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Comparison of Postoperative Pain between Pethidine and Paracetamol Recipients with Tibial Fractures Undergoing Nailing Surgery in Bahonar Hospital in Kerman, Iran

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Abstract

Background

The aim of the present study was to compare the postoperative pain intensity between pethidine and paracetamol (acetaminophen) recipients with tibial fractures who underwent nailing surgery.

Materials and Methods: This study is a double-blind clinical trial conducted on candidates (in the age range of 18-50 year-old) of orthopedic tibia fracture surgery referred to Shahid Bahonar Hospital in Kerman, Iran, in 2019. Samples were selected by the convenience sampling method and randomly assigned to paracetamol and pethidine groups. Spinal anesthesia and 0.05 bupivacaine were used for all patients. The pethidine group (1 mg/kg body weight), and the paracetamol group (15 mg/kg body weight) were injected half an hour before 6, 12, and 24 hours after surgery under local anesthesia. The mean postoperative pain intensity in terms of VAS scores at 6, 12, and 24 hours after surgery was compared between the two groups. The collected data were analyzed using SPSS ver. 19.

Results: A total of 96 patients participated in the study. The results of the independent t-test showed a statistically significant difference between the mean pain intensity of patients in paracetamol (65.47 ± 9.88), and pethidine (69.97 ± 11.65) recipients six hours after surgery (P=0.044). There was also a statistically significant difference between the paracetamol (45.37 ± 8.63) and pethidine (49.95 ± 9.93) recipients in terms of the mean pain intensity (P = 0.018). There was no statistically significant difference between the two groups in terms of demographic characteristics, i.e. age, weight, height, gender, and smoking.

Conclusion: Based on the results, paracetamol is more effective than pethidine in relieving postoperative pain in patients with tibial fractures.

Key Words: Pain, Pethidine, Paracetamol, Tibial fractures, Nailing surgery.

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1- INTRODUCTION

Acute pain treatment is an important issue in the healthcare system. Researchers estimate that in the United States, only a quarter of patients who undergo surgery receive adequate relief from acute surgical pain (1, 2). Acknowledgment of the prevalence of acute postoperative pain has led to the development of many socio-medical guidelines and, more importantly, new regulatory standards for the assessment and management of acute pain. New standards emphasize the routine evaluation of pain as the fifth vital sign (3). Postoperative pain not only leads to physical complications but also causes anxiety and psychological distress (4). Physical complications of postoperative pain include phlebothrombosis, pulmonary embolism, respiratory dysfunction, and even myocardial infarction (5).

Pain control is of particular importance among orthopedic patients as poor pain control in these patients can lead to delayed movement and limited joint movements (6). Proper pain relief leads to shorter hospital stays, reduced hospital costs, and increased patient satisfaction. The goal of postoperative pain control is to relieve pain with minimal complications. This is often best implemented using a multi-mode approach (7). Methods of pain control usually include the use of opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and other methods. Since pain is a multifactorial phenomenon, it usually cannot be controlled using only drug therapy (8). Paracetamol is an intravenous analgesic made by a Korean company and has analgesic effects similar to NSAIDs, but with fewer complications (9).

Intravenous paracetamol is a useful drug for the immediate treatment of mild to moderate pain and high postoperative fever. Paracetamol is also used when side effects of NSAIDs need to be considered (10). Paracetamol infusion, along with other local anesthetics, also increases hemodynamic stability and analgesia and reduces opioid-related side effects (11). Paracetamol alone induces stronger analgesia with fewer side effects than synthetic drugs such as fentanyl and leads to a reduction in the extra opioid used in the recovery rooms (2, 12). Pethidine is used to treat pain and chills after surgery. Although the exact mechanism of action of pethidine is unknown, it may exert its effect directly on the thermoregulatory center or through an agonist effect on μ and κ opioid receptors (13).

