Original Article

Bull Emerg Trauma 2013;1(4):152-157.

Bulletin of Emergency And Trauma

Effects of Meperidine on Pain Intensity and Accuracy of Clinical Diagnosis in Patients with Acute Abdominal Pain: A Randomized Clinical Trial

Vahid Hattami[1], Sajjad Hatami[1*], Khairolah Asadolahi[1], Mahtab Anvari[1]

[1]Department of Surgery, Ilam Medical School, Ilam University of Medical Sciences, Ilam, Iran

Corresponding author: Sajjad Hatami
Address: Department of Surgery, Ilam Medical School, Ilam University of Medical Sciences, Ilam, Iran.
e-mail: asamob44@yahoo.com

Received: August 21, 2013
Revised: September 20, 2013
Accepted: September 29, 2013

ABSTRACT

Objectives: To determine the effects of Meperidine (Pethedine®) on pain intensity, clinical findings, final diagnosis and management of patients with acute abdominal pain.
Methods: This was a randomized clinical trial including 100 patients, with lower abdominal pain lasting for less than 48 hours who were referred to the emergency department of Imam Khomeini hospital affiliated with Ilam University of Medical Sciences, over a period of 11 months. Hemodynamically unstable patients were not included in the study. The baseline pain severity was measured using a visual analogue scale (VAS). Patients were randomly assigned to receive 25 mg of intramuscular Meperidine (Pethedine®) (n=50) or 5 mL of intravenous normal saline as placebo intravenously (n=50). After 1-hour the patients were then re-examined and the pain severity was re-assessed and the clinical diagnosis was recorded.
Results: There was no significant difference between two study groups regarding the baseline characteristics. The mean pain score on arrival was comparable between groups (6.80 ± 1.6 *vs.* 6.81 ± 1.2; *p=0.956*). The abdominal tenderness was not affected in Meperidine group. Rebound tenderness disappeared in 4% of the Meperidine group and in 2% of the placebo group. Nausea was decreased in 14% of the Meperidine group and 32% of the placebo group. Changes in the clinical pattern and diagnostic peritoneal signs in patients were negligible and did not significantly interfere with the diagnosis (*p=0.133*). Diagnostic accuracy was 96% in the Meperidine group and 98% in placebo group, which was not significantly different (*p=0.554*).
Conclusion: Administration of Meperidine reduces pain intensity in patients with acute abdominal pain without interference with the clinical diagnosis. Thus analgesics could be safely administered to the patients with acute abdominal pain for increasing the patients comfort.

Keywords: Meperidine; Pain management; Clinical diagnosis; Acute abdominal pain.

Please cite this paper as:
Hattami V, Hatami S, Asadolahi Kh, Anvari M. Effects of Meperidine on Pain Intensity and Accuracy of Clinical Diagnosis in Patients with Acute Abdominal Pain: A Randomized Clinical Trial. *Bull Emerg Trauma.* 2013;**1**(4):152-157.

Introduction

Pain is an unpleasant feeling which follows a damage to body tissues. It is also a defense mechanism which leads to reaction against the cause of pain. Pain could also cause serious life threatening outcomes such as respiratory distress, metabolic disorders, gastrointestinal (GI) dysfunction, thromboembolism and psychological difficulties [1]. Pain is the most common symptom amongst those indicating a problem with the GI system and potentially leads to a surgical intervention more than any other GI symptom [2].

The term "acute abdominal pain" refers to any undiagnosed abdominal pain which begins abruptly

