

A Comparison Between Intravenous Acetaminophen (Paracetamol) and Intravenous Meperidine in Postoperative Pain Reduction of Patients Undergoing Appendectomy

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Background: Pain management after surgery is one of the most important proceedings after emergency appendectomy but there have been no studies on this issue.

Objectives: In this study, effects of intravenous acetaminophen (Apotel) are compared with intravenous pethidine (meperidine) in terms of post-operative pain management.

Patients and Methods: In this randomized clinical trial study, forty patients with ASA- class I or II who were candidates for emergency appendectomy were randomly divided into two groups. Induction and maintenance of anesthesia in the two groups were similar. The first group received 15 mg/kg intravenous acetaminophen (Apotel) and the second group received 0.5 mg/kg intravenous meperidine 30 minutes before ending surgery. The patients were asked for post-operative pain control using visual analog scale (VAS) at 1, 2, 6 hours after surgery. They were compared with regard to postoperative analgesic requirements and complications.

Results: VAS (visual analog scale) was higher in the meperidine group than Apotel group ($P = 0.006$). In the meperidine group, in the first 6 hours after surgery, VAS (visual analog scale) was higher than five and analgesics were administered. VAS in the acetaminophen group was lower in the first 6 hours and the need for analgesic was very low. Analgesic requirements were much lower in the Acetaminophen group. Frequency of ileus was higher in the Apotel group ($P = 0.023$). The patients were similar regarding other adverse effects.

Conclusions: Administration of intravenous Acetaminophen before ending appendectomy might be more effective than meperidine in postoperative pain management while having fewer complications.

Keywords: Appendectomy; Meperidine; Paracetamol; Pain

1. Background

Pain management is an important proceeding in post-operative period and most patients have an unpleasant experience of post-operative pain. Although there have been many improvements in analgesic systems, studies have shown the presence of medium to intense pain in more than 80% of patients (1). Opioids are still the drug of choice for relieving intense pain, however they are associated with several complications including addiction, tolerance, nausea, sedation and respiratory depression which postpone patients' discharge (2-5). Physicians are sometimes hesitant to use intravenous acetaminophen (IVA) in the perioperative period due to its cost and also the relatively limited amount of available data and supporting studies regarding its efficacy. Appendectomy is an acute abdomen

surgery, thus patients receive no analgesics preoperatively due to interference with the diagnosis. This results in experience of a lot of pain by the patients. The objective of this double blind randomized clinical trial was to compare two drugs that are widely available and have the least contradiction and complications and also have a low cost. These two drugs are intravenous acetaminophen and intravenous meperidine which were tested for relieving post-operative pain. The aim of this study was to determine which drug has fewer complications and is more effective in relieving pain after surgery (6, 7). The primary outcome was to compare pain scores between the two groups. The secondary outcome included comparison of postoperative analgesic requirements and adverse effects.

Implication for health policy makers/practice/research/medical education:

In this study we tried to use two drugs that are widely available and have the least contradiction and complications and also have a very low cost. These two drugs are intravenous acetaminophen and intravenous meperidine which were tested for relieving post-operative pain. The aim of this study was to determine which drug has less complications and more effectiveness in relieving pain after surgery. Use of intravenous Acetaminophen after appendectomy is more effective than meperidine while having less complications. Use of intravenous acetaminophen, reduces the need for auxiliary painkillers and decreases the period of ileus.

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2. Objectives

In this study, effects of intravenous acetaminophen (Apotel) are compared with intravenous pethidine (meperidine) in terms of post-operative pain management.