Pethidine has a weaker agonist effect and potency than other opioid drugs and, therefore, has fewer side effects such as respiratory suppression, nausea and vomiting, gastrointestinal side effects, and sedation and has a lower likelihood of addiction (14). Paracetamol and pethidine are two common analgesics used for patients after orthopedic surgery and are different in their side effects and costs imposed on the health system. Also, pethidine may have addictive effects and subsequent adverse psychological and social effects. However, there are few studies comparing the analgesic effect of these two drugs. Therefore, the present study aimed to compare pethidine and paracetamol in reducing postoperative pain in patients with tibial fracture undergoing nail surgery.

2- MATERIALS AND METHODS

2-1. Study design and population

This study is a controlled clinical trial with post-test design carried out at Shahid Bahonar Hospital of Kerman, Iran, in 2019. A total of 96 patients who were candidates for tibial fracture surgery and who had undergone nail surgery were included in the study and were randomly divided into two groups: pethidine (n = 48) and paracetamol (acetaminophen). Participants were selected using convenience sampling. Before injecting the analgesics, the patient was examined

for fracture complications, especially compartment syndrome. Spinal anesthesia was induced using 0.05 bupivacaine in all patients. The pethidine group (1 mg/kg body weight) and the paracetamol group (15 mg/kg body weight) received injections half an hour before 6, 12, and 24 hours after surgery under local anesthesia. Pain intensity during 6, 12, and 24 after surgery was measured using the VAS scale (15-18). Finally, the mean pain intensity between the two groups was evaluated and compared using VAS. It should be noted that patients were asked about their consent to inject analgesics at the baseline. If the patient did not want to, they were excluded from the study.

2-2. Sample size

The standard deviation was 1.2 based on the study of Kolahdooz et al. (19). Also, one unit of change in VAS score was considered important, and the sample size was 22 in each group taking into account α=0.05 and test power=80% (based on the World Health Organization sample size formula). Considering that the two groups are to be compared, the sample size in each group was determined 48 people using a correction factor.

$$n = \frac{2*(z_{(1-\infty/2)} + z_{(1-\beta)})^2 \sigma^2}{d^2} \times \sqrt{k-1}$$

2-3. Measuring tool

Research instruments included a demographic questionnaire containing questions on sex, age, etc. The second part included the visual analogue scale (VAS) to determine the pain intensity in patients. VAS consists of a straight line with the endpoints defining extreme limits with scores 10 and 0 indicating the worst pain and no pain, respectively. The pain intensity is determined by the patient on the line (**Figure.1**) (15, 20). VAS is the most widely used tool for measuring pain. In addition to its acceptable validity and reliability, the most important feature of this instrument is its simplicity of use. Scores of 1-3, 4-7, and 8-10 indicate mild, moderate, and severe pain, respectively (16). The validity and reliability of this instrument have been confirmed in several international studies (17, 20). The reliability of this scale in Iran has been confirmed with a correlation coefficient of r = 0.88 (18).

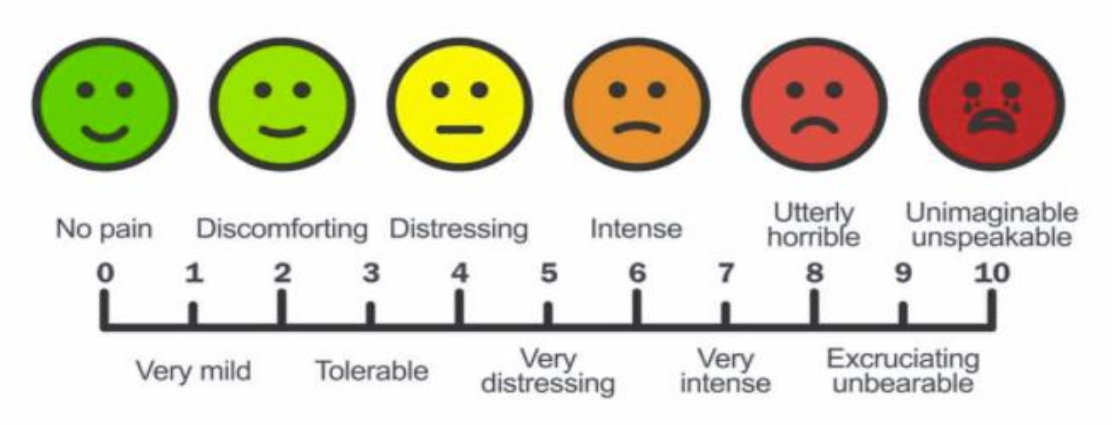

Fig.1: The visual analogue scale or visual analog scale (15, 20).

