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Comparison of Patient-Controlled Analgesia Using Morphine With and Without Paracetamol in Postoperative Pain Control

Mehryar Taghavi Gilani[1]* (MD); Alireza Bameshki[1] (MD); Arash Peivandi Yazdi[1] (MD); Reihaneh Hasanzadeh[1] (MD)

[1.] Cardiac Anesthesia Research Center, Imam Reza Hospital, School of Medicine, Mashhad University of Medical Science, Mashhad, Iran.

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ABSTRACT

Introduction: Postoperative pain control plays a pivotal role in reducing postoperative complications, hospitality time, and increasing satisfaction. This study aimed to evaluate the effect of paracetamol on the pain and complications caused by gastrectomy.

Materials and Methods: This randomized prospective study was conducted on 60 patients (two same group) who were candidate for gastrectomy in Imam Reza Hospital of Mashhad, Iran during August-September 2015. The first group received Patient-Controlled Analgesia (PCA) with morphine only, and in the second group, paracetamol (1 gram) infused with morphine every six hours. Level of pain, morphine intake, and side effects were evaluated in both groups.

Results: No significant difference was observed in the four-scale score of pain in the patients (morphine group: 0.64±0.1, morphine-paracetamol group: 0.6±0.1) (P=0.72). During the first 24 hours after the surgery, the morphine group had lower consciousness level (2.3±0.2) compared to the morphine-paracetamol group (1.7±0.3) (P=0.001). Moreover, infusion of paracetamol with morphine to control the pain after gastrectomy reduced the need for morphine analgesia. Morphine intake was 21.4±7.7 in morphine group, while it was 14.3±5.8 in the morphine-paracetamol group within the first 24 hours after the surgery (P=0.001). However, this level had no significant effect on postoperative complications such as itching, nausea, and arterial oxygen saturation.

Conclusion: According to the results of this study, intravenous paracetamol (one gram) administered every six hours with PCA using morphine could decrease morphine intake leading to better consciousness level during the first 24 hours after gastrectomy without further complications.

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Introduction

Postoperative pain control is one of the most essential factors for the improvement of the quality of postoperative care. Elimination of pain leads to higher patient satisfaction and increases the activity and mobility of the patient. Postoperative pain could give rise to pulmonary, cardiac, and metabolic complications, impair wound healing, and agitate the patient (1).

Currently, several methods and medications are used to alleviate postoperative abdominal pain; such examples are narcotics, nonsteroidal anti-inflammatory drugs, and use of epidural catheters and nerve blocks (2-5). As a potent and effective analgesic, morphine is one of the most common drugs used to eliminate postoperative pain. Some of the side effects associated with the use of morphine are respiratory depression, urinary retention, nausea and vomiting, dry mouth, and itching.

Limitation in the access and use of narcotic drugs has urged medical researchers to utilize more effective medications in order to manage postoperative pain in different patients (6).

In 1995, the American Society proposed the guidelines on the reduction of acute postoperative pain relying on standard care, use of epidural and Patient-Controlled Analgesia (PCA), and simultaneous

***Corresponding Author:** Mehryar Taghavi Gilani, Cardiac Anesthesia Research Center, Imam Reza Hospital, School of Medicine, Mashhad University of Medical Science, Mashhad, Iran. Email: Taghavim@mums.ac.ir

analgesic methods (7). Several studies have been performed in this regard proposing conflicting results. This study aimed to evaluate the effect of paracetamol on the management of postoperative pain and complications. Moreover, we assessed the effect of morphine dose on postoperative pain control and consciousness level of patients undergoing gastrectomy.

Materials and Methods

This randomized, double-blinded, prospective study was conducted on 60 patients with gastric cancer who were candidate for gastrectomy in Imam Reza Hospital of Mashhad, Iran during August-September 2015.

Study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences, and written informed consent was obtained from all the participants prior to the study.