3. Patients and Methods

This study was randomized clinical trial which was applied to all patients who were referred to emergency surgery department for acute abdomen and underwent appendectomy with Mcburney incision at Ghaem Educational and Research Hospital in Mashhad. Local ethical committee approved this study on August 11, 2012 (code: 900634). The data were observed and collected in the field. All patients who underwent appendectomy under general anesthesia were candidates for our study. Excluding criteria included: history of addiction, history of chronic painkiller abuse, patients whose surgery were done under regional anesthesia, history of liver insufficiency, duration of more than 2 hours, Change of diagnosis during surgery, midline incision for appendectomy. In this double-blinded clinical trial study, 72 patients were assessed for eligibility, 32 patients were excluded according to exclusion criteria. 40 patients who underwent appendectomy at Ghaem Hospital were selected and randomly divided into two equal groups (each group consisting of 20 patients).

$$n = (p_1(1 - p_1) + p_2(1 - p_2)) (z_{1-\alpha/2} + z_{1-\beta})^2 / (p_1 - p_2)^2$$

($p_1 = 0.26$, $p_2 = 0.78$)

Patients in both groups were anesthetized using the same method: After preoxygenation the patients received midazolam 0.04 µg/kg, and fentanyl 3 µg/kg, thiopental sodium 4 mg/kg and atracurium 0.6 mg/kg. Anesthesia was maintained with propofol infusion 100 µg/kg/min and using 50% N₂O in oxygen. At the end of surgery, patients received neostigmine and Atropine for reversal of muscle relaxant. The patients were randomly allocated to receive either intravenous Acetaminophen 15 mg/kg of body weight ($n = 20$) or intravenous meperidine 0.5 mg/kg of body weight ($n = 20$), 30 minutes before ending surgery. After the patients woke up, pain score was measured using VAS standard upon the first request for analgesic by the patients. Pain level was also evaluated and recorded 1 hour, 2 hours and 6 hours after surgery using VAS stan-

dard. In the case of intolerable pain in any patient (as VAS higher than 3), after measuring the degree of pain, an auxiliary analgesic (methadone) was administered. Then the data were analyzed and compared using the related software (8-10).

4. Results

All variables in this study have a normal distribution, so parametric statistical analysis was used. The patients were similar regarding demographic data. According to the statistical results obtained (t-test), the minimum age of patients was 13 years and the maximum age was 41 years. The average age of all patients was 25 ± 6.92 years. The average age of meperidine group was 25.85 ± 6.89 ; this number was 24.15 ± 7.02 for Apotel group. From a statistical standpoint using t-test, there was no meaningful difference between the two groups ($P = 0.444$). There were 15 women and 25 men among our patients that after being randomly divided into two groups, there were no statistical differences between the two groups using chi-squared test ($P = 0.327$) (Table 1). Average pain score in all patients, one hour after surgery was 2.75 ± 1.19 . In the second and sixth hour, were 3.13 ± 1.57 and 1.25 ± 0.70 , respectively. Pain intensity level in meperidine group, one hour after surgery, was 3.25 ± 1.41 . In the second and sixth hour were 3.15 ± 1.78 and 1.55 ± 0.76 , respectively. Pain intensity level in Apotel group, one hour after surgery, was 2.255 ± 0.64 . In the second and sixth hour, were 3.10 ± 1.37 and 0.95 ± 0.51 , respectively (Table 2, Figures 1 and 2).

It was shown that the pain score had a statistically significant difference between the two groups, one hour and also six hours after the surgery, with Apotel having lower levels (using t-test with $P = 0.006$ in the first hour and $P = 0.006$ in the sixth hour) But there were no statistical differences between the two groups in the second hour ($P = 0.921$). The number of requests for analgesic after the surgery was 10 for meperidine group (50%) while it was 6 in the Apotel group (30.33%). Using chi-squared test, it was shown that the number of requests had no statistical difference between the two groups ($P = 0.20$) (Table 2). Average pain score upon receiving the first analgesic after surgery in all patients was 5.31 ± 1.08 . It was 5.60 ± 0.97 in meperidine group and 2.83 ± 1.17 in Apotel group.

