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COMPARATIVE STUDY OF INTRAVENOUS PARACETAMOL AND TRAMADOL IN MANAGEMENT OF POST-OPERATIVE ANALGESIA IN PERCUTANEOUS NEPHROLITHOTOMY- RANDOMIZED CLINICAL STUDY

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ABSTRACT

Background: Postoperative pain is a critical aspect of surgical recovery, especially in procedures like percutaneous nephrolithotomy (PCNL), where inadequate pain management can delay healing and increase complications. Common analgesics such as intravenous (IV) Paracetamol and Tramadol are frequently used, but their comparative efficacy and safety in urological surgeries remain under-investigated. Paracetamol, a non-opioid analgesic, is known

for its favorable safety profile, whereas Tramadol, an opioid, may cause more adverse effects. This study aims to compare the efficacy and safety of IV Paracetamol and Tramadol in patients undergoing PCNL.

Methods : A randomized clinical trial was conducted at the Department of General Surgery, Sri Chamarajendra Hospital, Hassan Institute of Medical Sciences. Forty-six patients undergoing PCNL were randomly assigned to receive either IV Paracetamol (1g in 100 ml NS) or IV Tramadol (100 mg in 100 ml NS) postoperatively. Analgesic efficacy was assessed using the Visual Analog Scale (VAS) at multiple time points (T1 to T7), while adverse drug reactions (ADRs) were monitored using the Naranjo Scale. Statistical analysis included unpaired t-tests and chi-square tests.

Results: In this randomized clinical trial, both intravenous Paracetamol and Tramadol provided effective postoperative pain relief in patients undergoing percutaneous nephrolithotomy. The groups were comparable in age (Paracetamol: 41.87 ± 9.45 years, Tramadol: 43.43 ± 9.61 years; p 0.580) and sex distribution ($p = 0.767$). Paracetamol showed significantly lower VAS scores at T2 (2.87 ± 0.76 vs. 3.52 ± 1.20; $p = 0.033$) and T3 (2.13 ± 0.55 vs. 2.48 ± 0.52; $p = 0.031$), indicating better early pain control. From T4 to T7, VAS scores between the groups were similar with no statistically significant differences ($p > 0.05$). Adverse drug reactions were minimal, with probable ADRs in 13% of the Tramadol group and none in the Paracetamol group (p 0.111).

Conclusions: Intravenous Paracetamol and Tramadol were found to be equally effective in managing postoperative pain in patients undergoing percutaneous nephrolithotomy. Although Paracetamol showed slightly lower pain scores at certain early postoperative time, it can be considered as the first-line option for postoperative analgesia in this clinical setting.

Keywords: Postoperative analgesia, Paracetamol, Tramadol, Percutaneous Nephrolithotomy, Visual Analog Scale, Randomized Clinical Trial, Adverse Drug Reaction.

INTRODUCTION

Postoperative pain management is a crucial responsibility for clinicians, as many patients experience significant pain following surgery. The American Pain Society (APS), in collaboration with the American Society of Anesthesiologists (ASA), has developed comprehensive guidelines for managing postoperative pain in both adults and children. These guidelines emphasize the importance of preoperative patient education, the use of multimodal

approaches that include both pharmacological and non-pharmacological therapies, and the implementation of standardized pain management protocols within healthcare institutions. Common pharmacological options recommended include opioids, paracetamol, and non-steroidal anti-inflammatory drugs (NSAIDs), tailored to the nature of tissue injury during surgery and the intensity of the patient's pain[1].

Pain is an expected aspect of any surgical procedure, yet postoperative pain is often managed inadequately. Insufficient treatment of post-surgical pain can lead to both physical and psychological complications, such as splinting, reduced gastrointestinal motility, and delayed wound healing, which may negatively impact perioperative outcomes and prolong hospital stays. Effective recovery from surgery requires a holistic approach to managing postoperative pain[2]. Postoperative pain is most intense during the first 24-72 hours and gradually decreases thereafter. However, it remains a frequently overlooked issue that receives insufficient attention[3].