Inclusion criteria of the study were as follows: 1) age range of 40-70 years; 2) ability to be trained on the use of PCA pump based on the confirmation of the research physician; 3) ability to communicate and 4) normal pulse oximetry, electrocardiography (ECG), and intravenous location for morphine injection in preoperative evaluation.

Exclusion criteria for participation were as follows: 1) history of cardiac or liver failure, insulin-dependent diabetes, and renal disease; 2) allergy to morphine and acetaminophen; 3) body weight of more than 110 kg or less than 55 kg and 4) long-term use of narcotics or other analgesics.

During gastrectomy, all the patients received midazolam (2 mg/kg), fentanyl (3 mg/kg) and propofol (2 mg/kg). Afterwards, the patients received all-trans retinoic acid (ATRA 1.5 mg/kg) for the administration of maintenance propofol (50-200 mg/kg/min) and remifentanil (0.2-0.8 mg/kg/min), and morphine (0.1 mg/kg) 30 minutes before the end of the surgery. After the induction of proper breathing, all the patients were injected with relaxant reversed prior to extubation and transfer to the intensive care unit (ICU). In the ICU, they received monitoring and oxygen therapy with 40-50% FiO2 using a mask for 12-24 hours after the surgery (SaO2>92%). During the first 24 hours after the surgery, the patients were evaluated in terms of hemorrhage and ECG changes.Selected patients were randomly divided into two groups using numbered, closed envelopes. Patients in the morphine-only group received 1 mg of morphine via PCA pump as the individual need for at least a five-minute interval.

In addition, these patients were injected with 10 mg/kg paracetamol ampule as placebo every six hours. In the second group, in addition to receiving morphine via PCA pump, the patients were administered with an infusion of paracetamol ampule (1 gr) every six hours. In this study, the patients, anesthetists and ICU nurses were blinded to the procedures.

The first dose of morphine was prescribed in the presence of a nurse who trained the patient on the symptoms of tachycardia and high blood pressure, which were considered as the indicators of postoperative pain. When the patients were fully alert and responsive, they were asked to use the PCA system on their own. The patients were evaluated in terms of the consciousness level per hour, respiratory rate per minute, SaO2, and nausea and vomiting. Level of consciousness was measured in the ICU using simple numerical benchmark (awake=1, sometimes awake and asleep again=2, asleep most of the time=3, and difficult to awaken=4). In conscious patients, the rate of pain was measured using the Numeric Rating Scale (NRS) at 6, 12 and 24 hours based on the scoring system of rest and motion, as follows: no pain=0 (NRS=0), mild pain=1 (NRS=1-3), moderate pain=2 (NRS=4-7), and severe pain=3 (NRS=8-10).

Statistical analysis

Sample size in each group was determined based on the study by Fayaz (8) and variance of morphine intake. Considering the error in the estimated mean of 0.85, type I error of 0.05, and confidence of 80%, sample size of the study was calculated at 56 patients. However, we selected 60 patients for higher accuracy in terms of age, duration of surgery, and changes in arterial oxygen pressure and morphine intake.

Data analysis was performed in SPSS $V._{16}$, and morphine intake of the patients was compared using T-test. Moreover, non-parametric variables (e.g., consciousness level, pain, and nausea) were assessed using the Chi-square test, and the correlation between the consciousness level and morphine intake was evaluated as well. In all statistical tests, P value of less than 0.05 was considered significant.

Results

This study was conducted on 60 patients with gastric cancer within the age range of 40-70 years, who were divided into two groups. No statistically significant difference was observed between the two groups in terms of age, height, body weight, duration of surgery, and recovery time Table 1.