Table 1. Patients' Charectristics^a

	Pethidine	Apotel	Total	P Value
Count	20	20	40	-
Age, y	25.85 ± 6.89	24.15 ± 7.02	25.00 ± 6.92	0.444
Gender				0.327
Male	11 (55%)	14 (70%)	25 (62.5%)	
Female	9 (45%)	6 (30%)	15 (37.5%)	
Stay in ward, h	29.30 ± 21.80	26.55 ± 5.31	27.92 ± 15.71	0.587
Duration of ileus, h	13.10 ± 5.60	9.35 ± 4.30	11.10 ± 5.60	0.023

^a All data are presented in Mean ± SD and No. (%).

Table 2. Pain Intensity During Different Hours in Both Groups

	Pethidine	Apotel	Total	P Value
Pain in the first hour	3.25 ± 1.41	2.25 ± 0.64	2.75 ± 1.19	0.006
Pain in the second hour	3.15 ± 1.78	3.10 ± 1.37	3.13 ± 1.57	0.921
Pain in the sixth hour	1.55 ± 0.76	0.95 ± 0.51	1.25 ± 0.70	0.006
Pain level upon the first request for analgesic	5.60 ± 0.97	2.81 ± 1.17	5.31 ± 1.08	< 0.001
Number of requests for analgesic, %	10 (50%)	6 (33%)	16 (40%)	0.200
Time of first request for analgesic after surgery, h	1.80 ± 0.63	2.33 ± 0.52	4.56 ± 1.71	0.104

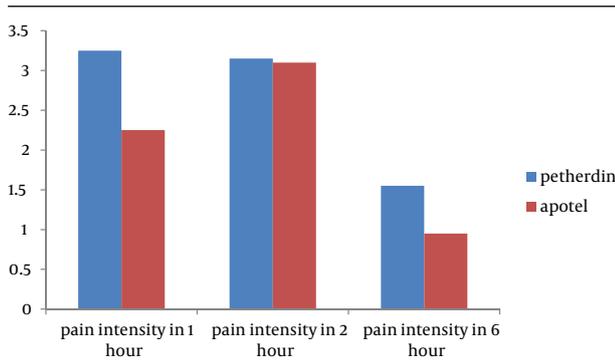


Figure 1. Pain Intensity During Different Hours in Both Groups

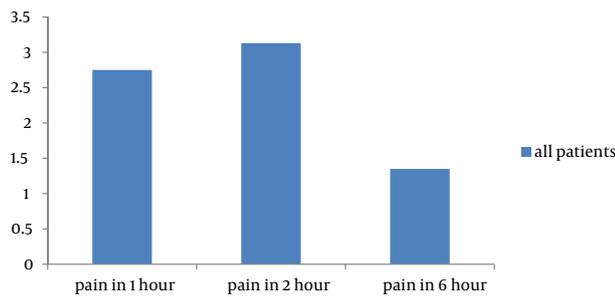


Figure 2. The Average Pain Score in All Patients

Using t-test, it was shown that the two groups have statistically meaningful difference in pain levels on the time of first request for analgesic ($P < 0.001$) (Table 2). Average time of first request for analgesic after surgery in all patients was 4.56 ± 1.71 . It was 1.80 ± 0.63 hours in meperidine group versus 2.33 ± 0.52 hours in Apotel group. T-test showed that the time of first request for analgesic between the two groups had no statistically significant difference ($P = 0.104$) (Table 2). Average duration of ileus was 11.10 ± 5.60 hours in all patients (13.10 ± 5.60 in meperidine group and 9.35 ± 4.30 hours in Apotel group). T-test showed that there is a statistically significant difference between the two groups ($P = 0.023$). Apotel group had a shorter period of ileus than meperidine (Table 1). Average duration of hospitalization after surgery in all patients was 27.92 ± 15.71 hours (29.30 ± 21.80 hours

in meperidine group and 26.55 ± 5.31 hours in Apotel group). T-test shows that the two groups had no statistically meaningful difference ($P = 0.587$).