2-4. Inclusion criteria

1. Patients with tibial fractures over 18 years and under 50 years of age that were candidates for tibial nail surgery.

2. Patients with tibial fracture, who were classified into 42a, 42b, and 42c groups according to AO classification.

2-5. Exclusion criteria

1. Any contraindications to paracetamol, including liver disease and allergies.

2. Any contraindications to the use of pethidine, including respiratory and drug-sensitive diseases.

3. When it is not possible to perform the tibial nailing (such as the presence of fractures at the end and beginning of the tibia bone that cannot be nailed or when the tibial canal diameter is less than 8mm and thus, the nail cannot pass, or the tibial physis is open where nailing is forbidden).

4. Lack of consent to participate in the research project.

5. Age over 50 years.

6. Opium consumption.

7. History of substance abuse (addiction).

8. People who received analgesics for any reason.

2-6. Ethical consideration

The present study was approved by the Ethics Committee of Kerman University of Medical Sciences with the code 97001049, (RCT code: TCTR20210802005). Informed consent was obtained from all patients. All stages and objectives of the study were described to patients and their unwillingness to participate in the study had no effect on their normal treatment process.

2-7. Data Analysis

The study data were coded and analyzed using SPSS ver. 19. Shapiro-Wilk test was first used to check the normality of the data. The t-test was used to compare the values of quantitative variables between the two groups in case of normal distribution, and Mann-Whitney-U statistical test was used in case of abnormal distribution. Paired samples t-test was used to compare variables before and after intervention in each group in case of normal distribution of data, and the Wilcoxon test was used in case of abnormal distribution. The p-value<0.05 was considered the statistically significant level in all tests.

3- RESULTS

A total of 96 patients over 18 and under 50 years of age with tibial shaft fractures that were candidates for tibial nail surgery participated in the study. Participants were assigned into pethidine (n=48), and paracetamol (acetaminophen) groups (n=48). The results of the Shapiro-Wilkes test showed that the main variables of the study, that is, pain intensity at 6, 12, and 24 hours after surgery, were normal and (quantitative) the demographic variables of age, weight, and height, were abnormal (**Table.1**).

The results of statistical tests showed no statistically significant difference between the two groups in terms of demographic characteristics such as age, weight, height, sex, and smoking (**Table.2**) (P>0.05), and the two groups were homogeneous in this regard.

Table-1: Test of normality of distribution of demographic variables.

Variables	Paracetamol Group, n=48		Results	Pethidine group, n=48		Results
	Shapiro-Wilkes test	P-value		Shapiro-Wilkes test	P-value	
Pain intensity at 6 hours after surgery	0.958	0.085	Normal	0.971	0.276	Normal
Pain intensity at 12 hours after surgery	0.973	0.325	Normal	0.975	0.386	Normal
Pain intensity at 24 hours after surgery	0.961	0.124	Normal	0.980	0.571	Normal
Age, year	0.846	P<0.001	Abnormal	0.881	P<0.001	Abnormal
Weight, kg	0.755	P<0.001	Abnormal	0.829	P<0.001	Abnormal
Height, cm	0.843	P<0.001	Abnormal	0.929	P<0.001	Abnormal

Table-2: Frequency distribution of demographic variables by pethidine and paracetamol groups (n=96).