Table1: Demographic parameters in two groups (Mean±Standard Deviation)

	Morphine	Morphine-Paracetamol	P-value
Gender (male/female)	19.11	21.9	0.14
Age (year)	65.3±11.3	66.8±10.1	0.6
Body Weight (kg)	62.8±17.8	63.4±10.9	0.21
Duration of Surgery (minutes)	273.3±51.9	251±76.2	0.44

According to our findings, there was no significant difference between the two study groups in terms of the consciousness level six hours after the surgery, while the level of consciousness was significantly lower in patients of the morphine-only group after 6-24 hours (P=0.001, P=0.021, P=0.016, and P=0.002 at 6, 12, 16, and 24 hours, respectively). Moreover, no significant difference was observed between the groups in terms of

pain intensity (P=0.66, P=0.54, P=0.56, and P=0.54 at 6, 12, 16, and 24 hours, respectively). Morphine intake was 21.4±7.7 in the morphine-only group and 14.3±5.8 in the morphine-paracetamol group during the first 24 hours after the surgery. Furthermore, no significant difference was observed between the study groups with regard to the postoperative complications Table 2.

Table2: Morphine intake, consciousness level, postoperative pain score, and opioid complications in two groups (Mean±Standard Deviation)

	Morphine	Morphine-Paracetamol	P-value
Total Morphine Intake	21.4±7.7	14.3±5.8	0.001
Nausea and Vomiting (%)	33.3	33.3	1.00
Pruritus (itching) (%)	20	13.3	0.79
SpO2 (%)	96.5±1.3	95.8±1.9	0.24
Consciousness Level	2.3±0.2	1.7±0.3	0.001
Postoperative Pain Score	0.64±0.1	0.6±0.1	0.72

Discussion

In the present study, we added paracetamol to morphine PCA in order to discover the most suitable method for postoperative pain control in surgical patients, as well as the most plausible medication in terms of effectiveness, complications, cost, and drug abuse. Patients commonly experience severe pain during the first 24 hours after surgery, and the intensity of pain depends on the type of surgical procedure and treatment protocol. In one study, Bameshki evaluated the level of postoperative pain after laparotomy, and the maximum pain during the first postoperative hours was reported to be 8.4±1.2, while the mean of pain intensity was 5.8±1.9 during the first 24 hours without proper protocol. In the current study, pain intensity during the first 24 hours after the surgery was equal in both groups. However, the level of morphine intake was lower in the morphine-paracetamol group compared to the morphine-only group, which indicates that use of non-opioid analgesics could reduce the consumption of narcotics.

In the present study, level of consciousness in patients of the morphine-only group was lower compared to the morphine-paracetamol group, which could be due to the higher dose of morphine in the first group. However, no significant difference was observed between the groups in terms of other side effects of opioids, such as nausea, vomiting, itching and oxygen desaturation.

In another research, Katabryj investigated the analgesic effect of paracetamol on postoperative pain in patients undergoing cardiac surgery, and the results suggested that combined, intravenous administration of paracetamol could effectually alleviate the postoperative pain in these patients (9). In 1998, one study was performed in Switzerland to compare the analgesic effects of paracetamol and morphine on postoperative pain. According to the results, paracetamol could be used as an alternative for morphine in the postoperative control of moderate pain. Furthermore, it was denoted that morphine exerted better short-term analgesic effects, while the effect of paracetamol remained for a longer period (10).

In another research performed in Russia in 2002 on the efficacy of proparacetamol in postoperative analgesia, 30 patients were evaluated with regard to the analgesic effects of paracetamol on postoperative pain. According to the results, use of paracetamol increased the severity of postoperative pain (11). Several studies have compared the analgesic effects of paracetamol with opioid painkillers reporting no significant difference between these two methods (12-15).

One of the limitations of the current study was the measurement of postoperative pain at fixed time intervals, and the primary outcome was rescue analgesic requirements, which may not truly reflect the length of analgesic effects and efficacy of the analgesics used in the study.

Conclusion

According to the results of this study, addition of intravenous paracetamol (1 gr) at six-hour intervals to the pain control protocol through morphine PCA after gastrectomy decreased morphine intake by 32% improving the consciousness of the patients during the first 24 hours after the surgery. However, this method had no effect on the other complications caused by morphine administration, such as nausea, vomiting and itching.

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