Original Article

Preemptive analgesia application in acute appendicitis

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ABSTRACT

Background: Preemptive analgesia with infiltration of anesthetics into surgical wounds before the incision has been shown to be effective in various elective surgeries. Although this application can decrease the postoperative pain, it is not known whether it is effective in surgery with acute pain or not. **Aims:** In this study, we evaluated whether the preincisional local anesthetic application will decrease the postoperative pain in patients undergoing appendectomy for acute appendicitis. **Materials and Methods:** Forty consecutive patients admitted to the Emergency Department with a tentative diagnosis of acute appendicitis were randomly divided into two groups. In Group 1, 1% prilocaine and 0.25% bupivacaine was injected to the planned incision site cutaneously, subcutaneously, and under the fascia of the external oblique muscle. The patients in Group 2 received the same volume of saline to the same anatomical sites. Initially, 1 mg/kg meperidine was administered intramuscularly to both groups for postoperative analgesia. If needed further, meperidine 0.5 mg/kg was administered intramuscularly. Postoperative pain was assed by visual analog scale during the first 24 hours. The analgesic needed and the doses required were recorded. **Statistical Analyses:** All data were stored using SPSS 11.0 for Windows. Wilcoxon test and two independent samples T-test was used as the non-parametric test. **Results and Conclusions:** No statistically significant difference was found between the two groups' pain score, the number of patients who needed analgesic, and the amount and the number of doses administered. In conclusion, we think that preincisional local anesthetic infiltration does not help to decrease the need for postoperative analgesic use in patients with acute pain, and this may be related with previous central sensitization.

Key Words: Anesthesia, preemptive analgesia, appendicitis

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INTRODUCTION

Post-operative pain can cause complications in many systems, mainly in the respiratory system, and can disturb the patient. Post-operative analgesia is one of the most important factors of perioperative anesthesia management. Various analgesic agents, mainly opioids, are used parenterally and/or regionally for this purpose. The most common agent used for this purpose is parenteral pethidine (Aldolan® [pethidine hydrochloride], meperidine etc.). The opioid use for the treatment of postoperative pain causes some side effects. Although decreasing the dose of the analgesic can help to decrease these side effects, this comes with a decrease in the effectiveness of the analgesic also. The respiratory and gastrointestinal side effects can be prevented by using local anesthetics.[1]

It has been demonstrated that local anesthetic application to the surgical area before incision (preemptive analgesia) decreases pain in elective surgeries like tonsillectomy, cholecystectomy, vaginal hysterectomy or orthopedic surgeries.[2-6] Theoretically, preemptive an-

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algesia controls the postoperative pain by preventing or limiting the stimulation of spinal neurons before the central nervous system receives the afferent signals.[7] It has been a rare interest in the clinical era whether this method can be useful in cases like painful acute appendicitis.[8,9] In this study we aimed to evaluate if the post-appendectomy pain can be relieved with preincisional local anesthetic infiltration.

MATERIALS AND METHODS

The study was designed in a prospective randomized manner and consecutive patients with a tentative diagnosis of appendicitis who presented to the Emergency Department between April and December 2003 were enrolled into the study. The approval from the Academy Ethical Committee was taken and patients gave the informed consent which informed them the nature of the procedure, reasonable alternatives to the proposed intervention, the relevant risks and benefits. Patients were consecutively randomized into two groups during their admittance to the clinic. Group 1 patients received preemptive analgesia with a combination of lidocaine and bupivacaine hydrochloride, and Group 2 patients served as controls with normal saline solution infiltration.

Patients were informed about the procedure but kept blinded about the group to which they were allocated. During the study, patients false diagnosed regarding to explorations findings and the pathologic specimen confirmation, sensitive to amide group local anesthetics, and the ones who did not agree with the procedure were excluded from the study and new patients were added as replacements.