Variables	Sub-group	Paracetamol Group, n=48	Pethidine l Group, n=48	Results
		Number (%)	Number (%)	
Age, year	<25	20 (41.7)	18 (37.5)	Mann-Whitney U=1089, p=0.643
	25-35	14 (29.2)	14 (29.2)	
	>35	14 (29.2)	16 (33.3)	
	Mean ± SD	28.39± 7.36		
	Minimum-Maximum	21-46	19-55	
Weight, kg	<75	33 (68.8)	32 (66.7)	Mann-Whitney U=1088.500, p=0.641
	75-85	11 (22.9)	2 (4.2)	
	>85	4 (8.3)	14 (29.2)	
	Mean ± SD	71.12±8.94	73.83 ±13.35	
	Minimum-Maximum	55-95	54-125	
Height, cm	<170	12 (25)	17 (35.4)	Chi-square=2.567, p=0.109
	170-175	18 (37.5)	26 (54.2)	
	>175	18 (37.5)	5 (10.4)	
	Mean ± SD	172± 5.55	170.01± 6.47	
	Minimum-Maximum	155-180	150-185	
Gender	Female	3 (6.2)	8 (16.7)	Chi-square=2.567, p=0.109
	Male	45 (93.8)	40 (83.3)	
Smoking	Yes	22 (45.8)	24 (50)	Chi-square=2.567, p=0.109
	No	26 (54.2)	24 (50)	

SD: Standard deviation.

The results of the independent t-test showed a statistically significant difference between paracetamol and pethidine groups in terms of the mean pain scores six hours after surgery (P=0.044). The mean score of patients' pain intensity at six hours after surgery was 65.47±9.88 in the paracetamol group and 69.97 ± 11.65 in the pethidine group. The results indicate a nearly 4-unit reduction in the mean score of pain intensity six hours after surgery in the paracetamol group compared to the pethidine group. The results of the independent t-test showed a statistically significant difference between paracetamol and pethidine groups in terms of mean

pain scores 12 hours after surgery (**Table.3**) (P = 0.018). The mean score of patients' pain intensity at 12 hours after surgery was 45.37 ± 8.63 in the paracetamol group and 49.95 ± 9.93 in the pethidine group. The results indicate an approximately 4-unit reduction in the mean pain intensity score at 12 hours after surgery in the paracetamol group compared to the pethidine group. The results of the independent t-test showed no statistically significant difference between paracetamol and pethidine groups in terms of mean pain scores at 24 hours after surgery (P = 0.436) (37.37 ±9.90 and 38.83 ± 8.30 in paracetamol and pethidine groups, respectively). The results indicate a nearly one unit change in that the mean score of pain intensity at 24 hours after surgery in the paracetamol group compared to the pethidine group (P> 0.05).

Table-3: Mean score of pain intensity in paracetamol and pethidine groups (n=96).

Variables	Groups	Mean± SD	Results*
Pain intensity at 6 hours after surgery	Paracetamol	65.47±9.88	P=0.044
	Pethidine	69.97±11.65	
Pain intensity at 12 hours after surgery	Paracetamol	45.37±8.63	P=0.018
	Pethidine	49.95±9.93	
Pain intensity at 24 hours after surgery	Paracetamol	37.37±9.90	P=0.436
	Pethidine	38.83±8.30	

*Independent T-test.

Table.4 shows paired comparisons of the mean score of postoperative pain intensity in the paracetamol and pethidine groups at different time intervals. The results of the paired t-test showed a significant difference in pain intensity score in the paracetamol and pethidine groups between all of the three time intervals (P <0.05). The difference between the mean scores of pain intensity in the two groups of paracetamol and pethidine shows a significant decrease in the pain intensity at 24-h time interval as compared to the 6-h time interval. **Figure.1** shows that the mean pain intensity score in the paracetamol group decreased compared to the pethidine group at different time intervals.

Table-4: The comparison of pain intensity scores at different times between the two groups of paracetamol and pethidine (n=96).

Variables	Times	Paracetamol group, n=48		Pethidine group, n=48	
		Mean difference	*P-value	Mean difference	*P-value
Pain intensity score	6 hours-12 hours	20.140± 1.497	P<0.001	20.021±1.882	P<0.001
	6 hours-24 hours	28.104±1.593	P<0.001	31.146±1.761	P<0.001
	12 hours-24 hours	8.01±0.983	P<0.001	11.125±1.419	P<0.001

*Paired t-test.

