Original Article

Comparison between intravenous paracetamol and fentanyl for intraoperative and postoperative pain relief in dilatation and evacuation: Prospective, randomized interventional trial

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Abstract

Background and Aims: Dilatation and Evacuation procedure involves pain, for which pain control measures need to be undertaken. The purpose of this study was to compare paracetamol with fentanyl for pain relief in dilatation and curettage procedures.
Materials and Methods: Sixty female patients were randomly included during the period from March 1, 2012 to February 28, 2013. All patients had received oral midazolam 7.5 mg as a premedication 30 min before procedure in the ward. Group P had received intravenous (IV) paracetamol 15 mg/kg in the waiting area of the operating room 15 min before starting the procedure. Group F had received IV fentanyl 2 ug/kg/min at induction of anesthesia. Pain scores on a numerical rating scale at 5, 15, and 30 min intervals after surgery were recorded.
Results: Mild pain was commonly observed in both groups, an insignificant difference between groups.
Conclusion: The study demonstrates the usefulness of IV paracetamol which may be as effective as fentanyl in dilation and curettage procedures.

Key words: Fentanyl, pain, paracetamol

Introduction

The World Health Organization estimates that worldwide approximately 42 million abortions take place each year.[1] Nearly 90% of abortions are performed in the first trimester of pregnancy, before 14 weeks of gestation.[2-3] There are two approaches to surgical abortion: Vacuum aspiration and dilatation and evacuation (D&E). D&E is a commonly performed daycare procedure in obstetrics. Due to requirement for an early discharge, this procedure requires an anaesthetic technique that can provide rapid recovery.[4] However, like any other surgical procedure, D&E involve pain, and therefore pain control measures have to be undertaken. Many patients still find this surgical procedure extremely uncomfortable; 78-97% report at least moderate procedural pain[5-7] and,[8] therefore, optimizing pain control should be a goal in every procedure.

Short acting narcotic analgesics are commonly used for intraoperative and postoperative pain relief in day care procedures. Fentanyl is a synthetic opioid, which is highly lipid-soluble and rapidly acting drug. Its onset of action is 2 min and duration of action is 30-60 min. Its adverse effects are respiratory depression, pruritus, skeletal and thoracic muscles rigidity, etc.,[9] may delay discharge especially in day care surgeries. It is also not freely available in our country.

Paracetamol is used as a nonopioid analgesic.[10] It is an effective and safe drug for managing mild to moderate pain. It rapidly passes through blood-brain barrier, reaches a high concentration in the cerebrospinal fluid and has an antinociceptive effect mediated by the central nervous system.[11,12] Injectable paracetamol was introduced for intravenous (IV) use in 2002, which provides the onset of pain relief within 5-10 min following administration. The peak analgesic effect is achieved in 1-h and the duration of this effect lasts 4-6 h.[13] It is devoid of any major adverse effects like respiratory and circulatory depression and has no sedative effect making it ideal for day care procedure with mild to moderate pain. The hypothesis is that IV paracetamol is comparable with

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Access this article online

Quick Response Code:

Website: www.joacp.org

DOI: 10.4103/0970-9185.150542

fentanyl for pain relief in D&E procedures. The objective of this study was to compare IV paracetamol with fentanyl for intra- and post-operative pain relief in dilation and curettage procedures.

Materials and Methods

After approval from departmental research and hospital Ethical Review Committee (2159-Ane-ERC-12) written informed consent was taken from all patients participated in the study. The study was conducted from March 1, 2012 to February 28, 2013. Sixty adult American Society of Anesthesiologists (ASA) I-II female patients aged >18 years who underwent elective D&E procedure requiring general anesthesia were enrolled. Gestational age more than 12 weeks, hypersensitivity to any of the study drugs, anticipated difficult airway, morbid obesity, inadequate fasting, or hepatic disorders were excluded.