Paracetamol a member of Nonsteroidal Anti inflammatory Drugs (NSAID) inhibits prostaglandin synthesis without affecting platelet function or causing nephrotoxicity, with adverse reactions occurring in fewer than 1 in 10,000 individuals. Tramadol, a member of the Opioids group, selectively targets mu receptors, inhibits synaptic norepinephrine reuptake, and enhances intrasynaptic serotonin release by modulating neuroamine transmission. Due to the minimal impact of both IV paracetamol and tramadol on the renal system, we chose these two drugs for comparison in urosurgical patients[4]

METHODS:

STUDY TYPE: Randomized Clinical Study

STUDY PLACE: HASSAN INSTITUTE OF MEDICAL SCIENCES, HASSAN, KARNATAKA

DURATION OF STUDY: 12months

Inclusion criteria:

1. Patients aged 18-65 years
2. Both sex

3. Patients scheduled for Percutaneous Nephrolithotomy
4. Normal baseline renal and liver function tests.
5. Patients who provide written informed consent.

Exclusion criteria:

1. Pregnant and lactating women
2. Known hypersensitivity or allergy to Tramadol, Paracetamol, or their excipients.
3. Patients under chronic analgesics medications
4. Renal failure, hepatic dysfunction, hemorrhagic disorder

Data were collected using a semi-structured questionnaire after obtaining ethical committee clearance. This randomized clinical trial was conducted in the Department of General Surgery at Sri Chamarajendra Hospital, Hassan Institute of Medical Sciences, Hassan, among patients undergoing percutaneous nephrolithotomy, after obtaining informed consent. Patients who met the inclusion criteria were recruited and informed about the study's objectives in their native language. They were then randomly assigned to two groups.

The study aimed to compare the efficacy and safety of paracetamol and tramadol using the Visual Analog Scale (VAS) for pain assessment and the Naranjo Scale for evaluating adverse drug reactions.

Group A received IV Paracetamol (1 g in 100 ml normal saline), while Group B received IV Tramadol (100 mg in 100 ml normal saline) immediately postoperatively. Subsequent doses of either IV paracetamol (1 g) or IV tramadol (100 mg) were administered at 6, 12, and 18 hours postoperatively. Pain intensity was assessed using a 10-point Visual Analog Scale (VAS; 0 = no pain, 10 = worst imaginable pain) at the following time points: before analgesic administration (T0), and at 0.5 hours (T1), 1.5 hours (T2), 3 hours (T3), 6 hours (T4), 12 hours (T5), 18 hours (T6), and 24 hours (T7) postoperatively.

The Naranjo Scale was used to evaluate any adverse drug reactions observed during the study.

STATISTICAL ANALYSIS:

The estimation of the sample size for this study was determined using the formula:

$$n = \frac{2(Z_\alpha + Z_\beta)^2 S^2}{\gamma^2}$$

Where, $Z_{\alpha=1.96,}$ z $Z_{\beta=0.842,}$ SD1=9.48, SD2+ 2.48

S=(SD1+SD2)/2; S=5.98

n= $2(1.96+0.842)^2 (5.98)^2/25$

n= 22.3

According to the study conducted by Ajaydeep et al[4], VAS score for Paracetamol group(SD1) and Tramadol group(SD2) has been obtained.

Attrition =5%, hence, by using this formula an estimated sample size was 23 for each group

Total- 46

RESULTS

The present study was done in HIMS, Hassan. A total of 46 patients who underwent percutaneous nephrolithotomy followed up in their postoperative period for postoperative analegesia with paracetamol vs tramadol

The results from the tables and figures in our study can be interpreted as follows:

Table 1 shows the mean age in the Paracetamol group was 41.87 ± 9.45 years, while in the Tramadol group it was 43.43 ± 9.61 years. There was no statistically significant difference between the groups (p = 0.580). This indicates both groups were age-matched. Hence, age is unlikely to have influenced outcome differences.

