

## Effect of Intravenous Paracetamol on Acute Post-operative Pain, Nausea, and Vomiting after Outpatient Diagnostic Laparoscopy for Infertility

Sussan Soltani-Mohammadi<sup>1</sup>, Negar Adhami<sup>2</sup>, Gita Shoeibi<sup>1</sup>

<sup>1</sup> Associate Professor, Department of Anesthesiology, Critical Care and Pain Medicine, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

<sup>2</sup> Resident, Department of Anesthesiology, Critical Care and Pain Medicine, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

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### Abstract

**Background:** Post-operative pain, nausea, and vomiting (PONV) are significant causes of morbidity among patients undergoing outpatient diagnostic laparoscopy. However, the optimal strategy for prevention of these side effects remains unclear. Many drugs and their combination have been used to attenuate these adverse responses. We conducted a study to evaluate the effect of intravenous (IV) paracetamol on attenuation of acute post-operative pain and opioid consumption and as a result PONV at the same time in infertile women undergoing diagnostic laparoscopy.

**Methods:** A total of 104 American Society of Anesthesiologists Class I-II infertile women aged 18-40 years, who were scheduled for elective diagnostic laparoscopy under general anesthesia, were included and anesthetized with the same technique. The paracetamol group received IV infusion of 1000 mg paracetamol in 100 ml saline, and the placebo group received the same volume of saline after induction of anesthesia. Pain score at the end of surgery and 1 hour later, PONV and fentanyl consumption as rescue analgesic at the recovery room were all recorded and compared between the two groups.

**Results:** There were no significant differences between the two groups regarding demographic data. Mean pain score was  $2.8 \pm 2.7$  in paracetamol group and  $4.3 \pm 3.5$  in placebo group at the end of surgery ( $P = 0.016$ ). Mean pain score was  $3.7 \pm 2.1$  in paracetamol group and  $4.6 \pm 2.2$  in placebo group 1 hour after surgery ( $P = 0.030$ ). Nearly 36% of patients in placebo group and 14% in paracetamol group need additional fentanyl for pain relief after surgery ( $P = 0.008$ ). Incidence of post-operative nausea was 16.3% and 14.5% in placebo and paracetamol groups, respectively, ( $P = 0.150$ ). Incidence of post-operative vomiting was 6% and 0 in placebo and paracetamol groups, respectively, ( $P = 0.040$ ).

**Conclusions:** IV paracetamol reduced post-operative pain and nausea in infertile women undergoing diagnostic laparoscopy for assisted reproductive techniques.

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### Introduction

Gynecological laparoscopy is a common procedure in assisted reproductive technologies. Anesthesia for these patients is a challenge, particularly in the day surgery population. Post-operative nausea and vomiting and poor analgesia can cause distress to the patient and increased cost for the health system because of overnight admission (1).

It is essential that the analgesia and pain control for these group of patients to be sufficient by the evening in an ambulatory surgeries where patients have limited access to health-care providers and analgesic and antiemetic medications (2-6).

Multimodal or balanced analgesia, utilizing regional analgesic techniques (where possible), and nonopioid analgesics appear to represent a viable strategy to decrease systemic opioid consumption and improve post-operative analgesia (7).

In a study by Sreenivasulu et al. (8) on 60 patients, the effect of pre-emptive use of 1 g intravenous (IV) paracetamol on post-operative pain scores and analgesic requirements in patients undergoing laparoscopic surgeries under general anesthesia were evaluated. They found that paracetamol provided satisfactory analgesia, decreased post-operative tramadol consumption, and also, post-operative pain, nausea, and vomiting (PONV).

**Corresponding Author:** Sussan Soltani-Mohammadi

Department of Anesthesiology, Critical Care and Pain Medicine, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran  
Tel/Fax: +98 21 88633039, E-mail: soltanmo@sina.tums.ac.ir

In a qualitative review by Hyllested et al. (9) for comparing paracetamol with non-steroidal anti-inflammatory drugs (NSAIDs) and their combination on post-operative pain, they concluded that paracetamol is a viable alternative to NSAIDs because of low incidence of adverse effects, but addition of NSAIDs to paracetamol may confer additional analgesic efficacy compared with paracetamol alone.