5. Discussion

Pain management is an important proceeding in post-operative period. Studies show the presence of medium to intense pain in more than 80% of patients in spite of improvements in analgesic systems (1). Opioids are still the drug of choice relieving intense pain but have many complications (2-4). Intravenous acetaminophen (IVA), or paracetamol, was available in Europe in 2002, but it was only approved for use in the United States on November, 2010. IVA has both rapid and effective analgesic properties and is considered to be safe and well tolerated (11). We tried to use two drugs that are widely available and have the least contradiction and complications and also a very low cost. These two drugs are intravenous acetaminophen and intravenous meperidine which were tested for relieving post-operative pain. The aim of this study was to determine which drug has fewer complications and more effectiveness in relieving pain after surgery (6, 7). From a statistical standpoint using t-test, there was no significant difference between the two groups, average age ($P = 0.444$) and sex ($P = 0.327$). Acetaminophen (IV) was shown in several studies to decrease the amount of opiates consumed after surgery, but the reduction of adverse effects associated with opioids has mixed results (12, 13). In our study, it was shown that the pain score had a statistically significant difference between the two groups, one hour and also six hours after the surgery, with Apotel (IV acetaminophen) having lower levels (using t-test with $P = 0.006$ in the first hour and $P = 0.006$ in the sixth hour) but there were no statistical differences between the two groups in the second hour ($P = 0.921$). The use of acetaminophen (IV) is approved by the food and drug administration for the management of mild to moderate pain, the management of moderate to severe pain with opioid analgesic adjuncts, and fever reduction (14). It was shown that Pre-emptive (before surgical incision) versus preventive (after surgical incision) use of IVA had no difference in pain control, but both groups had a decrease in pain scores 6 h after surgery compared with placebo ($P < 0.001$) (15). In our study, the number of requests for analgesic after

the surgery was 10 for meperidine group (50%) while being 6 in the Apotel group (30.33%). Using chi-squared test, it was shown that the number of requests had no statistical difference between the two groups ($P = 0.20$). Several studies suggest that patients receiving IVA may have a reduction in postoperative nausea and vomiting, although this has yet to be formally evaluated (16). In our study, the average time of ileus was 11.10 ± 5.60 hours in all patients (13.10 ± 5.60 in meperidine group and 9.35 ± 4.30 in Apotel group). T-test showed that there is a statistically meaningful difference between the two groups ($P = 0.023$). Apotel group had a shorter period of ileus than meperidine. Average period of hospitalization after surgery in all patients was 27.92 ± 15.71 (29.30 ± 21.80 in meperidine group and 26.55 ± 5.31 in Apotel group). T-test shows that the two groups had no statistically meaningful difference ($P = 0.587$).

In this study we showed that the pain score in the first hour and also in the first sixth hours after surgery was different between Apotel and meperidine groups, with Apotel yielding lower levels of pain ($P = 0.006$ for the first hour and $P = 0.006$ for the sixth hour). But pain score was not statistically different in the second hour ($P = 0.921$). Apotel group had a shorter period of ileus than pethidine group. Though in the comparison of time of first request for analgesic after surgery, the two groups had no statistically significant differences ($P = 0.104$). The number of requests for analgesic after surgery was 10 in meperidine group (50%) and six in Apotel group (30.33%) which showed no statistically significant difference ($P = 0.20$). In this study, Apotel had a substantial effect in reducing post-operative pain in appendectomy patients. Use of intravenous acetaminophen reduces the need for auxiliary analgesic and decreases the duration of ileus. As Apotel provides good pain control and little side effects, we recommend the use of Apotel for post-operative pain in patients undergo appendectomy.

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Authors' Contribution

Masoomeh Tabari: study concept and design, writing manuscript; Mohamad Alipour: analysis and interpretation of data, final approval of the manuscript; Akram Asadpour: drafting of the manuscript, collecting of data; Nasser Mogharabian: critical revision of the manuscript for important intellectual content; Shahram Amini: revision of the manuscript, literatures search.

