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The Effect of Intramuscular Midazolam on Postoperative Pain Resulting from Herniorraphy

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The main purpose of this study was to assess the effect of intramuscular midazolam on postoperative pain and to test our hypothesis that the patients are more comfortable and suffering less pain after operation. Eighty male patients with ASA class (I, II), aged 15-60 years whom were scheduled for elective inguinal herniorraphy, were enrolled in this study in a double blind fashion. Patients were randomly assigned to two groups of forty, whom were randomly allocated for this study. Group A the test group received 0.1 mg kg^{-1} midazolam and group B the control group received 0.02 cc kg^{-1} saline, intramuscularly, just after inducing anesthesia with fentanyl 3 μg kg^{-1}, thiopental 5 mg kg^{-1} as well as atracurium 0.5 mg kg^{-1}. Popular McGill questionnaires were filled for pain severity assessment in four stages (1, 2, 3 and 8 h after operation) and the patients' vital signs were charted in five stages (preoperative and 1, 2, 3 and 8 h after operation). The data so obtained was analyzed statistically using Student t-test and Chi-square. First hour after operation, pain score average in group A was 2.3 in comparison with 6.6 in group B ($p<0.05$). After second and 3rd h of operation scores of 3.6 and 3.8 in comparison with 6.4 and 6.2 were related to group A and group B, respectively ($p<0.05$). Vital signs of the patients in group A were more stable than group B during the first hour of recovery period ($p<0.05$). Moreover, the need of intravenous opiate for relieving pain during recovery period in group A was less than group B ($p<0.05$). Intramuscular midazolam just after inducing anesthesia appears to cause pain relief after herniorraphy, particularly during early recovery period.

Key words: Postoperative pain, intramuscular, midazolam, herniorraphy

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INTRODUCTION

Acute postoperative pain is a complex response to different factors such as tissue damage, visceral distention and diseases. Postoperative pain could result to a variety of physiologic damages of different organs throughout the human body. Despite of different senses among patients which are related to factors such as age, sex and physiological stability, postoperative pain is inevitable without a good management. Effective pain control after operation is an essential point in both managing and caring of the surgical patients (Katz *et al*., 1996; Shah *et al*., 2003; Bergendahl *et al*., 2004).

Factors related to postoperative pain severity are due to those linked to the site and the duration of operation, the quality of surgery, physiologic status and patient's psychological situations as well as preoperative medication along with kinds of induction of anesthesia. On the other hand, we could add surgical procedures, anesthesia related events and postoperative pain management as three major factors related to postoperative pain (Ong *et al*., 2004).

Postoperative complications which can be related to acute postoperative pain are divided to vital organ damage such as cardiovascular problem, pulmonary dysfunction and non vital organ damage which are not observed at firs glance (Katz *et al*., 1996; Kain *et al*., 2000).

The advantages of effective postoperative pain management include patient's comfort and therefore his/her satisfaction, early mobilization, fewer pulmonary and cardiovascular complications as well as reduced in deep vein thrombosis and faster recovery (Richardson *et al*., 1997).

To our knowledge, it has not been mentioned in literatures about an accurate method for managing postoperative pain, particularly among those patients who are more sensible to surgical stress. Therefore, we carried out an investigation to characterize the role of intramuscular midazolam on relieving pain after operation among patients whom were scheduled for elective inguinal herniorrapphy.

MATERIALS AND METHODS

Eighty male patients aged between 15-60 years with ASA class I and II whom were scheduled for elective open inguinal herniorraphy in 2005 at Shahrekord University affiliated hospital (Kashani Hospital) in Iran, were enrolled in this study. Individually, each patient signed a consent form according to the local Ethic Committee of the university. Exclusion criteria such as allergy, coexisting diseases, suspected or known drug abuse and pregnancy as well as duration of operation less than 15 min and more than 45 min were considered curiously and study was done based on a double blind manner. Remembering that patients' demographic data (age, weight) were recorded before operation.