Table 2 shows distribution of VAS score in time intervals, **T1**: No significant difference in mean VAS scores at T0 (p 0.764), suggesting similar baseline pain levels postoperatively. **T1**: No significant difference in mean VAS scores at T1 (p 0.266), suggesting similar baseline pain levels postoperatively. **T2**: Paracetamol group had significantly lower VAS (2.87 ± 0.76) than Tramadol (3.52 ± 1.20) at T2 (p 0.033), indicating better early pain control. **T3**: A statistically significant lower VAS score was observed in the Paracetamol group (2.13 ± 0.548vs 2.48 ± 0.51; p 0.031), supporting better analgesia. **T4 to T7**: No significant differences in VAS scores were found (p > 0.05), suggesting comparable analgesic effects over time.

Table 3 shows rescue analgesic time using unpaired t-test. The mean time to rescue analgesia was significantly longer in the Paracetamol group (6.78 ± 0.80 hours) compared to the Tramadol group (4.96 ± 0.83 hours).This difference was highly significant (p < 0.001).

It indicates prolonged analgesic effect with Paracetamol. Thus, Paracetamol provided longer-lasting pain relief postoperatively.

In Table 4 using Chi-square test sex distribution of the participants done. The distribution of males and females was similar between groups (Paracetamol: 56.5% female; Tramadol: 52.2% female). No statistically significant difference was observed (p 0.767). This confirms gender was well balanced across groups. Hence, sex-related bias is unlikely to affect outcomes.

Table 5 shows commonest side of surgery. Left-sided surgeries were slightly more common in the Paracetamol group (65.2%) compared to the Tramadol group (52.2%). However, the difference was not statistically significant (p 0.369). Both groups had a fairly even distribution of surgical sides. Thus, the surgical site is not a confounding variable.

Table 6 shows adverse drug reactions in the participants. The Chi-square test (p 0.111) indicates no statistically significant difference in adverse drug reactions (ADRs) between the Paracetamol and Tramadol groups. In the Tramadol group, 13.0% had probable ADRs, while none were reported in the Paracetamol group. Doubtful ADRs were equally reported (8.7%) in both groups. Most participants had no ADRs—91.3% with Paracetamol and 78.3% with Tramadol.

Figure 1 depicts the distribution of VAS score in the participants with paracetamol and tramadol.

The study found that both intravenous Paracetamol and Tramadol were effective in managing postoperative pain following percutaneous nephrolithotomy. Pain scores were comparable at most time points, with Paracetamol showing significantly lower VAS scores at T2 (2.87 ± 0.76 vs. 3.52 ± 1.20) and T3 (2.13 ± 0.55 vs. 2.48 ± 0.52), indicating better early pain relief. No significant differences were observed from T4 to T7. Adverse drug reactions were minimal and not statistically different between the groups. Overall, both drugs demonstrated similar efficacy and safety profiles.

DISCUSSION

The findings of our study can be contrasted with the results from the Saleh et al study, which evaluated postoperative analgesic efficacy of intravenous Paracetamol and Tramadol in PCNL

patients. In the Saleh et al study, both analgesics were used equally among 36 patients (18 each). Patients receiving Paracetamol had a slightly lower mean VAS score (2.44 ± 0.51) compared to those receiving Tramadol (2.67 ± 0.48), but the difference was not statistically significant (p 0.186), suggesting comparable efficacy between the two drugs[1].

In contrast, our study showed a statistically significant difference in pain scores at specific time points. At T2 and T3, patients in the Paracetamol group had significantly lower VAS scores (2.87 ± 0.76 and 2.13 ± 0.55, respectively) compared to the Tramadol group (3.52 ± 1.20 and 2.48 ± 0.52), with p-values of 0.033 and 0.031, respectively. Additionally, the time to rescue analgesia was significantly longer in the Paracetamol group (6.78 ± 0.80 hours vs. 4.96 ± 0.83 hours; p < 0.001), and fewer adverse drug reactions were observed. Both studies support that Paracetamol and Tramadol are effective for postoperative pain relief in PCNL patients[1].