and continues for less than 7 days, and more often less than 48 hours [3,4]. An abdominal pain lasting for more than 6 hours is usually caused by important surgical problems [5]. Acute abdominal pain is one of the most common complaints in the emergency departments (ED) and comprises 6.4% of 100 million ED patients [6-9]. Acute abdominal pain occurs in almost 25% of general surgery operations [10]. Besides, abdominal pain is the chief complaint of 25% of patients with pain who to hospital [11]. Acute abdominal pain is the most common surgical emergency problem and the most frequent reason for admission amongst non-traumatic surgical problems, which involves 1% of all hospital admissions, and could affect visceral and peripheral abdominal region [12]. The primary purpose in the evaluation of patients with acute abdominal pain is to determine whether they need an emergency surgical intervention, which sometimes could be very controversial and challenging. In this context, about two-third of the patients referring with acute abdominal pain, do not need any surgical intervention [13]. Decision-making about the surgical intervention in patients with acute abdominal pain is guided by taking an accurate history of the patient, physical examination and physicians' experience [14]. Administration of different analgesics for pain placebo in these patients has always been one of the most challenging and controversial problems among surgeons, since many physicians and surgeons believe that giving analgesic to these patients will change the pain pattern and clinical findings and interfere with the proper diagnosis and management [15-18]. However, administering analgesic drugs should be supported by clinical evidence that they do not interfere with accurate diagnosis. If the aforementioned controversy and concern over administration of analgesics are disproved, they can be used as effective pain relieving agents in patients with acute abdominal pain [15-19]. Many studies have been designed to show that analgesics do not affect clinical findings, but could merely help relieve pain and be safely used in such patients [15-21]. Another study showed that analgesics may cause some negligible changes in clinical findings which could not interfere with the diagnosis and management [17]. In addition, some blinded studies have shown prosperous effects of analgesics in comparison with placebo on decreasing pain in these patients without interference in their management [22]. Studies have also proved more satisfying outcome in patients receiving analgesics [23]. Two main categories of analgesic agents are nonsteroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics. NSAIDs, like salicylate and related agents, are usually used to placebo inflammatory pain. In severe Meperidines of pain, opioid analgesics are often used as the first line pain reliever. Acetaminophen which is different from these two agents is the most important and efficient drug used to placebo mild to moderate pain [8].

The objective of the present study was to evaluate the pain relieving property of Meperidine (Pethedine®) with respect to pain severity, clinical findings, final diagnosis, possible side effects and management plan of patients with acute abdominal pain, so that if proven safe and harmless it, could be used normally without any concern for pain placebo in these patients.

Materials and Methods

Study Population

This was a randomized clinical trial being performed in Imam Khomeini hospital, a tertiary healthcare center affiliated with Ilam University of Medical Sciences during and 11-month period from March 2010 to February 2011. We included 100 patients with lower abdominal pain for less than 48 hours who referred to the ED of Imam Khomeini during the study period. The patients excluded from the study were those with unstable hemodynamic (systolic blood pressure less than 90 mmHg and heart rate more than 100 per minute), under 18 years of age, having pain in another region of the body besides abdomen, unable to communicate easily, having a prior medical condition, history of allergy to Meperidine, and trauma, pregnancy, history of addiction or drug abuse and subjects with history of opium, analgesics or anti-inflammatory drug consumption before admission and finally those unwilling to participate in the study. The study protocol was approved by the institutional review board (IRB) of Ilam University of Medical Sciences. The approval of hospital medical research ethics committee was also achieved before the study. The study protocol as well as the advantages and disadvantages of the study were described to the patients and inform written consents were signed by all the eligible patients.

Study Protocol

The patients were randomly selected from those referred to our ED over the above mentioned period, and fulfilled the inclusion criteria and did not meet the exclusion criteria. Patients were randomly selected from those referring to our center. All the included patients were examined by the attending physician and history and clinical examination positive findings were recorded in a data gathering form. Then the patients were randomly assigned to two study groups including Meperidine and placebo groups. All the patients were given an admission number based on the order of referral. Then they were randomly divided into two categories using a computer random

digit generator.

All demographic data, including age, sex, occupation, medical and drug histories were gathered and recorded in the data collecting forms. Initially, the history of the present illness was then taken for each patient which focused on the degree of pain according to visual analogue scale, the duration, in hours, of the pain until referring to hospital, the location of pain using 4 quadrants of the abdominal regions and the characteristics of pain. Patients were also asked about the radiation of the pain, history of nausea, vomiting and anorexia. A thorough physical examination was then carried out, focusing on the presence of tenderness, rebound tenderness, guarding and Rovsing's sign.

Having collected the primary data, patients in Meperidine group received 25 milligrams of Meperidine (Pethedine®) intramuscularly (n=50) and those in placebo group were given 5 milliliters of normal saline intravenously (n=50). The patients were re-examined after1 hour, and based on patients' response their pain severity was recorded. Notes were also taken of the incidence of drug adverse effects, primary diagnosis which guided the type of management including surgical or medical procedures.

Patients were followed and examined after 7 to 10 days, and if, due to previous misdiagnosis, the initial abdominal pain persisted, the treatment schedule was changed accordingly. Patients were also reminded to refer to the center if the pain did not resolve in due course. Additional complementary work-ups were then carried out to determine the treatment of choice for the patients. All the patients and the nurses who administered drug where blinded toward the groups of the patients. In addition, the physician measuring the pain intensity and who performed the clinical examinations was blinded toward the study groups.

