DETERMINING THE EFFECT OF INTRAPERITONEAL PETHIDINE ON POSTOPERATIVE PAIN

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Abstract

The main problem in the postoperative period is pain relief. Adequate postoperative analgesia not only leads to patient's comfort but also decreases morbidity, nursing care and time of hospitalization.

Determination of the effect of intraperitoneal pethidine on postoperative pain in women scheduled for elective tubal ligation was undertaken.

In a double blind clinical trial study of 60 women, ASA I, 25-45 years old, were enrolled for elective tubal ligation in Kosar hospital in Qazvin, IRAN.

Patients were randomly divided in two equal groups (30 each).One group received pethidine intraperitoneally and the other group received equal amount of placebo in the same region. The intensity of postoperative pain was evaluated by visual analogue scale (VAS) for about 8 hours. Incidence of nausea was also evaluated. Data was transformed to SPSS software. Then data analysis was performed by U-test.

There was no significant statistical difference with regard to age, weight, and time of operation between the two groups. The mean score of pain was significantly lower in intraperitoneal pethidine group than placebo group but the incidence of nausea in the intraperitoneal pethidine group was more than in placebo group ($P < 0.05$).

Thus, intraperitoneal pethidine decreases postoperative pain but increases postoperative nausea.

Key words: Intraperitoneal pethidine, Postoperative pain, Postoperative analgesia.

Introduction

Today, several operations are being done in operating rooms of the world. In this regard the main problem is pain relief. Insufficient pain control is associated with acute and chronic side effects. Attenuation of perioperative pathophysiology that occurs during surgery by reduction of nociceptive input in to the CNS and optimization of perioperative analgesia may decrease complications and facilitate the patients' recovery[1,2].

The transmission of nociceptive stimuli from the periphery to the CNS results in the neuroendocrine stress response, a combination of local inflammatory substance and systemic mediators of the neuroendocrine response. The dominant neuroendocrine responses to pain involve hypothalamic-pituitary-adrenocortical and sympathoadrenal interaction[1]. Suprasegmental reflex responses to pain result in increased sympathetic tone, increased catecholamine secretion,

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and decreased secretion of anabolic hormones. A hypermetabolic, catabolic state occurs[1].

The stress response may be an important factor in the postoperative development of hypercoagulability which leads to deep vein thrombosis, vascular graft failure, and myocardial ischemia. The stress response also may potentiate immunosuppression[1].

Hyperglycemia from the stress response may contribute to poor wound healing and depression of immune function. Uncontrolled pain by activation of the sympathetic nervous system may be important in the development of myocardial ischemia and infarction and may also delay return of postoperative gastrointestinal motility that may lead to paralytic ileus[1]. Thus attenuation of postoperative pain will decrease perioperative morbidity and mortality.

Many options are available for the treatment of postoperative pain, including systemic (opioid and nonopioid) analgesics and regional (neuroaxial and peripheral) analgesic techniques. By considering patient's preferences and an individualized assessment of the risks and benefits of each treatment modality, the anesthetist can optimize the postoperative analgesic regimen for each patient[1].

Complete intraoperative blockade of afferent pain signal to the central nervous system by some type of medications through different routs is fundamental in decreasing postoperative pain[3]. Thus during operation, interruption of nociceptive input and blockade of N-methyl D-aspartate activation by some drugs such as opioids (specially morphine) or local anesthetics may be necessary to provide effective postoperative analgesia[4,5]. Pethidine may be a good choice for treatment of postoperative pain because it is an opioid which has also local anesthetic effect[1].

Therefore the purpose of this study is to determine the effect of intraperitoneal pethidine administration during surgery on postoperative pain instead of intramuscular pethidine injection in postoperative period.

Methods

Prior permission of institution's of human subjects committee, and patients' informed consent, were procured. In a double blind clinical trial study 60 women, ASA class I, 25-45 years old, scheduled for elective tubal ligation, were enrolled. Exclusion criteria consisted of opium addiction, long term abuse of non-steroidal anti-inflammatory drugs or analgesic and the positive history of anaphylactic reaction to pethidine.

Patients were randomly assigned into two groups (intraperitoneal pethidine and intraperitoneal placebo) according to their colored cards. The patients were asked to rate the severity of pain via a visual analogue scale (VAS) ranging from no pain (0), mild pain (1-3), moderate pain (4-6) and sever pain (7-10)[6]. The use of these measures was explained to all patients before surgery. An independent investigator blinded to the treatment group obtained the scores every two hours till 8 hour after termination of operation.

Premedications (midazolam 20 μ/kg, fentanyl 1.5 μ/kg), induction (sodium thiopental 5 mg/kg and succinylcholine 1.5 mg/kg) and maintenance of anesthesia (halothane 1% in combination with oxygen 50%/N2o 50%) were the same in the two groups. Intraoperative monitoring consisted of electrocardiogram, pulse oximeter and noninvasive blood pressure. At the end of the operation, the patients allocated to group A received 50 mg (1 ml) pethidine which was diluted with 29 ml of normal saline (total volume 30 ml) intraperitoneally. Patients in group B received only 30 ml normal saline intraperitoneally.