Financial Disclosure

All of authors had no financial interests related to the material in the manuscript.

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References

1. Sinatra R. Role of COX-2 inhibitors in the evolution of acute pain management. *J Pain Symptom Manage*. 2002;**24**(1):S18-27.
2. Mehmet Turan I, Nilgun Sahin C, Fatma Senay TIV. Paracetamol Infusion is better than I.V meperidine infusion for postoperative analgesia after caesarean section. *Internet J Anesthesiol*. 2007;**15**.
3. Gadsden J, Hart S, Santos AC. Post-caesarean delivery analgesia. *Anesth Analg*. 2005;**101**(5S Suppl):S62-9.
4. Dashti GA, Amini S, Zanguee E. The prophylactic effect of rectal acetaminophen on postoperative pain and opioid requirements after adenotonsillectomy in children. *Middle East J Anesthesiol*. 2009;**20**(2):245-9.
5. Ebrahimzadeh MH, Mousavi SK, Ashraf H, Abubakri R, Birjandinejad A. Transdermal fentanyl patches versus morphine intravenous patient-controlled analgesia for Postoperative Pain, a randomized trial and literature review. *Iran Red Cres J*. 2014;In Press.
6. Elia N, Lysakowski C, Tramer MR. Does multimodal analgesia with acetaminophen, nonsteroidal antiinflammatory drugs, or selective cyclooxygenase-2 inhibitors and patient-controlled analgesia morphine offer advantages over morphine alone? Meta-analyses of randomized trials. *Anesthesiol*. 2005;**103**(6):1296-304.
7. Schug SA, Manopas A. Update on the role of non-opioids for postoperative pain treatment. *Best Pract Res Clin Anaesthesiol*. 2007;**21**(1):15-30.
8. Durak P, Yagar S, Uzuner A, Kilic M, Dilber E, Ozgok A. [Post-operative pain therapy after laparoscopic cholecystectomy: paracetamol versus diclofenac]. *Agri*. 2010;**22**(3):117-20.
9. Romsing J, Moiniche S, Dahl JB. Rectal and parenteral paracetamol, and paracetamol in combination with NSAIDs, for postoperative analgesia. *Br J Anaesth*. 2002;**88**(2):215-26.
10. Shafer SL. Tattered threads. *Anesth Analg*. 2009;**108**(5):1361-3.
11. Candiotti KA, Bergese SD, Viscusi ER, Singla SK, Royal MA, Singla NK. Safety of Multiple-Dose Intravenous Acetaminophen in Adult Inpatients. *Pain Med*. 2010;**11**(12):1841-8.
12. Memis D, Inal MT, Kavalci G, Sezer A, Sut N. Intravenous paracetamol reduced the use of opioids, extubation time, and opioid-related adverse effects after major surgery in intensive care unit. *J Crit Care*. 2010;**25**(3):458-62.
13. Sinatra RS, Jahr JS, Reynolds L, Groudine SB, Royal MA, Breitmeyer JB, et al. Intravenous acetaminophen for pain after orthopedic surgery: an expanded analysis. *Pain Pract*. 2012;**12**(5):357-65.
14. Pasero C, Stannard D. The role of intravenous acetaminophen in acute pain management: a case-illustrated review. *Pain Manag Nurs*. 2012;**13**(2):107-24.
15. Khalili G, Janghorbani M, Saryazdi H, Emaminejad A. Effect of preemptive and preventive acetaminophen on postoperative pain score: a randomized, double-blind trial of patients undergoing lower extremity surgery. *J Clin Anesth*. 2013;**25**(3):188-92.
16. Macario A, Royal MA. A literature review of randomized clinical trials of intravenous acetaminophen (paracetamol) for acute postoperative pain. *Pain Pract*. 2011;**11**(3):290-6.