The vascular way was opened and a three-way stopcock inserted to the vein. The monitorization of the vital signs was recorded by a non-invasive pressure monitor (Critikon, Dinamap, Vital Signs Monitor 1846 SX, USA), EKG and pulse oximeter (Model 400, Palco Laboratories, USA).

Non-depolarizing muscle relaxant (vecuronium 0.1 mg/kg), opioid (phentanile 1-2 μg/kg), and thiopental 5 mg/kg were used to induce anesthesia. After endotracheal intubation, anesthesia was maintained with, 3 l/kg oxygen + 3 l/kg nitrous oxide + 1-2% isoflurane and vecuronium 0.02-0.03 mg/kg intravenously (iv). A combination of 10 ml of 1% prilocaine and 10 ml of 0.25% bupivacaine was infiltrated into the planned incision site cutaneously, subcutaneously, and under the fascia of the external oblique muscle of the patients in Group 1. The patients in Group 2 were injected with the same volume of saline to the same anatomical sites. All patients received the standard incision on the right bottom quadrant. The patients were classified as normal, suppurative, gangrenous, and perforated appendicitis by the surgeons. At the end of the surgery, inhalation of the anesthetics stopped and the patients received 0.06 mg/kg neostigmine + 0.02 mg/kg atropine IV for decurarization. The patients who had enough spontaneous respiration were taken to the recovery room and monitored for blood pressure, respiration rate, and peripheral oxygen saturation. When the patients somnolence score was 1, the pain levels was evaluated by a 10-cm visual analog scale (VAS). Patients had to estimate their experienced pain intensity based on this scale from 0 = no pain, to 10 = most extreme pain. The patients who had VAS ≥4 received 1 mg/kg meperidine HCl intramuscularly (IM). On the 2-hour follow-up controls, patients who had VAS ≥4 received additional meperidine HCl at a dose of 0.5 mg/kg IM. The additional doses applied in 24 hours were recorded.

Statistical analysis was done by Wilcoxon test and two independent samples T-test was used as the non-parametric test. The level of significance was selected as $P<0.05$.

RESULTS

Forty consecutive patients were included in the study (31 males and 9 females). The average age of the patients was 21.15±0.7 and 20.90±0.7 in Group 1 and Group 2, respectively (Table 1). There was no significant difference between the groups based on the patient characteristics.

Two patients in Group A and three patients in Group B who were false diagnosed regarding exploration findings and the pathologic specimen confirmation were excluded from the study and new patients were added to the study as replacements.

There was no difference between the two groups' systolic and diastolic arterial pressure, heart rate, and peripheral oxygen saturation values. There was no difference between the two groups' somnolence score (Table 2). The VAS values recorded at 0, 6, 12, and 24 hours (Table 3) showed no statistical difference between the patients' VAS values at no time points. In Group 1, three patients had nausea, two had vomiting, and one had urinary retention. In Group 2, one patient had nausea, one had respiratory depression (Table 4).

Total drug doses as mg/kg (1.92 ± 0.5 in Group A and

Table 1: Demographic characteristics of the patients

	Group I (n=20)	Group II (n=20)
Gender (F/M)	4/16	5/15
Age (years)	21.15 ± 0.74	20.90 ± 0.78
Weight (kg)	73.15 ± 8.23	72.50 ± 7.31
Operation time (min)	89.00 ± 16.43	88.25 ± 18.86

Table 2: Somnolence scores of the patients

	5 min	10 min	20 min
Group I	2.11 ± 0.32	2.00 ± 0.0	1.00 ± 0.0
Group II	2.09 ± 0.43	2.05 ± 0.21	1.05 ± 0.21

Table 3: VAS values (mean ± SD)

Hour	0	6	12	24
Group A	6.05 ± 1.10	4.03 ± 0.95	3.01 ± 1.06	1.81 ± 0.66
Group B	5.99 ± 1.05	4.12 ± 1.01	2.97 ± 0.82	1.65 ± 0.52

Table 4: Distribution of side effects

	Group A	Group B
Nausea	3	1
Vomiting	2	-
Urinary retention	1	-
Sweating	1	1
Somnolence	1	1
Hypotension	1	1
Respiratory Depression	-	1

1.97 ± 0.6 in Group B) and numbers of application during the study (4 in both groups) showed no statistical difference between the groups.