All patients were premedicated with oral diazepam (10 mg), 2 h before entering the operative room. And they were randomly assigned according to a paper-generated random number list in to two groups of forty, just after entering the operating room. Routine intra operative monitoring devices (ECG, Pulse Oximetry, Non invasive blood pressure monitor) were attached. After insertion of a 18-Gage intravenous (i.v.) cannula, all patients received 10 mL kg^{-1} balanced crystalloid Ringer solution over 10 min as well as 0.1 mg kg^{-1} morphine sulfate intravenously before inducing anesthesia towards controlling pain during operation.

General anesthesia was induced with fentanyl 3 μg kg^{-1}, sodium thiopental 5 mg kg^{-1} and atracurium 0.5 mg kg^{-1}, intravenously. Anesthesia was maintained with halothane 1 Mac, nitrous oxide 50% with oxygen and atracurium 0.1 mg kg^{-1} during general anesthesia and operation was performed by the same surgeon in all patients.

Patients were randomly assigned to two groups of forty each and Group A (The Test Group or Midazolam Group) received Midazolam 0.1 mg kg^{-1} through their left deltoid muscle and Group B (The Control Group or Saline Group) received 0.02 mL kg^{-1} saline through their left deltoid muscle using 2 cc syringe with 23-Gage needle, just after inducing anesthesia.

All patients in both groups were closely observed either during operation or during 8 h after operation in the recovery room and the surgery ward which were the same. Intermittent postoperative pain intensity assessment (1, 2, 3 and 8 h after operation) was done according to McGill questionnaire pain score assessment (Sensory, Affective and Evaluative descriptors). The Present Pain Intensity (PPI) was considered based on a 1-5 intensity scale. Based on evaluating the intensity of pain by the patients, Visual Analog Scale (VAS) ranging from 0-10 was considered for additional analgesic requirement and VAS>3 was the main point for intravenous injection of meperidine 0.5 mg kg^{-1} for controlling pain during recovery period if necessary.

The mean of sum of three major classes of word descriptors (Sensory, Affective and Evaluative) based on 1-5 intensity scale was used for statistical analysis. Moreover, vital signs were assessed during postoperative period.

Statistical analysis was performed with the SPPS (SPSS for Windows Release 11.0) statistical package. The collected data were analyzed using Student t-test and Chi-Square and ($p<0.05$) was considered statistically significant.

RESULTS AND DISCUSSION

Neither demographic data nor surgery time was different between groups, ($p>0.05$) (Table 1).

Difference of mean of Total Present Pain Intensity score (PPI) between groups was significant during postoperative 3 h period in contrast to 8 h after operation which was not significant, ($p>0.05$) (Table 2).

Also analgesic requirement among the patients in group A was (22±2.1 mg) lower than group B (38±2.8 mg), $p<0.05$. And the time until administration of the first analgesic drug after the end of surgery in group A was 46±3.1 min in comparison with group B which was 21±2.3 min, $p<0.05$.

Difference of mean of vital signs was not significant before operation, ($p>0.05$) (Table 3). With the exception of respiratory rate differences between the groups during the first 3 h after operation, there were not significant differences in blood pressure and pulse rate between groups, except during the first hour after operation (Table 3).

We found no major complications among patients in both groups except agitation and hallucination which were seen in group A (2 and 3) and in group B (3 and 5), respectively which were not significant.

Present study showed that intramuscular injection of midazolam just after inducing anesthesia can reduce pain intensity after minor operation, particularly during the first three-h period after operation. The most important point in this study is that the stability of vital signs (Blood Pressure, Pulse Rate and Respiratory Rate) is statistically maintained. However, there was no acceptable result after this period of time. The result of our study is different from those studies in which opiates were used for decreasing postoperative pain (Suzuki *et al*., 1999; Phillips and Currier, 2004).

Although opiates are popular analgesic drugs that are widely used for postoperative pain management, new drugs should be considered curiously by investigators because of various complications related to opiates consumption and this important point could result towards not desirable drug response. Some researches showed that most of the patients, whom were treated with narcotics for relieving severe acute postoperative pain, had experienced unwanted pain in their recovery periods (Phillips and Currier, 2004).