Statistical Analysis

The Statistical Package for Social Science, SPSS for Windows, version 16.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Independent t-tests was used to compare the parametric data between two study groups while chi-square tests were for comparing the categorical data. A two-sided *p*-value less than 0.05 were considered statistically significant.

Results

During the study period, 100 patients, 49 (49%) males and 51 (51%) females, with acute abdominal pain chosen randomly from all patients referred and admitted to the ED of the Imam Khomeini hospital, Ilam, Iran, met the inclusion criteria and enrolled in this study. None of the patients were lost to follow-up and none of them were excluded because of adverse effects. Thus final number of patients undergoing final analysis was 50 in each study group. Patients were classified into 3 age ranges, including 18 to 31 years with 71 (71%), 32 to 43 years with 22 (22%) and 44 to 57 years with 7 (7%) patients. Mean age of patients was 28.53 ± 2.3 years, with minimum of 18 and maximum of 57 years. The baseline characteristics of patients is summarized in Table 1. Surgical intervention was carried out in 35 patients of Meperidine group and 42 of placebo group as their treatment plan and others received medical treatment. The prevalence of differential diagnoses in our patients could be determined by post-surgical follow up. The diagnosis was confirmed in 48 (96%) patients of the Meperidine and 49 (98%) patients of the placebo group. However, in 3 (3%) remaining patients with sustained abdominal pain, further evaluation was done to arrive at appropriate diagnosis. Patients were divided into 3 groups according their duration of pain before referral to the hospital. The mean pain duration in Meperidine groups was 10.84 ± 2.6 compared to 9.86 ± 2.9 hours in the placebo group (*p=0.322*). Table 2 shows the degree of pain in both groups before and one hour after administration of analgesic or placebo. 1-hour after administration of Meperidine or placebo the pain scores decreased to 9.39 ± 2.1 and 9.26 ± 1.8 in Meperidine and placebo groups respectively (*p=0.769*). The frequency of severe (*p=0.041*) and very severe (*p=0.039*) pain decreased significantly in Meperidine groups compared to placebo.

Table 3 demonstrates the prevalence of signs and symptoms in the patients before and 1 hour after administration of the drugs. The abdominal tenderness was not affected in Meperidine group. Rebound tenderness disappeared in 4% of the Meperidine group and in 2% of the placebo group. Nausea was decreased in 14% of the Meperidine group and 32% of the placebo group. Vomiting reduced to about 40% in both groups. Changes in the clinical pattern and diagnostic peritoneal signs in patients were negligible and did not significantly interfere with the diagnosis (*p=0.133*). Diagnostic accuracy was 96% in the Meperidine group and 98% in placebo group, which was not significantly different (*p=0.554*).

Discussion

As stated previously, physicians are divided over administering analgesics to patients with acute abdominal pain, as some believe that it will change the pattern of peritoneal signs and interfere with the proper diagnosis. Tahmasebi Rad *et al*. indicated that 82.8% of surgeons did not prescribe analgesia before reaching a diagnosis [24]. In 2005, Hashikawa *et al*. evaluated the tendency of physicians to prescribe

Table 1. Baseline characteristics of 100 patients with acute abdominal pain receiving Meperidine (n=50) or placebo (n=50) as analgesics.

	Meperidine (n=50)	Placebo (n=50)	*p*-value
Age (years)	29.12 ± 8.6	27.6 ± 7.8	0.856
18-31 (%)	35 (70%)	36 (72%)	
44-57 (%)	12 (24%)	10 (20%)	0.791
32-43 (%)	3 (6%)	4 (8%)	
Sex			
Male (%)	24 (48%)	25 (50%)	0.901
Female (%)	26 (52%)	25 (50%)	
Pain duration (hours)	10.84 ± 2.6	9.86 ± 2.9	0.322
3-9 (%)	30 (60%)	27 (54%)	
10-18 (%)	16 (32%)	16 (32%)	0.214
19-27 (%)	4 (8%)	7 (14%)	
Pain intensity at admission	6.80 ± 1.6	6.81 ± 1.2	0.956
Final diagnosis			
Acute appendicitis (%)	17 (34%)	26 (52%)	
Suppurative appendicitis (%)	12 (24%)	12 (24%)	
Appendicular Abscess (%)	3 (6%)	0 (0%)	
Gangrenous appendicitis (%)	4 (8%)	4 (8%)	0.291
Renal colic (%)	1 (2%)	1 (2%)	
Gastroenteritis (%)	1 (2%)	2 (4%)	
Mesenteric lymphadenitis (%)	1 (2%)	0 (0%)	
Unknown (%)	11 (22%)	5 (10%)	
Treatment			
Surgical (%)	35 (70%)	42 (84%)	0.063
Medical (%)	15 (30%)	8 (16%)	

