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Comparison of Postoperative Pain in Two Groups of Children with Bone Fractures Receiving Pethidine and Paracetamol in Kerman Bahonar Hospital: A Clinical Trial Study

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Abstract

Background

Paracetamol and Pethidine are two prevailing analgesics prescribed for postoperative orthopedic patients, each having different side effects and impacts on fracture healing. The present study was conducted to compare the impacts of Paracetamol and Pethidine on postoperative pain relief of children with bone fractures.

Materials and Methods: Fifty children with orthopedic bone fracture surgery candidates were selected in a double-blinded clinical trial study. A random number table was utilized to classify children into two groups of Paracetamol or pethidine treatment. First, the pain intensity of each group was checked using the Visual Analog Scale (VAS). Six hours after the surgery, the first group received Pethidine (1mg/kg of body weight), and the second group received Paracetamol (1gr). Moreover, the VAS scales were checked for both groups 6, 12, and 24 hours later. Afterward, the pain intensity of both groups was assessed according to the VAS scale.

Results: Independent t-test results revealed a significant difference between the pain intensity of paracetamol (44.24 ± 6.44), and Pethidine (52.68 ± 10.47) groups 6 hours after the surgery (p=0.03). Moreover, there was also a significant statistical difference between the pain intensity of two groups 12 and 24 hours after the surgery.

Conclusion

Given the effectiveness of Paracetamol and Pethidine on postoperative pain, both medications can be used for children with bone fractures.

Key Words: Children, Pethidine, Paracetamol, Clinical Trial Study.

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1- INTRODUCTION

Traumatic injuries, specifically fractures, and dislocations, are among the main reasons for medical services in Pediatric Emergency Units (PEU) (1). Moderate to severe pain in children's most common complaints after surgery, especially over the first 24 hours after common or even minor surgeries (2). After reoccurring pains, permanent changes such as autonomic nervous system stimulations happen that might cause behavioral problems and impairments in neurodevelopment and learning abilities among children. Children's reaction to pain is derived from interactive and complex factors such as experience, genetics, and developmental factors. The significant role of personal life experiences resulting in different reactions and responses must not be ignored. These factors potentially intensify the pain response; therefore, medical staff must be aware of their significant role. The pain reinforces a child's reaction and might result in phobias or fear of being treated (3). Moreover, lack of proper diagnosis and inadequate treatment of pain in children results in the delayed recovery process, emotional damages, and changes in children's pain processing. The resent studies have indicated that experiencing pain results in behavioral changes and expressions of stress among children (5).

Several studies have indicated that sedatives and painkillers are being abused in Pediatric Emergency Units for patients with closed fractures or dislocations. The ideal medicine for analgesia and sedation in these cases must be effective, safe, and have proper instruction to use (1). Pain control is significant in orthopedic patients since poor pain control might result in delayed movement recovery and limited joint movements (4). Proper postoperative pain control has various advantages, such as reduced postoperative complications and faster patient discharge, and reduced costs (5). Pethidine is a synthetic opioid with around one-tenth of the strength of Morphine and around 2-3 hours of action duration. Since it affects the brain and is fat-soluble (with a higher fat solubility compared to Morphine), Pethidine has a high abuse risk and might be preferred over morphine cases where acute pain needs to be controlled. Pethidine is delivered every 4 hours with 25-50 mg doses using a slow intravenous injection. The required time for the peak of plasma concentration using the Opioid is around 30 minutes after rectal administration and 6-10 minutes after intravenous injection (6). Besides, there are several methods for controlling severe postoperative pain, including the prescription of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), and Paracetamol (5). The most significant advantage of Paracetamol over NSAIDs is the noninterference with platelet functions and is safe to prescribe for patients with asthma of gastric ulcer history (7). Long-term use of NSAIDs could result in incision bleeding, gastrointestinal bleeding, and renal failure (8). Pethidine and Paracetamol are two prevailing postoperative analgesics prescribed for orthopedic patients, their different side effects, impacts on fracture healing, a considerable difference in terms of cost imposed on the healthcare system, and no study has yet compared their analgesic effects on children. Accordingly, the present study was conducted to compare the effectiveness of Pethidine and Paracetamol among the children with postoperative pain relief of bone fractures.