DISCUSSION

In the last decade, our knowledge about the mechanisms of acute pain increased and treatment protocols that are more logical and specific to the mechanisms responsible for the development of the pain, replaced the empiric treatments.[7] The method called "preemptive analgesia" is one of these new treatment protocols.

The traditional approach for postoperative analgesia is to begin the analgesic treatment when the pain starts in the postoperative period. It is stated that the intense painful stimulus of the surgical incision causes some functional changes in the central nervous system (sometimes called "windup"). It is hypothesized that applying local anesthetic techniques and potent analgesics (preemptive therapy) before surgery will decrease the postoperative analgesic need.[10]

Preemptive analgesia is to decrease the postoperative pain by preventing the intense nociceptive bombardment of the central nervous system due to surgery.[11] The term "preemptive" here means to decrease the postoperative pain by applying preoperative therapies. Actually, the application time or method of the treatment is not that important. Regardless of the time and method applied, preventing the central nervous system's hyperstimulatory state is important.[7] In order to achieve this, the treatment must cover all the possible causes and the periods of this painful stimulus.

The intense painful stimuli are not only caused by surgical incisions, but chemical substances and enzymes released from the injured tissue play a role in this mechanism as well.[11] For this reason, the approach to prevent the painful stimulus must target both the stimuli due to incision and the stimuli of the released substances. Many drugs and methods were used in preemptive analgesia research and it has been shown that the postoperative pain can be prevented by these preemptive methods. These methods include infiltration of local anesthetic in the surgical wound, opioid use, regional blocks and use of non-steroid anti-inflammatory drugs during the preoperative period.[12-14]

It has been suggested that the most effective method is to combine preincisional and postincisional infiltration.[15] This observation is in correlation with the hypothesis of two different phases of the pain, the first of which is the incisional pain, and the other phase is the secondary pain due to the inflammatory response of the traumatized tissue.

Brull *et al*[16] showed a decrease in VAS scores and postoperative opioid needs of patients who had graft removal from their crista iliaca and received local anesthetic via a catheter put in their wounds.

Willard *et al*[9] conducted a study evaluating the effect of a combination of 1% lidocaine mixed with 0.25% bupivacaine and 1:400,000 epinephrine in equal volumes before incision compared to a control group which received normal saline. They concluded that preincisional local anesthetic use does not reduce pain in patients after appendectomy operation. A similar study was done by Ko *et al*[8] from California. By comparing patients who received preemptive analgesia with a combination of lidocaine hydrochloride and bupivacaine hydrochloride, preemptive analgesia with saline infiltration and nothing, they concluded that preemptive analgesia did not reduce postoperative pain, reduce analgesic requirements, or shorten the length of hospital stay. We have observed similar results confirming these studies.

In this study, we showed that preincisional infiltration did not have a significant contribution on the postoperative analgesia. We think that, as preemptive analgesia prevents or limits the spinal neuron excitability before perceiving the afferent stimuli, it may not be helpful in patients with intense pre-operative pain.

In another study, it is stated that the application of infiltration both in pre-operative and post-operative periods is more helpful.[15] We think that post-operative infiltration may reduce the second phase of the pain, but it may not be enough because of central sensitization.

It has been reported that the major cause of the pain in acute appendicitis is the inflammation of the parietal peritoneum.[17] In this experiment, we did not apply local anesthetic to the peritoneal area, so we are unable to comment on this issue.

One of the most important components of the post-

operative pain is the intraoperative anesthesia method. As we applied a standard protocol to all our patients, we cannot evaluate this factor.

In conclusion, preincisional local anesthetic infiltration did not help to decrease the need of post-operative analgesic in acute painful surgical cases. This may be due to previous central sensitization.

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