analgesics to patients with abdominal pain and found that 97% of ED physicians were inclined to give analgesics to these patients after primary evaluation and 93% of them favored administration of opioid analgesics [25]. Wolfe JM *et al*. investigated the common pattern of analgesic administration by physicians. In this context, 85% of those who answered their questionnaires believed that these drugs did not interfere with the diagnosis, but added that they should be used after fulfilling surgical evaluation and planning [26]. The Effectiveness of analgesics in patients with abdominal pain without any change in the clinical pattern has been supported by many studies [12,17,27]. On the contrary, adverse effects of these agents in patients with abdominal pain have been reported by other investigators [28].

In 2009, Tade *et al*. performed a prospective study whereby they assessed the effects of Pentazocine on patients with acute abdominal pain. They concluded that Pentazocine can dramatically reduce the pain in these patients; however, it could potentially hide some clinical features and interfere with the diagnosis. They suggested 2 hours of admission for better evaluation of patients receiving Pentazocine [29]. Attard shows that early administration of Papaverutum to patients with acute abdominal pain not only reduced pain, but it helped and did not interefere with correct diagnosis [30]. In 1996, Pace and colleagues evaluated the effect of intravenous Morphine Sulfate on patients with acute abdominal pain as safe, effective and unproblematic [31]. However, Lovecchio and his colleagues in 1997 re-assessed the effect of Morphine Sulfate and declared that this agent had adversely affected the physical examination of patients with abdominal pain and that further studies were needed to arrive at definitive conclusion [32]. Other studies in

Table 2. Pain intensity in both study groups before and one hour after administration.

	Before administration			1 hour after administration		
	Meperidine	**Placebo**	***p*-value**	**Meperidine**	**Placebo**	***p*-value**
1 – 3 (mild)	0 (0%)	2 (4%)	0.166	6 (12%)	4 (8%)	0.097
3 – 6 (moderate)	22 (44%)	21 (42%)	0.752	30 (60%)	25 (50%)	0.058
6 – 9 (severe)	19 (38%)	21 (42%)	0.687	14 (28%)	18 (36%)	0.041
9 < (very severe)	9 (18%)	6 (12%)	0.107	0 (0%)	3 (6%)	0.039

Journal compilation © 2013 Trauma Research Center, Shiraz University of Medical Sciences, http://www.beat-journal.com

Table 3 Frequency of signs and symptoms of the patients of two study groups before and 1 hour after administration.

	Before administration			1 hour after administration		
	Meperidine	**Placebo**	***p*-value**	**Meperidine**	**Placebo**	***p*-value**
Pain radiation (%)	23 (46%)	19 (38%)	0.413	**7** (14%)	12 (24%)	0.203
Nausea (%)	41 (82%)	37 (74%)	0.338	34 (68%)	21 (42%)	0.009
Vomiting (%)	32 (64%)	26 (52%)	0.223	12 (24%)	8 (16%)	0.317
Anorexia (%)	27 (54%)	25 (50%)	0.688	23 (46%)	24 (48%)	0.841
Tenderness (%)	50 (100%)	50 (100%)	0.998	50 (100%)	50 (100%)	0.998
Rebound Tenderness (%)	27 (54%)	22 (44%)	0.316	25 (50%)	21 (42%)	0.423
Guarding	1 (2%)	1 (2%)	0.998	3 (6%)	2 (4%)	0.640
Rovsing's sign (%)	3 (6%)	2 (4%)	0.640	2 (4%)	1 (2%)	0.554

1995 and 2002 showed that Morphine was an efficient drug for pain management in these patients with no adverse effect on their diagnosis [15,19,33,34]. The comparable result was reported about Diclofenac [35]. In another study performed by Ranji and colleagues in 2006, showed that administration of opiate analgesic may alter the findings of physical examination, but these changes did not significantly increase the management errors [6]. Thomas and Silen, reviewed 8 trials about the effect of analgesia on accuracy of physical examination findings and proper diagnosis, and showed that there was no association between analgesia and diagnostic impairment [36].