2- MATERIALS AND METHODS

2-1. Study design and population

The present double-blinded clinical trial study was conducted on 50 children who were candidates of bone fracture orthopedic surgery. The sampling took four years during 2016-2020. The present study is a part of more comprehensive

research entitled "Comparison of postoperative pain in two groups of children with bone fractures receiving pethidine and paracetamol in Kerman's Bahonar Hospital".

2-2. Method

Fifty children with bone fractures who were selected using the convenience sampling were classified into two groups using a random number table. Six hours after the surgery, patients of the first group and the second group received Pethidine and Paracetamol, respectively. A coding method was also used to double-blind the study. Therefore, a researcher colleague would fill the syringe with 2cc of the determined drug according to the random allocation list and would deliver the coded syringes to the researcher to be distributed. Accordingly, at the end of the research and after opening the coding boxes, the researcher would know which patients were treated using which analgesic. The patients were examined for fracture complications-specifically the compartment syndrome before being injected. All patients were placed under spinal anesthesia. The syringes had the same color and size. Using the Visual Analog Scale (VAS), the researcher then asked the children to define their pain intensity as a number from 0-100, 0 being painless, and 100 being maximum imaginable pain. Afterward, the VAS was checked for both groups after 6, 12, and 24 hours. The related VAS was recorded and statistically analyzed.

2-3. Samples

Consistent with the study of Kolahduz et al. (8), a standard deviation of 1.2 was considered. Moreover, one unit of change in the VAS scale was considered to be significant. Considering $\alpha=0.05$ and the power of 80%, the sample size was calculated to be 22 in each group (according to the sample size determination reference, WHO). Given that the two groups must be compared, the total sample size across the two groups was determined to be 50 according to the correction coefficient.

2-4. Visual Analog Scale (VAS)

This scale consists of a horizontal line scaled from zero to 100, in which zero indicates painless, and 100 indicates insufferable pain. Pain symptoms improvement was assessed visually, the validity of which is confirmed using Ferreira-Valente (9).

2-5. Intervention

The pain intensity was first checked using the VAS in both groups. Six hours after the surgery, the first group received Pethidine (1mg/kg of body weight), and the second group received Paracetamol (1gr). The VAS scales for both groups were checked 6, 12, and 24 hours later.

2-6. Ethical consideration

The required permits were received from the Ethical Committee of Karman Medical Sciences University before the onset of the research (IR.KMU.REC.1398.586). Also, this project was registered at the Clinical Trial Center with number of TCTR20200921002. At the onset of the research, the participants were provided with a complete and clear explanation of research methods and project objectives, and all of them signed informed consent. The present study was carried out according to the 2016 Helsinki declaration of acceptable principles. To protect the private information of the participants, the obtained data was only available to the original authors, and access of other individuals to research data was prevented.

2-7. Inclusion and exclusion criteria

The inclusion criteria of the study were the parents' consent and the age of under 18 years old. Exclusion criteria included ant Paracetamol restrictions due to liver disorders and allergies, and Pethidine

restrictions due to respiratory disorders, and allergy, and opioid abuse due to addiction.

2-8. Data Analysis

The data were analyzed using SPSS software version 20.0 after data collection. First, a Kolmogorov-Smirnov test was conducted to check data normality. To compare the quantitative variables between the two groups, at-test was used in case of data normality, and Mann-Whitney-U statistical test was used in case of data abnormality. Moreover, to compare the before and after the status of variables in each group, a paired samples t-test was conducted in case of data normality, and the Wilcoxon test was used in case of data abnormality. A p-value lower than 0.05 was considered to be statistically significant in all analyses.