If the VAS score was greater than 3, 1 mg/kg IM pethidine was administered every 4 hour during 8 hour after termination of operation. During this time, the percent of patients who received pethidine was determined. Also the percent of patients who experienced nausea was evaluated. Nausea was classified as mild (no need for treatment), moderate (can be treated with 10 mg metoclopromide), and severe (no response to 10 mg metoclopromide). Finally, statistical analysis was performed by using the U-test. P-value <0.05 was meaningful.

Results

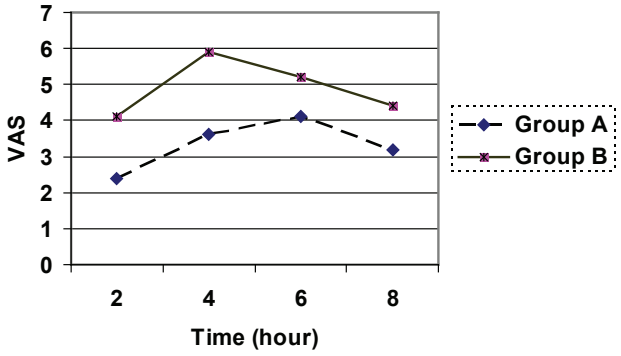
The demographic data with regard to age, weight and duration of surgery revealed no statically significant difference between the two groups (Table 1).

Table 1
Demographic data (mean ± SD)

Parameters	Group A	Group B
Age (years)	33.6 ± 5.4	32.9 ± 6.1
Weight (kg)	64.3 ± 5	63.1 ± 4
Duration of operation (min)	24.6 ± 6.2	25.1 ± 6.8

During 8 hour after operation, the pain score was significantly lower in Group A than in Group B ($p < 0.05$) (Fig. 1).

Fig. 1
Comparison of postoperative VAS in the two groups



The percent of patients who received pethidine for analgesia was 23.3% in Group A and 80% in Group B. This difference was statistically significant ($P < 0.0001$).

About postoperative nausea, 70% in Group A developed mild nausea and 13.3% developed moderate one. Only 20% of patients in Group B had mild nausea. Thus incidence of nausea was higher in Group A than Group B, which was statistically meaningful ($P < 0.0001$).

Discussion

Postoperative pain leads to some reversible or irreversible side effects especially in high risk patients. Thus the most important aim of anesthetists is pain relief through different methods.

About mechanism of postoperative analgesia by opioids, Opioid agonists not only produce a local anesthetic like effect on the surface of excitable cell membrane[1,7] but also affect serotoninergic pathways and in this way modulate opioid mediated analgesia[1]. Local anesthetic effects of opioids, most prominent with pethidine occur at the proximal end of the dorsal root as it passes the dorsal root entry zone[1,8].

Previous investigators have postulated that the analgesic effect of intraperitoneal pethidine resulted from local anesthetic activity at the surgical site and/or from central activity after systemic absorption[9].

Because of this dual local anesthetic and analgesic properties of pethidine, the opioid which selected in this study was pethidine, rather than morphine or fentanyl[10]. The effects of pethidine appear to be produced by its actions on two independent pathways; the opioid receptor pathways, which subserve analgesic action, and the sodium channels, which lead to local anesthetic action[11].

Profound blood flow of peritoneum seems likely to increase drug absorption into circulation and through this pathway, medication reaches to target point adequately. Thus intraperitoneal administration of drugs such as pethidine or lidocaine may be effective for producing clinical effects.

After absorption of pethidine from peritoneum to blood, it highly binds to plasma protein principally 70% to α_1-acid glycoprotein and only to a minor extent to plasma albumin[1]. Then it reaches to several target points such as surface of excitable cell membrane, proximal end of dorsal root, and serotoninergic pathways[1].

The peritoneum is exposed to block of visceral nociceptive conduction, thereby providing an additional mechanism of analgesia[11]. However, absorption from the large peritoneal surface may also occur, and this may be a further mechanism of analgesia[12].

In one study by O'Hanlon DM et al, intraperitoneal pethidine was compared with intramuscular pethidine in laparascopic cholecystectomy.

Conclusion of this study was superiority of intraperitoneal pethidine to intramuscular one for postoperative pain relief[13].

In another study by Visalyaputras et al, effectiveness of intraperitoneal lidocaine, intramuscular morphine or both drugs together for pain relief in postpartum tubal ligation was evaluated and they concluded that installing lidocaine in the abdominal cavity effectively decreases intraoperative pain in this type of operation[14].

Our study has demonstrated that intraperitoneal pethidine administration provides postoperative

analgesia so that it decreases requirement for postoperative intramuscular pethidine injection significantly, but was associated with mild to moderate nausea.

It is hoped that intraperitoneal administration of drugs may lead ultimately to improvement in convalescence and reduces the risk of hospital readmission after minimally invasive surgery and decreases postoperative morbidity[12].

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