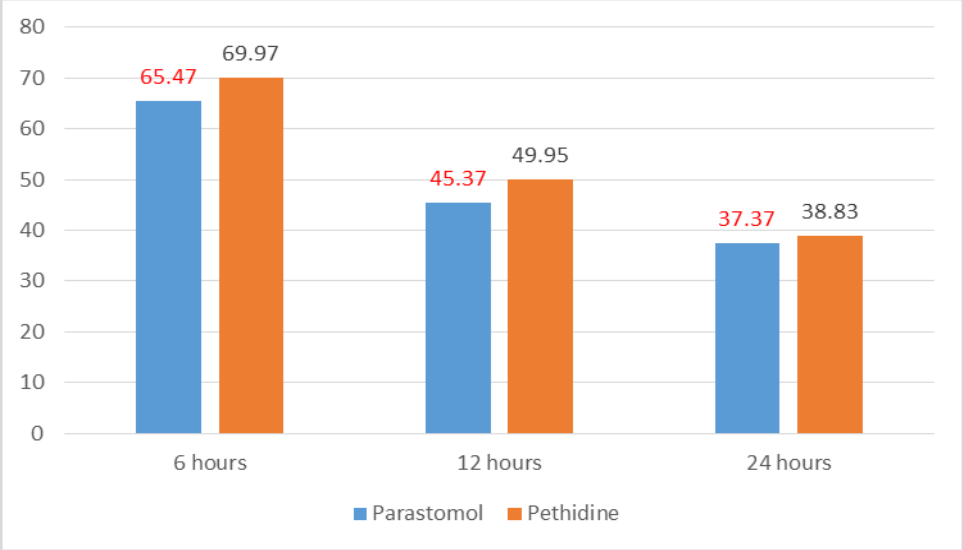

Fig.1: Mean pain intensity score of patients after surgery in the two groups of paracetamol and pethidine in three time periods of 6, 12 and 24 hours after surgery.

4- DISCUSSION

The aim of this study was to compare the postoperative pain intensity between pethidine and paracetamol (acetaminophen) recipients with tibial fractures referred to Bahonar Hospital in 2019. The results showed a significant decrease in the postoperative pain intensity in the paracetamol group in comparison with the pethidine group at different time intervals. The literature review showed no similar study comparing the effects of pethidine and paracetamol in orthopedic surgery. However, two studies were found that compared the effect of pethidine and paracetamol on non-orthopedic surgeries. The findings of the present study are inconsistent with the study by Jarineshin et al. They compared the analgesic effect of pethidine with paracetamol on post-cesarean section pain of two groups of 35 women in Bandar Abbas. They found that pethidine reduced the pain score better than paracetamol (21). This difference can be due to the difference in the type of surgery as well as the extent of communication between the researcher and the patient, which affects the level of pain. Studies have shown that communication between the treatment staff and patients is effective in reducing the pain among patients. Other reasons for the difference between the results include the difference in dose, dose interval, and duration of administration of the two drugs. On the other hand, the results of the present study are consistent with the findings of Kolahdouzan et al. (2013) who compared the analgesic effect of intravenous paracetamol with intravenous pethidine on 100 patients undergoing urology surgery aged 18-62 years in Tabriz. They showed that pain intensity in intravenous paracetamol recipients was significantly lower than the pethidine recipients six hours after surgery ($P < 0.001$). The pethidine group needed additional doses of analgesics more than the paracetamol group (15). The present study shows that the efficacy of pethidine differs from that of paracetamol. This difference may be related to the mechanisms of action of the two drugs. Pethidine acts as an analgesic through ascending and descending receptors and neurons of the hypothalamic basal ganglia, limbic structure, and cerebral cortex (22). On the other hand, the

mechanism of action of paracetamol includes inhibition of prostaglandin synthesis. The first enzyme in the prostaglandin production cycle is cyclooxygenase, and paracetamol prevents its production by entering the cycle and exerts its analgesic effect (23). In the present study, there was a downward trend in pain reduction in the pethidine group. Although this study did not have a pretest group, the findings are consistent with the studies of O'Hara et al. (24), Imani et al. (25), Noroozinia et al. (26), and Vetter (27). O'Hara et al. (1987) evaluated the effectiveness of pethidine and morphine in controlling pain among children in the first 48 hours after orthopedic surgery. Twenty-five children between the ages of 7 and 17 were randomly divided into two groups of morphine and pethidine recipients. The results showed that both drugs significantly reduced pain intensity and the number of children with no pain in the pethidine group was significantly higher than the morphine group on both the first and second days (24).