Table 1: Patients' demographic data and surgery time between groups

Parameters	Midazolam group (Group A)	Saline group (Group B)	p-value*
Age (year)	35.38±11.99	32.67±10.22	0.66
Weight (kg)	71.42±8.50	70.65±8.00	0.42
Surgery time (min)	28.07±5.85	28.47±5.63	0.19

*$p<0.05$ is significant, Data are presented as mean±SD

Table 2: Postoperative total pain intensity scores between groups during different hours

Time	Midazolam group (Group A)	Saline group (Group B)	p-value*
1 h after operation	2.3±1.0	6.6±1.4	0.00*
2 h after operation	3.6±1.2	6.4±1.3	0.00*
3 h after operation	3.8±0.9	6.2±1.2	0.00*
8 h after operation	6.3±1.3	6.1±1.2	0.41

*$p<0.05$ is significant, Data are presented as mean±SD

Table 3: Preoperative and postoperative vital sign between two groups

Vital signs	Midazolam group (Group A)	Saline group (Group B)	p-value
Systolic blood pressure (mm Hg)			
Before operation	127±13	128±12	0.927
1 h after operation	110±13	133±16	0.000*
2 h after operation	130±15	131±28	0.300
3 h after operation	128±23	130±18	0.710
8 h after operation	123±12	125±16	0.370
Pulse rate (per min)			
Before operation	79±6	81±6	0.160
1 h after operation	69±4	90±8	0.000*
2 h after operation	78±7	82±9	0.300
3 h after operation	86±8	91±7	0.710
8 h after operation	86±7	85±6	1.000
Respiratory rate (per min)			
Before operation	19±2	19±1	0.290
1 h after operation	15±2	21±1	0.000*
2 h after operation	18±2	22±1	0.000*
3 h after operation	19±1	22±3	0.000*
8 h after operation	20±2	20±1	0.340

*$p<0.05$ is significant, Data are presented as mean±SD

Midazolam is the most important drug among benzodiazepines, because of its unique characteristics. Fortunately, there are no major problem with this water soluble drug (Bauer *et al*., 2004). The patients didn't suffer from most complications related to opiates such as nausea, vomiting, urinary retention and itching as well as other side effects, whenever midazolam was used (Brosius and Bannister, 2001; Bauer *et al*., 2004).

The advantages of using midazolam in this study for relieving acute postoperative pain are shown not only because of its effects on patients' relaxation and comfort but also because of having no major complications and side effects mentioned in previous studies (Brosius and Bannister, 2001; Bergendahl *et al*., 2004; Bauer *et al*., 2004; Boussofara *et al*., 2006).

The main goal in this study was to assess acute pain intensity during 8 h postoperative period, but on the other hand, complications along with opiate induced analgesia were closely focused. Fortunately, there were no major complications and discomfort among the patients in both

groups. Moreover, Brosius and his colleague showed that the recovery period among their patients aged 1 to 10 years, was not shorter than usual (Brosius and Bannister, 2001). Present study showed that the patients in both groups had no significant agitation and hallucination.

Klain and his colleagues considered using lorazepam and midazolam for relieving pain after abdominal hysterectomy. They noted that there was no need for additional analgesic drug for managing postoperative pain during the recovery period (Klain *et al*., 2001). The result of their study was similar to our study, except using lorazepam, the night before surgery. Other studies' results are paralleled with our finding, particularly in relieving pain after surgery (Stegmann and Bester, 2001). Most of these studies are based on intravenous injection of midazolam during operation. As Sen *et al*. (2001) noted, intrathecal midazolam was used as a premedication for caesarean section and unwanted cardiovascular complications as well as other side effects was not seen, but only short duration of pain relief was observed.

CONCLUSION

Although, the short acting characteristic of midazolam is expected to play a minor role in managing acute postoperative pain, especially after major surgery, this study showed that present pain intensity score (PPI) was significantly decreased during recovery period, which was normally unexpected. In spite of probable minor side effects of this short acting benzodiazepine which was not a problem in our study, we concluded that this randomized double blind study presents a new message towards substitution of new drugs and techniques for an ideal postoperative pain management.

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