In the Shahid et al study, two groups of postoperative patients were compared for analgesic efficacy, with group I receiving intravenous Paracetamol and group II receiving intravenous Tramadol. The demographic parameters and types of surgeries were comparable between the groups, minimizing confounding. The mean VAS scores at 30 minutes were 5.76 (group I) and 6.23 (group II), and at 24 hours were 1.83 and 2.10 respectively. Although there was a gradual fall in VAS scores in both groups, the difference was not statistically significant (p 0.653), indicating comparable analgesic efficacy[2].

In comparison with our study, showed statistically significant differences in early postoperative pain scores. Specifically, at T2 and T3, Paracetamol demonstrated significantly lower VAS scores than Tramadol (2.87 ± 0.76 vs. 3.52 ± 1.20 at T2, $p = 0.033$; and 2.13 ± 0.55 vs. 2.48 ± 0.52 at T3, p 0.031). Additionally, the time to rescue analgesia was longer in the Paracetamol group ($p < 0.001$), and adverse drug reactions were fewer compared to Tramadol[2].

While both studies conclude that IV Paracetamol and Tramadol are effective for postoperative pain management, Shahid et al. reported no statistically significant difference at any time point. In contrast, our study demonstrates significantly better early analgesia with Paracetamol, suggesting that it may be more beneficial for controlling immediate postoperative pain, especially in procedures like PCNL.

The Agrawal et al study presents a comparison of intravenous Paracetamol (Group P) and Tramadol (Group T) for postoperative analgesia, focusing on VAS scores, rescue analgesic requirements, and hemodynamic parameters such as pulse rate (PR). While both groups were

comparable demographically and surgically, notable differences in outcomes were observed. Agrawal et al study shows the mean VAS score immediately after extubation was lower in Group P (1.86 ± 2.40) than in Group T (3.03 ± 2.42), although the difference was not statistically significant ($p > 0.05$). In contrast, our study reported statistically significant lower VAS scores in the Paracetamol group at early postoperative intervals — particularly at T2 (2.87 ± 0.76 vs. 3.52 ± 1.20; p 0.033) and T3 (2.13 ± 0.55 vs. 2.47 ± 0.52; p 0.031), indicating paracetamol and tramadol were equally efficacious[3].

The Agrawal et al study found a significantly lower mean number of rescue analgesic doses in the Paracetamol group (1.6 ± 1.16) compared to the Tramadol group (2.7 ± 0.95), with $p <$ 0.0001. Similarly, in our study, time to rescue analgesia was significantly longer in the Paracetamol group (6.78 ± 0.80 hours vs. 4.96 ± 0.83 hours; $p < 0.001$), suggesting a longer duration of analgesic effect[3].

The Vilochan et al study presents a detailed comparison between intravenous Paracetamol and Tramadol for postoperative pain control, with findings that closely align with the outcomes of our study, though with some distinctions in onset and pattern of analgesic effect[4].

Both studies had comparable baseline characteristics in terms of age and sex distribution between the Paracetamol and Tramadol groups, eliminating significant demographic bias. For instance, in Vilochan et al study, the mean ages were nearly identical (42.86 ± 8.56 vs. 42.76 ± 8.45; p 0.953), and sex distribution was not significantly different (p 0.648). Similarly, in our study, the groups were matched for age and gender (e.g., p 0.580 for age and p 0.767 for sex), supporting the internal validity of both studies[4].

