Does Pethidine Hydrochloride Analgesia in Patients with Acute Appendicitis Alter the Diagnostic Accuracy of Clinical Evaluation: a Randomized Double-Blind Clinical Trial

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ABSTRACT

Background: Prevalence of cancers associated with the use of oral tobacco (OT) is rising very rapidly and prevention of use is the best option to tackle this scenario. This cross-sectional study estimated the proportion of OT use and predictors associated with its initiation and determined the knowledge, attitude A total of 354 students (15-30 years age) in five colleges were interviewed by medical students and completed a peer reviewed, pre-tested, self-administered questionnaire. Chi square test and logistic regression analyses were applied to the results.

Method: Thirty nine (11.0%) students were lifetime users of smokeless tobacco among which nineteen (5.4%) were occasional users, seven (2.0%) were current users and thirteen (3.6%) fulfilled the criterion for established users. Paan was the most commonly used form of smokeless tobacco followed by Nass. On univariate analysis, lifetime use of smokeless tobacco showed significant associations with the use of cigarettes, student gender (M > F), individual condition (native > guest) and kind of the College (Engineering > Psychology).

Results: Although pain scores significantly reduced in pethidine group and there was a significant difference between the pethidine and placebo groups ($p<0.05$). Pethidine administration did not alter the physical signs, delay time to surgery, or diagnostic accuracy.

Conclusion: According to the result of the study, use of pethidine does not affect the accuracy and time of surgical diagnosis and can effectively reduce the pain among patients with acute abdominal pain due to appendicitis.

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►*Implication for health policy/practice/research/medical education:*
Use of pethidine does not affect the accuracy and time of surgical diagnosis

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1. Introduction:

Traditional surgeons' reluctance towards the use of opioid analgesia in patients with acute abdominal pain prior to a definitive diagnosis was a common practice for decades. "Cope" in his book claimed that analgesia would mask signs and symptoms of acute abdomen, delay diagnosis, and could lead to increased morbidity and mortality (1). Recently, with development of medical diagnostic techniques, more accurate definitions of clinical signs, and due to ethical concerns regarding pain management (2, 3), this point of view has been challenged (4, 5). Many studies stated that employment of analgesics would not increase morbidity (6-10) and possibly might not affect diagnostic accuracy (11, 12). In this study, we evaluated patients with acute appendicitis in order to investigate whether a single dose of intravenous pethidine hydrochloride can relieve pain without affecting the diagnostic accuracy.

2. Materials and Methods:

In this randomized double-blind controlled clinical trial which was conducted in Vali Asr Hospital of Arak, Iran, patients over 16 years of age who were suspected of having acute appendicitis were considered eligible for the study. Exclusion criteria were: previous appendectomy, opioid allergy, recent consumption of analgesic or psychotropic medications, pregnancy, pain onset>48hrs, loss of consciousness, renal, hepatic or respiratory insufficiency and systolic blood pressure<100mmHg. From December 1, 2008 to July 1, 2009, 106 patients fulfilled the inclusion criteria and were enrolled in the study. This study was ethically approved by the research ethics committee of the Arak University of Medical Sciences. Written informed consents were obtained from all patients or their relatives before the trial.

All of the enrolled patients were randomized to receive single-doses of 1mg/kg intravenous pethidine hydrochloride (n=53) or equivalent volumes of normal saline as placebo (n=53). The patients and the surgical resident who was responsible for visiting them remained blind during the trial and the same surgical resident examined all of the patients before and after drug administration. Clinical symptoms, physical signs and pain intensity (based on "Visual Analog Pain Scale" (VAS)) were recorded prior to, and 30 minutes after the injections. The surgical assessment included evaluation of abdominal tenderness, rebound tenderness, psoas, obturator, and Rovsing signs and pain with jumping or coughing. Based on the pathological reports, the accuracy of diagnosis was established.

All statistical analyses were performed with SPSS 16 software using t-test, paired t-test and chi-square and statistical significance was considered at $P \leq 0.05$.

3. Results:

There was no significant difference between two groups with regard to age, sex and initial clinical evaluation and VAS score ($p>0.05$. table 1).

The VAS scores upon admission to the hospital and after 30 minutes of pethidine hydrochloride or placebo administration were compared (table 2). Significant reduction in pain score was reported in pethidine group and there was a significant difference between pethidine and placebo group ($p<0.05$).