Imani et al. also showed that intra-articular injection of pethidine at the end of knee arthroscopy could be an alternative to bupivacaine. Besides, the mixture of pethidine and bupivacaine can exacerbate the effects of either drug alone (25). Noroozinia et al. used diclofenac (100 mg) and pethidine (50 mg) suppositories to relieve pain in patients with inguinal hernia after induction of anesthesia. Results showed an almost similar pain relief in both groups (26). Vetter (27) randomly divided 50 children aged 6 to 16 years into morphine or pethidine groups. The results showed that the postoperative pain intensity was significantly reduced in both groups (27). In the present study, the trend of pain reduction in the paracetamol group had a downward pattern. Although the present study did not have a pretest group, its findings are consistent with the studies of Safari et al. (28), Parish et al. (2), Baghianimoghadam et al. (29), Moon et al. (30), Hassan (31), and Landwehr et al. (32). Safari et al. compared the analgesic duration of bupivacaine and intravenous paracetamol alone and in combination after spinal surgery. The results showed that infusion of 15 mg/kg paracetamol 20 minutes before the end of surgery with 10 ml of 0.125% extradural bupivacaine in major spinal surgeries increased hemodynamic stability, increased analgesia, and reduced opioid-related complications (28). Parish et al. randomly divided patients with lumbar disc herniation who were candidates for lumbar disc surgery into two groups (n=26 patients per group). In the intervention group, intravenous paracetamol (15 mg/kg paracetamol dissolved in 100 ml of normal saline) was infused as a single dose within 20 minutes. In the control group, normal saline (100 ml) was administered within 20 minutes. There was a significant difference between the two groups in terms of the drug dose received after entering and discharge from the recovery room so that the drug dose was lower in the intervention group than the control group (2).

Baghianimoghadam et al. (2014) showed that IV paracetamol is an effective factor for better management of pain after cesarean section without significant neonatal complications in women undergoing cesarean section and general anesthesia. VAS pain score was significantly lower in the paracetamol group than in the placebo group at all measurement times. The paracetamol group required a lower analgesic dose to relieve postoperative pain than the placebo group ($P<0.05$) (29). Moon et al. showed that preoperative paracetamol in patients undergoing abdominal hysterectomy reduced the use of narcotic analgesics and their side effects (30). The results of a study by Hassan showed that the effect of paracetamol in controlling postoperative pain is comparable to narcotic analgesics,

and the administration of paracetamol and pethidine is effective in patients undergoing cesarean section under general anesthesia (31). Besides, Landwehr et al. showed that paracetamol and metamizole had similar analgesic effects (32). It is suggested that the long-term effects of these drugs on postoperative pain be investigated in future studies. It is recommended to design future studies using a cost-effectiveness analysis approach. It is also recommended that the effects of paracetamol in combination with other opioids be evaluated.

4-1. Study Limitations

In the present study, the short sampling duration limited the generalizability of the findings. Further research with longer follow-ups is recommended to confirm the reported findings. The second limitation of the present study was that the results cannot be generalized to other orthopedic surgeries. Larger sample size and other drug doses in other orthopedic surgeries are recommended.

5- CONCLUSION

The results showed a significant difference between the paracetamol and pethidine groups in terms of pain intensity score in all of the three measurement times (6, 12, and 24 hours after surgery). The difference between the mean pain intensity scores in the paracetamol and pethidine groups showed a significant reduction in pain intensity at 24 hours after surgery as compared to six hours after surgery. Therefore, paracetamol is more effective than pethidine in relieving postoperative pain in patients with tibial fractures. Considering the small size and follow-ups, the findings of the present study should be interpreted with caution.

6- AUTHORS' CONTRIBUTIONS

Study conception or design: FF, AA, and AR; Data analyzing and draft manuscript preparation: MS, and MJ, and AR, Critical revision of the paper: FF, AR, AA, and RA, Supervision of the research: AR, NN, and AA; Final approval of the version to be published: FF, MS, MJ, RA, SN, AA, and AR.

7- CONFLICT OF INTEREST: None.

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