In another study by Soltani Mohammadi et al. (10), rectal paracetamol reduced propofol consumption and post-operative pain in infertile women undergoing outpatient surgery for oocyte retrieval.

A meta-analysis and systemic review by Apfel et al. (11) showed that prophylactic IV acetaminophen reduces post-operative nausea and vomiting with an effect size that compares well with data known from other antiemetics. They suggested that the antiemetic effect of IV acetaminophen is not mediated through the reduction of post-operative opioid consumption but through direct mechanisms or through the reduction of post-surgical pain.

Paracetamol rapidly passes the blood-brain barrier, reaches a high concentration in the cerebrospinal fluid, and has an antinociceptive effect mediated by the central nervous system (12). This central effect has been regarded primarily as an indirect and reciprocal influence through cyclooxygenase enzyme inhibition, and probably through the serotonergic system as well. Besides this central effect, it is accepted that paracetamol has a peripheral anti-inflammatory influence although this effect is somewhat limited (13).

The primary end point of this study is evaluating the effect of IV paracetamol on acute post-operative pain, and secondary end point is to evaluate its effect on reducing PONV due to reducing opioid consumption, after diagnostic laparoscopy in infertile women undergoing outpatient surgery.

## Materials and Methods

This randomized, double-blind clinical trial was approved by the Ethical Committee of Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran, protocol number 342 on January 20, 2015. The study was performed at the Center of Reproductive Medicine, Dr. Shariati Hospital, between March and July 2015. A total of 120 American Society of Anesthesiologists Class I-II infertile women aged 18-40 years, who were scheduled for elective diagnostic laparoscopy under general anesthesia, were included, and written informed consent was given from each patient before surgery. The patients those having contraindications to paracetamol (allergy and liver disease), history of treatment by steroids, NSAIDs, or opioids before surgery were excluded. The patients were divided into two groups. Randomization was by means of computer-generated codes. Sealed envelopes

containing the information of the randomization code and were kept in the patient's folder until the end of the study. All members of the surgical team, patients, and the anesthetist were unaware of the allocation.

After transferring the patient into the operating room, a 20 Gauge IV cannula was inserted for each patient and 3 ml/kg ringer lactate solution was infused. Standard monitoring, including electrocardiogram, arterial oxygen saturation, non-invasive blood pressure, and end-tidal carbon dioxide monitoring, were used throughout the operation. Before surgery, the patients were educated about the numeric rating scale in which 0 = no pain and 10 = worst imaginable pain. All patients were premedicated with midazolam 0.03 mg/kg and fentanyl 2 µg/kg IV.

Anesthesia was induced by IV propofol 2.5 mg/kg and trachea was intubated by injecting IV atracurium 0.5 mg/kg with appropriate size endotracheal tube. Maintenance of general anesthesia was accomplished by propofol infusion 100 µg/kg/min and oxygen. The study drug was prepared by an anesthesia staff that was unaware of the allocation and gave it to the patients. The paracetamol group received IV infusion of 1000 mg paracetamol in 100 ml saline and the placebo group received the same volume of saline after induction of anesthesia during 30 minutes. Post-operative pain at the end of surgery and 1 hour later and PONV at the recovery room were all recorded and compared between the two groups. The patients with numerical rating scale (NRS) ≤ 3 were considered have no pain and patients with NRS > 4 were considered to have pain and IV fentanyl 1 µg/kg was injected when needed. Patients with post-operative vomiting were treated with ondansetron IV.