In the current study, the mean score of pain on admission among the patients of the Meperidine group, according to the visual analogue scale for pain, was 6.8 compared to 6.81 in the placebo group. The mean of the pain scores in Meperidine group who received Pethedine® decreased by 1.45 after 1 hour, whereas it decreased by 0.6 in the placebo group who received placebo. In the study performed by Amoli and his colleagues on morphine as analgesic, this mean decreased by 1.85 in Meperidine group and by 0.2 in placebo group who received placebo [15]. The study of Tade *et al*. on Pentazocine, showed pain reduction of more than 1.2 in 62.5% of the Meperidine group, compared with 30% of placebo group [29]. In studies that assessed the effects of Morphine on these patients, and approved its safety, this mean decreased by 1.4 in patients of Meperidine group and by 0.1 in those of the placebo group [19,34].

Abdominal tenderness was not affected in Meperidine group. Rebound tenderness disappeared in 4% of the Meperidine group and 2% of the placebo group. Nausea was decreased in 14% of the Meperidine group and 32% of the placebo group. Vomiting decreased about 40% in both groups. Changes in the clinical pattern and diagnostic peritoneal signs in our patients were approximately comparable to those of the abovementioned studies [19, 34] and did not significantly interfere with the diagnosis (p=0.331). Diagnostic accuracy was 96% in Meperidine group and 98% in placebo group, and the difference between them was not significantly different (p=0.554), and was consistent with other reports [19,34], indicating no interference with patient's diagnosis.

In conclusion, Administration of Meperidine reduces pain intensity in patients with acute abdominal pain without interference with the clinical diagnosis. Thus analgesics could be safely administered to the patients with acute abdominal pain for increasing the patients comfort.

Conflict of Interest: None declared.

References

1. Berti M, Danelli G, Albertin A, Deni F, Moizo E, Muzzolon F. Systemic analgesia after peripheral block. *Minerva Anestesiol* 2001;**67**(9 Suppl 1):195-9.
2. Fischer JF, Nussbaum MS, Chance WT, Luchette F. Manifestation of gastrointestinal disease. Society of American Gastrointestinal Endoscopic Surgeons, Vol 3,1999; p. 1033-1080.
3. Elahi B. Body Anatomy. Jeyhoun Publication, Tehran; 2000.
4. De dombal FT. Diagnosis of acute abdominal pain, 2nd ed. Churchill Livingstone, London; 1991.
5. Silen W. Cope`s early diagnosis of acute abdomen. 17th ed. Oxford University Press, New York; 1990.
6. Purcell TB. Nonsurgical and extraperitoneal causes of abdominal pain. *Emerg Med Clin North Am* 1989;**7**(3):721-40.
7. Guyton AC, Hall JE. Textbook of medical physiology. 11th ed. Elsevier, 2006; p. 609-620.
8. Kutzung B. Basic and Clinical Pharmacology. Translation by Fathollahi A. 11th ed. Arjomand Publication, Tehran; 2008.
9. Ciccone A, Allegra JR, Cochrane DG, Cody RP, Roche LM. Age-related differences in diagnoses within the elderly population. *Am J Emerg Med* 1998;**16**(1):43-8.
10. Burkitt HG, Quick CRG, Gatt D. Essential Surgery: Problems, Diagnosis, Management. 2nd ed. Singapore: Churchill Livingstone, 1996; p. 183.
11. Cordell WH, Keene KK, Giles BK, Jones JB, Jones JH, Brizendine EJ. The