Both studies agree that Paracetamol provides superior pain control over time, especially from 3 to 24 hours postoperatively. In the Vilochan et al study, Tramadol had a faster onset of analgesia with slightly better VAS scores at 30 minutes. However, Paracetamol consistently outperformed Tramadol from 1 hour onward, with significant differences at 3h, 6h, 12h, and 24h[4].

In our study, although the earliest time points (T2 and T3) already showed slightly better significant pain relief with Paracetamol, no further significant differences were seen from T4 to T7, although the trend favored Paracetamol.

Based on the comparative analysis of our findings with multiple previous studies—including those by Saleh et al., Shahid et al., Agrawal et al., and Vilochan et al.—it is evident that while

both intravenous Paracetamol and Tramadol are effective for postoperative analgesia, Paracetamol consistently demonstrates superior outcomes in terms of early pain control, longer duration of analgesia, and fewer adverse drug reactions. Our study further strengthens this evidence by showing statistically significant advantages of Paracetamol in the early postoperative period and a more favorable safety profile. Therefore, intravenous Paracetamol can be considered a more effective and safer alternative to Tramadol for managing postoperative pain in patients undergoing percutaneous nephrolithotomy.

LIMITATION OF THE STUDY

Small sample size, being conducted at a single center, short follow-up duration, which may limit the generalizability of the findings.

CONCLUSION

Both Paracetamol and Tramadol were equally effective for early postoperative pain control, with fewer probable adverse drug reactions and longer-lasting analgesia. Paracetamol can be a preferable option in clinical settings for managing postoperative pain.

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DECLARATIONS

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Table 1: Age distribution

Unpaired t test					
	Group	N	Mean	SD	p
AGE	Paracetamol	23	41.87	9.450	0.580
	Tramadol	23	43.43	9.610	

Table 2: VAS Score

Unpaired t test					
	Group	N	Mean	SD	p
VAS (T0)	Paracetamol	23	6.00	0.904	0.764
	Tramadol	23	6.08	1.040	
VAS (T1)	Paracetamol	23	5.43	1.161	0.266
	Tramadol	23	5.83	1.193	
VAS (T2)	Paracetamol	23	2.87	0.757	0.033
	Tramadol	23	3.52	1.201	
VAS (T3)	Paracetamol	23	2.13	0.548	0.031
	Tramadol	23	2.47	0.518	
VAS (T4)	Paracetamol	23	2.26	0.810	0.344
	Tramadol	23	2.48	0.730	
VAS (T5)	Paracetamol	23	2.17	0.778	0.331
	Tramadol	23	2.39	0.722	
VAS (T6)	Paracetamol	23	2.17	0.834	0.178
	Tramadol	23	2.48	0.665	

VAS (T7)	Paracetamol	23	2.57	0.992	0.403
	Tramadol	23	2.78	0.736	

Table 3: Rescue Analgesic Time

Unpaired t test				
	Group	Mean	SD	p
RESCUE(Hr/Nil)	Paracetamol	6.78	0.795	<0.001
	Tramadol	4.96	0.825	

Table 4: Sex Distribution of the participants

Chi-Square Test					
			Group		p
			Paracetamol	Tramadol	
SEX	Female	Count	13	12	0.767
		% within Group	56.5%	52.2%	
	Male	Count	10	11	
		% within Group	43.5%	47.8%	

Table 5: Surgical side of the participants

Chi-Square Test					
			Group		p
			Paracetamol	Tramadol	
Surgery side (R/L)	Left	Count	15	12	0.369
		% within Group	65.2%	52.2%	
	Right	Count	8	11	
		% within Group	34.8%	47.8%	

Table 6: Adverse Drug Reactions

Chi-Square Test					
			Group		p
			Paracetamol	Tramadol	
ADR	Doubtful ADR	Count	2	2	0.111
		% within Group	8.7%	8.7%	

	Nil	Count	21	18	
		% within Group	91.3%	78.3%	
	Probable ADR	Count	0	3	
		% within Group	0.0%	13.0%	

Figure 1: VAS score in the participant groups