Since 50% of patients after diagnostic laparoscopy have pain according to the previous studies, a sample size of 58 patients in each group would be required to detect a 25% difference in post-operative pain with an alpha error of 0.05 and power of 85% (95% confidence interval). The normality of distribution was tested by Kolmogorov-Smirnov test. Data were analyzed by SPSS software (version 19, SPSS Inc., Chicago, IL, USA). Independent sample t-test and chi-square test were used for comparing demographic data. Fisher's exact test was used for comparing NRS and PONV between the study groups.

## Results

A total of 120 patients were enrolled in the study. A total of 16 patients were excluded due to fulfilling criteria or changing the plan of surgery to operative procedure. Finally, 52 patients in paracetamol group and 49 in placebo group were included. Subject enrollment and allocation are summarized in a CONSORT flow diagram (Figure 1). Demographic data were not statistically different between the study groups (Table 1).

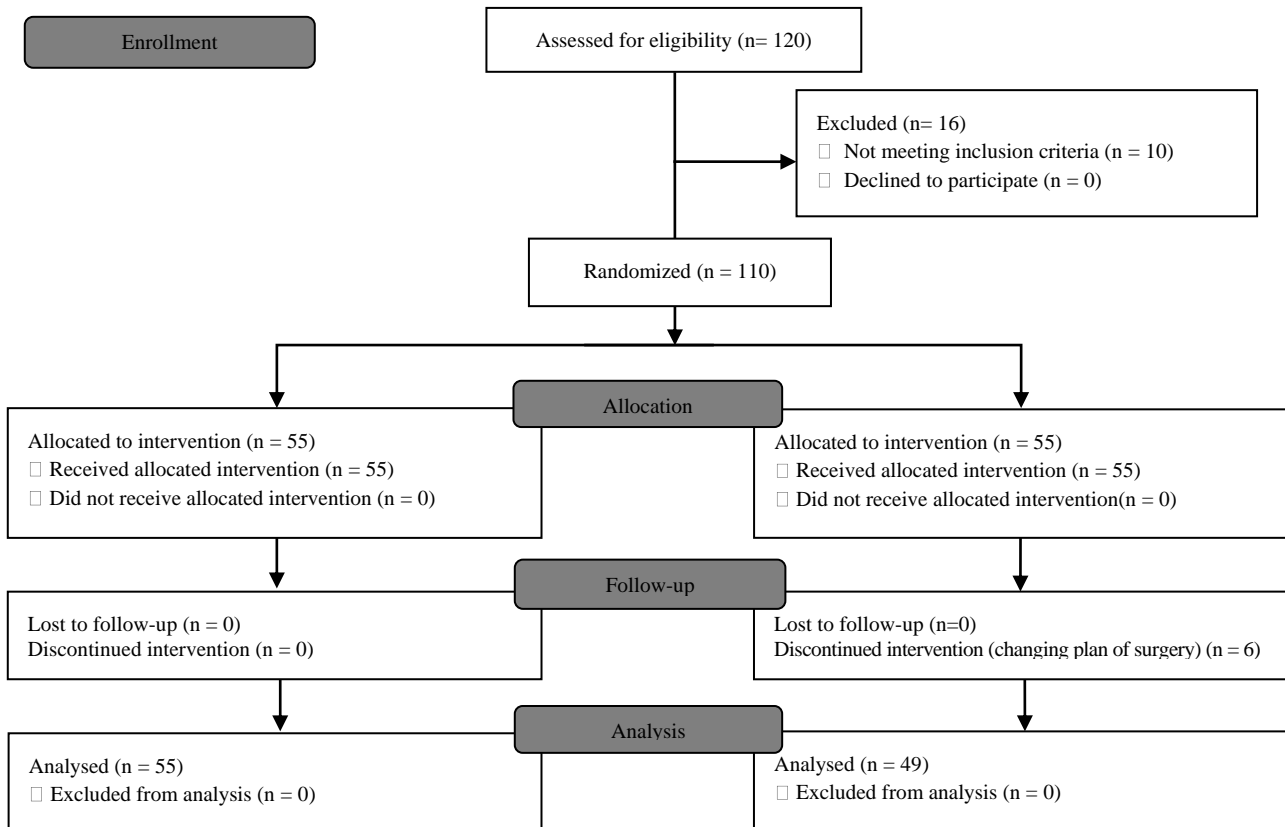


Figure 1. Consort flow diagram

Mean pain scores were statistically different between the study groups at the end of surgery and 1 hour later. Incidence of post-operative nausea was not different between the two groups, but post-operative vomiting was less in paracetamol group. Less additional fentanyl was needed in paracetamol group for post-operative pain relief (Table 2).

**Discussion**

This study showed that IV administration of 1000 mg paracetamol after induction of anesthesia reduced post-operative pain, PONV, and fentanyl consumption in early post-operative period in infertile women undergoing diagnostic laparoscopy as outpatient’s setting. In a study by Sreenivasulu et al. (8), 60 patients undergoing laparoscopic surgeries were randomized into two groups, who were given either an IV placebo or an IV injection of 1 g paracetamol, 15 minutes before induction. They

evaluated post-operative pain and consumption of tramadol as rescue analgesic in the post-operative period and also PONV. They concluded that pre-emptive administration of 1 g of IV paracetamol in patients undergoing laparoscopic surgeries provided satisfactory analgesia and decreased post-operative tramadol consumption and PONV. Their results were similar to ours except that we gave paracetamol after induction of anesthesia and our rescue analgesic was fentanyl.