3- RESULTS

The average age of children was 12.26 ± 2.1. The age (p=0.128), and gender (p=0.0120) of the children was similar in both groups. The Independent t-test revealed a significant difference between the pain intensity of Paracetamol and Pethidine groups (p=0.03). The average pain intensity of patients for 6 hours after the surgery was 63.6 ± 8.51 and 70.2 ± 12.24 in the paracetamol and pethidine groups, respectively. Thus, the results indicate that the average pain intensity value for 6 hours after the surgery was around seven units lower in patients receiving Paracetamol compared to those receiving Pethidine (**Table.1**). Independent t-test indicated a significant difference between the Paracetamol and Pethidine patient groups in terms of the average pain intensity value for 12 hours after the surgery (p=0.018). The average pain intensity value of patients for 12 hours after the operation was 44.24 ± 6.44 and 52.68 ± 10.47 in the Paracetamol and Pethidine groups, respectively. Thus, results indicate that the average pain intensity value for 12 hours after the surgery was around eight units lower in patients receiving Paracetamol compared to those receiving Pethidine (**Table.1**). The Independent t-test indicated no significant difference between the pain intensity values of patients in Paracetamol and pethidine groups (p=0.048). The average pain intensity value of patients for 12 hours after the surgery was 19.2 ± 7.8 and 32.4 ± 11.75 in the Paracetamol and pethidine group, respectively. Thus, results indicate that the average pain intensity value for 24 hours after the operation was around 13 units lower in patients treated with Paracetamol compared to those treated with Pethidine (**Table. 1**).

Table-1: VAS scores in paracetamol and pethidine groups, n=50.

Variables	Group	Mean± SD	P-value*
6 hours after the operation	Paracetamol	63.6±8.51	0.03
	Pethidine	70.2±12.24	
12 hours after the operation	Paracetamol	44.24±6.44	0.018
	Pethidine	52.68±10.47	
24 hours after the operation	Paracetamol	19.2±7.8	0.048
	Pethidine	32.24±11.75	

*T-test.

Table. 2 indicates the results of pairwise comparisons of patients' average pain intensity values in two groups in different hours after the surgery using a pairwise t-test. The results showed significant differences in pain intensity value of the two groups in all three measured times after the operation (p<0.001). The difference between the average pain intensity of Paracetamol and Pethidine

groups showed that postoperative pain declines significantly 24 hours after the surgery compared to 6 hours after the surgery (**Table. 2**, **Figure. 1**). Moreover, the results reveal that the patients' average pain intensity value was lower in the Paracetamol group compared to Pethidine groups in various postoperative hours.

Table-2: Pair comparison of VAS scores in paracetamol and pethidine groups, based on different times, n=50.

Variables	Pair comparison in different times	Paracetamol		Pethidine	
		Mean difference	P-value*	Mean difference	P-value*
VAS score	6 hours-12 hours	7.53±15.160	<0.001	12.85 ±17.52	<0.001
	6 hours-24 hours	8.52±40.2	<0.001	14.95 ±37.96	<0.001
	12 hours-24 hours	9.11 ±25.04	<0.001	13.555±20.44	<0.001

*T-test.

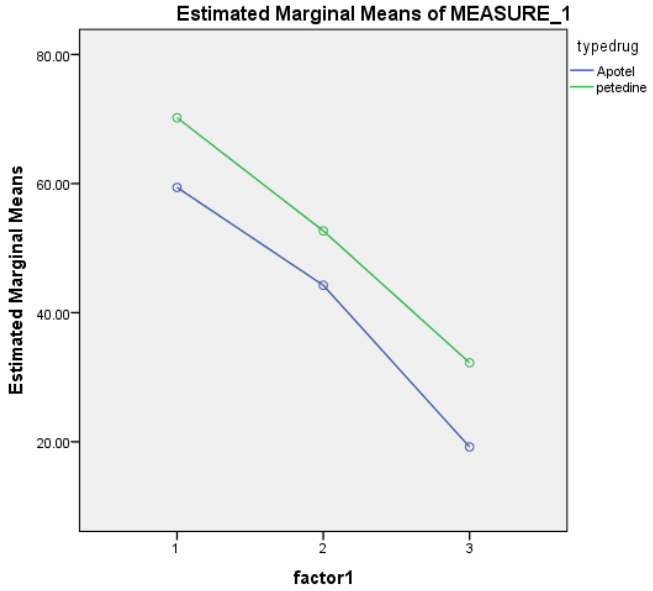

Fig.1: Mean pain intensity score of patients after surgery in the two groups of Paracetamol and Pethidine in three time periods after surgery (6, 12, 24 h).