high prevalence of pain in emergency medical care. *Am J Emerg Med* 2002;**20**(3):165-9.
12. Irvin TT. Abdominal pain: a surgical audit of 1190 emergency admissions. *Br J Surg* 1989;**76**(11):1121-5.
13. Delcore R, Ycheung LY. Acute abdominal pain. ACS Surgery, Principles and Practice. WebMD Inc. 2002; p. 225-240.
14. Taghinezhad H, Tahmasebi P. Pain and its care. Ilam University of Medical Sciences, 2007.
15. Amoli HA, Golozar A, Keshavarzi S, Tavakoli H, Yaghoobi A. Morphine analgesia in patients with acute appendicitis: a randomised double-blind clinical trial. *Emerg Med J* 2008;**25**(9):586-9.
16. Aydelotte JD, Collen JF, Martin RR. Analgesic administration prior to surgical evaluation for acute appendicitis. *Curr Surg* 2004;**61**(4):373-5.
17. Ranji SR, Goldman LE, Simel DL, Shojania KG. Do opiates affect the clinical evaluation of patients with acute abdominal pain? *JAMA* 2006;**296**(14):1764-74.
18. Kokki H, Lintula H, Vanamo K, Heiskanen M, Eskelinen M. Oxycodone vs placebo in children with undifferentiated abdominal pain: a randomized, double-blind clinical trial of the effect of analgesia on diagnostic accuracy. *Arch Pediatr Adolesc Med* 2005;**159**(4):320-5.
19. Yuan Y, Chen JY, Guo H, Zhang Y, Liang DM, Zhou D, et al. Relief of abdominal pain by morphine without altering physical signs in acute appendicitis. *Chin Med J (Engl)* 2010;**123**(2):142-5.
20. Bromberg R, Goldman RD. Does analgesia mask diagnosis of appendicitis among children? *Can Fam Physician* 2007;**53**(1):39-41.
21. Armstrong FD. Analgesia for children with acute abdominal pain: a cautious move to improved pain management. *Pediatrics* 2005;**116**(4):1018-9.
22. Mahadevan M, Graff L. Prospective randomized study of analgesic use for ED patients with right lower quadrant abdominal pain. *Am J Emerg Med* 2000;**18**(7):753-6.
23. Marinsek M, Kovacic D, Versnik D, Parasuh M, Golez S, Podbregar M. Analgesic treatment and predictors of satisfaction with analgesia in patients with acute undifferentiated abdominal pain. *Eur J Pain* 2007;**11**(7):773-8.
24. Tahmassebi Rad M, Goharian V, Sehat S, Abasion K. Surgeon`s attitude in utilizing opiats in patients with acute abdomen and evaluating the chang in their in attitude following CME. Iranian Association of Surgeon; 2006.
25. Hashikawa C, Burke TF, Pallin DJ, Briggs-Malonson M. Analgesia administration for acute abdominal pain: a survey of emergency physicians. *Ann Emerg Med* 2007;**50**(1):91-2.
26. Wolfe JM, Smithline HA, Phipen S, Montano G, Garb JL, Fiallo V. Does morphine change the physical examination in patients with acute appendicitis? *Am J Emerg Med* 2004;**22**(4):280-5.
27. Soroush AR, Khorgami J. The effect of analgesics (morphin) on the symptoms and clinical manifestation s of patients with acute abdomen. Iranian Association of Surgeons; 2006.
28. Lee JS, Stiell IG, Wells GA, Elder BR, Vandemheen K, Shapiro S. Adverse outcomes and opioid analgesic administration in acute abdominal pain. *Acad Emerg Med* 2000;**7**(9):980-7.
29. Tade AO, Salami BA, Ayoade AB. Pentazocine pain relief in adult patients with acute abdominal pain: A prospective randomized clinical trial. *East and Central African Journal of Surgery* 2009;**14**(2):44-9.
30. Attard AR, Corlett MJ, Kidner NJ, Leslie AP, Fraser IA. Safety of early pain relief for acute abdominal pain. *BMJ* 1992;**305**(6853):554-6.
31. Pace S, Burke TF. Intravenous morphine for early pain relief in patients with acute abdominal pain. *Acad Emerg Med* 1996;**3**(12):1086-92.
32. LoVecchio F, Oster N, Sturmann K, Nelson LS, Flashner S, Finger R. The use of analgesics in patients with acute abdominal pain. *J Emerg Med* 1997;**15**(6):775-9.
33. Gallagher EJ, Esses D, Lee C, Lahn M, Bijur PE. Randomized clinical trial of morphine in acute abdominal pain. *Ann Emerg Med* 2006;**48**(2):150-60, 160.e1-4.
34. Vermeulen B, Morabia A, Unger PF, Goehring C, Grangier C, Skljarov I, et al. Acute appendicitis: influence of early pain relief on the accuracy of clinical and US findings in the decision to operate--a randomized trial. *Radiology* 1999;**210**(3):639-43.
35. Aram FO. Preoperative use of analgesia in appendicitis. *Saudi Med J* 2008;**29**(6):859-62.
36. Thomas SH, Silen W. Effect on diagnostic efficiency of analgesia for undifferentiated abdominal pain. *Br J Surg* 2003;**90**(1):5-9.