In a study by Soltani Mohammadi et al. (10) on 80 infertile women who were scheduled for oocyte retrieval, the patients were anesthetized with fentanyl and propofol and anesthesia was maintained with propofol infusion to achieve bispectral index value between 45 and 65. They concluded that pre-operative rectal paracetamol reduced propofol consumption and post-operative pain. Although the route of drug administration was different, their results for reducing post-operative pain were similar to ours.

Table 1. Comparing demographic data between the study groups

Variable	Paracetamol group (n = 55)	Placebo group (n = 49)	P-value
Age (years)	32.2 ± 5.6	30.7 ± 6.4	0.180
Weight (kg)	67.1 ± 11.8	70.6 ± 14.3	0.160
Height (cm)	161.5 ± 3.4	163.4 ± 2.8	0.120
ASA Class I/II	51/4	43/6	0.290
Duration of surgery (minutes)	51.5 ± 19.6	53.3 ± 23.7	0.660

Data are presented as mean ± SD, P < 0.050 between groups. SD: Standard deviation; ASA: American Society of Anesthesiologists

**Table 2.** Comparing post-operative pain scores, nausea, vomiting, and opioid consumption between the study groups

Variables	Paracetamol group (n = 55)	Placebo group (n = 49)	P-value
Pain score at the end of surgery	2.8 ± 2.7	3.5 ± 4.3	0.016*
Pain score 1 hour after surgery	2.1 ± 3.7	2.2 ± 4.6	0.030*
Post-operative nausea (%)	14.5	16.3	0.150
Post-operative vomiting (%)	6	0	0.040*
Need for additional fentanyl (%)	14	36	0.080

Data are presented as mean ± SD and percent, \*P < 0.050 between groups. SD: Standard deviation

In a systemic review and meta-analysis by Apfel et al. (11), they showed that prophylactic IV acetaminophen reduces post-operative nausea and vomiting with an effect size that compares well with data known from other antiemetics through direct mechanisms or through the reduction of post-surgical pain. Their results were similar to ours in reducing post-operative pain and vomiting. In conclusion with using one drug, paracetamol, PONV, and opioid consumption can be reduced.

IV administration of 1 g of paracetamol provided satisfactory analgesia, decreased fentanyl consumption in early post-operative period and PONV in patients undergoing diagnostic laparoscopy for treatment of infertility as outpatients setting.

### Conflict of Interests

Authors have no conflict of interests.

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