4- DISCUSSION

The present study aimed to compare the postoperative pain intensity of patients with bone fractures between two groups of Paracetamol (Apotel), and Pethidine in Kerman Bahonar hospital in 2019. The results showed that the pain intensity of patients in the Paracetamol group was lower compared to the Pethidine group in various hours after the surgery. The results of the present study are consistent with some previous studies and inconsistent with some others. No study was found to compare the effects of Paracetamol and Pethidine in other orthopedic surgeries according to authors' desk research. However, two studies were found comparing the effects of Pethidine and Paracetamol in non-orthopedic surgeries. The first study was conducted by Jarineshin et al. (2017), which is relatively comparable with the present study, except that the operation type (C-section vs. Tibia operation). The results of the present study are consistent with those of Jarineshinan et al.'s. The study, as mentioned above, was conducted in Shariati hospital of Bandar Abbas and examined the analgesic effects of Paracetamol and Pethidine after Cesarean Section surgery between two

groups with 35 participants each, indicating that Pethidine has a stronger analgesic effect than Paracetamol (11). The result of another study conducted by Kolahduz et al. comparing the analgesic effects of intravenous Acetaminophen and intravenous Pethidine on 100 patients with 18-62 year-old who had outpatient urology surgery in Imam Reza hospital of Tabriz, 2013 were inconsistent with the results of the present study. The results of the present study indicated that the pain intensity value of patients treated with intravenous Acetaminophen was significantly lower compared to those treated with meperidine ($p<0.0001$).

The meperidine group patients needed higher analgesic doses compared to those receiving Acetaminophen (9), which might be due to the difference in surgery type (Kolahduz et al. 's study was conducted on patients who had urological surgery). Moreover, this inconsistency might be the extent of the researchers' communication with the patients. The healthcare staff's communication with the patient attenuates the pain levels. The level of the researchers' communication with the patients might be different in the two studies. Further potential inconsistency reasons include dose variability, treatment intervals, and duration of administration. The present study indicated that Pethidine and Paracetamol are different in terms of effectiveness. The difference between the two studies might be due to different action mechanisms. As an analgesic, Pethidine acts through ascending and descending neuron receptors of the hypothalamic basal ganglia, limbic structure, and cerebral cortex (12); while Paracetamol's action mechanism is inhibition of prostaglandin synthesis. Paracetamol inhibits the synthesis of Cyclooxygenase -the first enzyme in the cycle of prostaglandin production- by entering the cycle and, therefore, exerts its analgesic impact (13). Saryazdi et al. showed that both intravenous Ketorolac and intravenous Pethidine were effective in reducing postoperative inguinal hernia surgery pain. However, Ketorolac performed more effectively compared to intravenous Pethidine in terms of reducing the postoperative pain score (14). Hara et al. (1987) conducted a study to compare Pethidine's and Morphine's effectiveness in soothing children's pain during the first 48 hours after orthopedic surgery. Twenty five children with 7-17 years old were randomly classified into two groups. The first group was treated with oral Morphine, while the second group received Meperidine. Both drugs reduced pain intensity significantly; however, the number of children feeling no pain was significantly higher in the Morphine group compared to the Meperidine group in both the first and second days after the operation (15). Vetter et al. conducted a study in which 50 children with 6-16 years old were randomly classified into two groups of Morphine or Meperidine. The postoperative pain reduced significantly across both groups; however, this decline was significantly higher in the group treated with Morphine ($p=0.001$). Results indicate that Morphine is a better sedative compared to Pethidine for children (16). The study of Stanley et al. revealed no significant distinction in terms of pain relief, postoperative sedation, nausea, patient satisfaction, and antibiotic requirements (17). Pethidine might result in different analgesic impacts on children and adults. Moreover, further studies are suggested to incorporate a sample large enough to compare Pethidine effects on children and adults. According to the study of Imani et al., injecting Intra-articular Pethidine at the end of knee arthroscopy can be a substitute for Bupivacaine. Besides, a combination of Pethidine and Bupivacaine can aggravate the effects of either of them alone (17). In a study conducted by Norooznia et al., Pethidine (50 mg), and Diclofenac (100 mg)