Pethidine administration did not alter most physical signs. Positive psoas sign reduced significantly in the case group but there was no significant difference considering

Table 1: Baseline characteristics upon admission to the hospital in patients suspected of acute appendicitis in Vali Asr Hospital of Arak

Parameters	Pethidine group	Control group	P values
Age (years)	30.57±10.3	29.27±9.6	0.340
Male/Female (n)	33/20	33/20	-
Mean initial pain score	64.6±18.4	67±21.4	0.075
Right lower quadrant tenderness (%)	100%	100%	-
Rebound tenderness (%)	64.2%	67.9%	0.682
Positive Rosving sign (%)	62.2%	51%	0.375
Positive psoas sign (%)	47.1%	56.6%	0.211
Positive obturator sign (%)	45.2%	47.2%	0.640
Pain with jumping or coughing (%)	92.5%	79.2%	0.138

Table 2: abdominal pain scores (VAS) before and after drug injection in patients suspected of having acute appendicitis in Vali Asr Hospital of Arak

Groups	Before administration	After 30 min administration
Pethidine hydrochloride	64.5±18.4	37±17.5*†
Control(normal saline)	67±21.4	57.5±24

***** p<0.05, compared to the control group
† p<0.05, compared to before the administration of pethidine

other physical findings before and after drug administration in either group (P> 0.05) (Table 3).

All of the 106 patients underwent appendectomy and based on pathological reports, 78 cases (73.6%) had a final diagnosis of appendicitis. The elapsed time to surgery in pethidine group was 100±49 minutes vs. 119±58 minutes in the control group. There was no significant difference in the delay time to surgery and the accuracy of surgical decision-making

Table 3: Changes of physical signs of acute appendicitis before and after administration of pethidine or normal saline (%)

Physical Signs	Pethidine Group		Control Group	
	Before administration	After 30 min administration	Before administration	After 30 min administration
Right lower quadrant tenderness (%)	74.7	41.5	75.5	47.2
Rebound tenderness (%)	64.2	43.4	67.9	37.7
Positive Rosving sign (%)	11.3	1.9	5.7	0
Positive psoas sign (%)	9.4	3.8*	3.8	0
Positive obturator sign (%)	7.5	26.4	3.8	50.9
Pain with jumping or coughing (%)	20.8	9.4	15.1	13.2

Table 4: Diagnostic accuracy of appendicitis based on pathological report in pethidine and normal saline groups

Group	Correct diagnosis (Appendicitis)	Wrong diagnosis(normal pathology)
Pethidine	40(75.5%)	13(24.5%)
Normal saline(control)	38(71.7%)	15(28.3%)
Total	78(73.6%)	28(26.4%)

between pethidine and placebo group.

Based on pathological report, surgery was appropriate in 75.5% of pethidine recipients vs. 71.7% of placebo cases (p= NS) (Table 4) All of the 106 patients underwent appendectomy and based on pathological reports, 78 cases (73.6%) had a final diagnosis of appendicitis. The elapsed time to surgery in pethidine group was 100±49 minutes vs. 119±58 minutes in the control group. There was no significant difference in the delay time to surgery and the accuracy of surgical decision-making between pethidine and placebo group. Based on pathological report, surgery was appropriate in 75.5% of pethidine recipients vs. 71.7% of placebo cases (p= NS) (Table 4).

4. Discussion:

According to Rupp and Delaney's review (2004), the inadequacies in the treatment of pain appeared to stem from multitude of barriers that include: lack of educational emphasis on pain management in medical schools, inadequate or nonexistent clinical quality management programs of pain, clinicians attitude toward opioid analgesics that result in inappropriate diagnosis of drug-seeking behavior in patients complaining of acute pain, concerns about addiction, unsuitable apprehension about the safety of opioids, and the fact that patients and doctors have different conception of pain (13).

In 2000, the American College of Emergency Physicians stated that pain relief in acute abdomen is safe and could be used after early assessment by physicians (14). Due to developments in medical techniques and better clinical examination methods, in some recent studies, administration of opioid analgesia during the initial evaluation of acute abdominal pain leads to pain relief without affecting the diagnostic accuracy (12,15).

Our study demonstrated that administration of pethidine considerably reduced the intensity of pain in patients who received it compared to the pain score before pethidine administration and also in the control group ($p<0.05$). The patients' signs and symptoms are always the most important clues to the diagnosis of acute abdomen and appendicitis. This study showed that pethidine administration had no apparent effect on clinical evaluation, elapsed time to surgery, and the accuracy of diagnosis. It suggests that opioid analgesia does not increase the risk of delayed or missed diagnoses of appendicitis and does not influence the rate of unnecessary laparotomies. It seems that in patients suspected of acute appendicitis, using appropriate pain relief is more humane approach than the traditional method and can reduce patients' suffering.

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