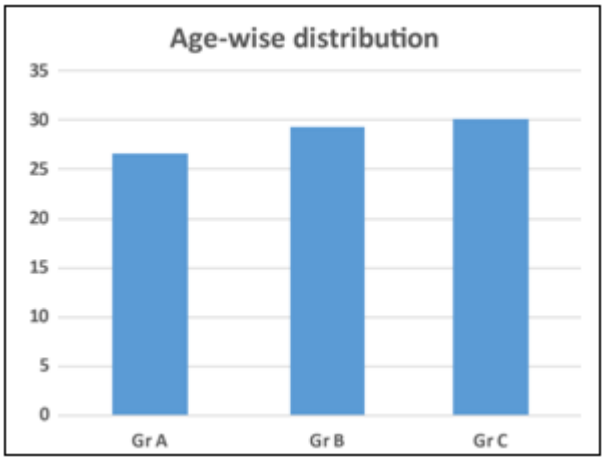
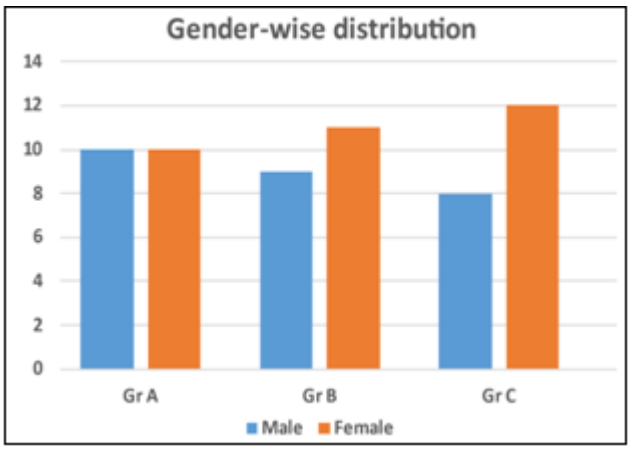


Figure 2: Visual analogue scale

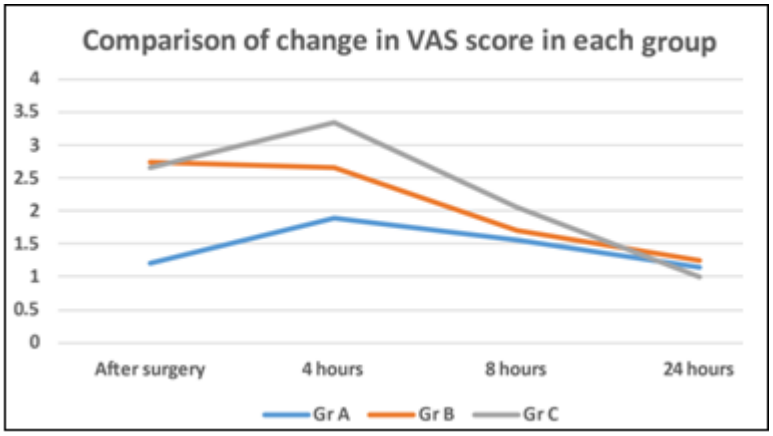
Graphs



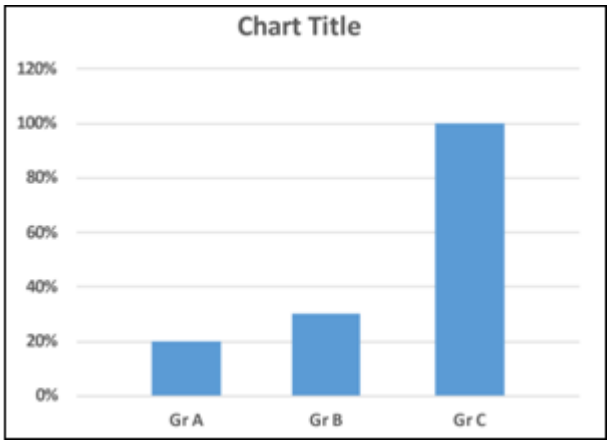
Graph 1: Age-wise distribution



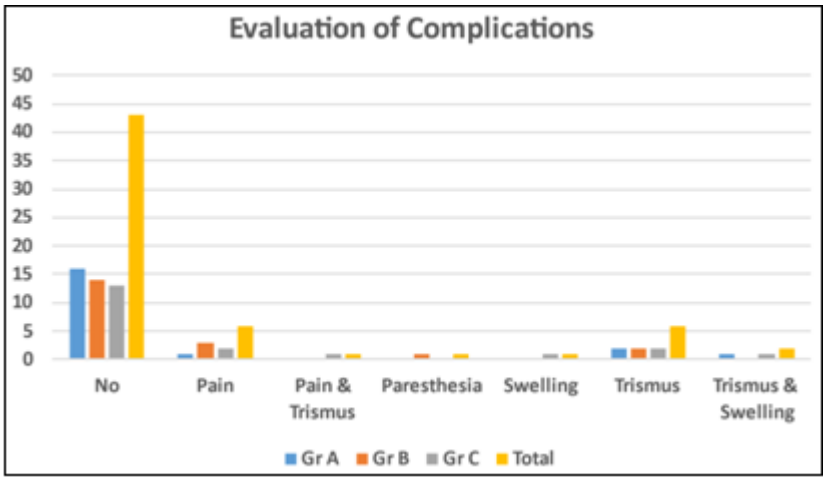
Graph 2: Gender-wise distribution



Graph 3: Comparison of change in VAS score in each group



Graph 4: Comparison of number of patients with rescue analgesia required



Graph 5: Evaluation of complications