suppositories were used after anesthesia induction to ease the pain of patients who were inguinal hernia candidates. The sedation effects of the medicines were revealed to be relatively similar (19). Rod et al., aimed to control pain in children who had undergone orthopedic or general operation through the injection of intravenous Propacetamol and Morphine in the recovery room. Accordingly, Morphine was more effective compared to Propacetamol in relieving pain induced by orthopedic and general pediatric surgeries. Therefore, Acetaminophen does not result in complete analgesia and must be used in combination with Morphine, according to the findings as mentioned above (20). However, considering the few relevant studies and the small samples used in this study, further studies with larger samples must be conducted to examine the side effects, cost-effectiveness, and pain relief time control as secondary consequences. Another study by Haghighi et al. discovered that the administration of Acetaminophen caused a significant analgesic effect after lower extremity surgeries. Additionally, Acetaminophen was more effective compared to Fentanyl and had fewer side effects on the patients (21). The study of Safari et al. aimed to compare the duration of intravenous Paracetamol Bupivacaine analgesic effects alone and together after spinal surgeries. They indicated that in massive spinal surgeries, infusion of 15 mg/kg Paracetamol 20 minutes before the end of the surgery combined with the infusion of 10ml Bupivacaine with a concentration of 0.125% on the extradural area by the surgeon increases analgesia duration and hemodynamic stability as well as reducing opioid side effects. Systolic and diastolic blood pressure changes, average arterial blood pressure, heart rate, and pain score at various times indicated no significant difference between the three groups of patients ($p>0.05$). In another study, Mohammadsadegh et al. delivered 15 mg/kg Paracetamol to 10 patients, while the patients in the control group received no drugs. The results of this study showed no significant difference between the intervention and control groups in terms of average pain before and after the intervention. Moreover, no significant difference between the amounts of opioids during the study was observed between the two groups (13). Parish et al. classified the patients with lumbar disc herniation who were candidates for lumbar disk surgery into two 25-individuals groups. The first group received Acetaminophen in a single dose (15 mg/kg acetaminophen dissolved in 100 ml normal saline serum) within 20 minutes. The second group was prescribed with 100ml normal Saline serum within 20 minutes. The statistical analysis showed a significant difference between the two groups in terms of the opioids received after being admitted into recovery and when being discharged from the recovery, so that the intervention group had lower opioid levels compared to the control group (23). The study of Baghianimoghadam et al. (2014) showed that Paracetamol IV is an influential factor in better postoperative pain management without notable infant side effects for women who have undergone Caesarean section and general anesthesia. The VAS pain score was significantly lower in those treated with Paracetamol compared to Placebo at all measurement times. The Paracetamol group needed a lower sedative dose to relieve the postoperative pain compared to the group had received a placebo ($p<0.05$) (24). Moon et al., indicated that in patients undergoing abdominal hysterectomy, administering Paracetamol before the surgery decreased patients' use of narcotic analgesics and their respective side effects (25). The results of a study conducted by Hassan et al. indicated that Paracetamol is comparable with narcotic analgesics in terms of postoperative pain control, and administration of Meperidine and

Paracetamol is effective on maintaining Hemodynamic stability and reducing postoperative pain in patients undergoing C-section or general anesthesia (26). Besides, Landwehr et al. indicated that Metamizole and Paracetamol have similar analgesic effects (27).

4-1. Study Limitations

One of the first and most central limitations of the present study is attributed to the methodology. The short duration of research has restricted the generalization of the results. Further studies are recommended to confirm the results of the present study through longer follow-up. The second limitation of the study, the results might not be generalizable to other orthopedic surgeries. The third limitation is related to blinding. The medicines must be delivered in constant doses and at equal intervals to ensure proper blinding; however, Pethidine and Paracetamol were administered in different doses and at different intervals, which limits the blindness of the study.

5- CONCLUSION

Considering the effectiveness of Pethidine and Paracetamol, both can be used to relieve postoperative pains in children with bone fractures. However, Paracetamol is a more effective analgesic compared to Pethidine. Given the limitations of the findings due to the research methodology, the generalization of these results must be cautiously interpreted.

6- CONFLICT OF INTEREST: None.

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