Each patient fulfilling the inclusion criteria was explained about study purpose and numerical rating scale by primary investigator in the wards/surgical day care unit. All patients were randomly allocated in two groups (30 each) by sealed envelope technique. The envelopes were prepared using a computer generated randomization table. The patients were explained in the ward about study purpose and assessment of pain by Visual Analog Scale (VAS) on 0-10 scales. The interpretation of pain scores was assessed as follows: 0 - no pain, 1-4 mild, 5-7 moderate and 8-10 - severe. All patients had received oral midazolam 7.5 mg as a premedication 30 min before procedure in the ward. Group P had received IV paracetamol 15 mg/kg in the preoperative area 15 min before the start of surgical procedure. Patients in Group F were given IV fentanyl 2 μg/kg at induction of anesthesia.

The conduct and technique of general anesthesia was same for both groups. After application of standard monitoring (noninvasive blood pressure [NIBP], electrocardiogram, and pulse oximetry) (SpO_2), patients were preoxygenated for 3 min. IV propofol 2 mg/kg was used for induction of anesthesia. After loss of consciousness, laryngeal mask airway (LMA) was inserted. Anesthesia was maintained with isoflurane 1.5% in oxygen and nitrous oxide (40:60). NIBP which includes systolic, mean and diastolic pressures, heart rate, pulse oximetry, respiratory rate, and end-tidal CO_2 were recorded. These readings were observed by one of the study author every 3 min from start of surgical procedure until the end. Inadequate pain control during the surgical procedure was assumed if heart rate, blood pressure and respiratory rate are increased 20% above the baseline, which was regarded as preinduction time period. The rescue analgesia consisting of fentanyl was administered in 25 μg increments in the intraoperative period for both groups.

At completion of surgery, patients were allowed to regain consciousness and LMA was removed when patients responded to verbal commands and thereafter transferred to the recovery room. Same study author who recorded intraoperative observations visited the patients in the recovery room and observe pain scores on a numerical rating scale at 5, 15, and 30 min intervals after surgery. If pain score was greater than 3 according to numerical rating scale, rescue analgesia with fentanyl 25 μg in increments was administered. The total dose of rescue analgesia used was also being recorded.

All statistical analysis was performed using statistical packages for social science version 19 (SPSS Inc., Chicago, IL). Quantitative data were presented as mean and standard deviation and analyzed by Student's *t*-test, while qualitative data were presented as frequency and percentage and analyzed by Chi-square test. We took percentage change (PC) in mean hemodynamics (heart rate, systolic blood pressure, and diastolic blood pressure) ranges from baseline to 20% and percentage change in variation (CV) of hemodynamics ranges from baseline to 15%. We calculated the sample size using $n = (Z_{\infty/2} + Z\beta)\ 2\ (CV)^2\ [1 + (1-PC)^2/(PC)^2$ formula at 5% level of significance and 80% power, 60 patients with 30 in each group were selected for this study.

Results

A total of 60 patients who underwent elective D&E due to missed abortions requiring general anesthesia were studied. They were randomly allocated in IV fentanyl and paracetamol group. There was no drop out during the study. It was observed that there was no significant difference between the groups with respect to age, weight, height, and ASA status as shown in Table 1. The measured vital signs did not indicate any significant differences in mean heart rate, blood pressure (systolic, diastolic, and mean arterial pressure) and respiration between the two groups during the course of study as presented in Figures 1-4, respectively.

The pain score based on visual analog score (VAS) were assessed at 5, 15, and 30 min in the recovery room. At 5 min mild pain was observed in both groups, mean pain scores were 1.57 ± 1.1 and 0.97 ± 1.3 in paracetamol and fentanyl groups, respectively except in 2 patients of paracetamol group who faced moderate pain and received rescue analgesia as shown in Table 2, while at 15 and 30 min, pain was observed "mild" in all patients for both groups. We did not observe any significant side-effects of drugs in either group.

Discussion

Poor pain control during the perioperative period leads to complications in both long- and short-term periods. With a good analgesic treatment plan, the anxiety, morbidity, cost

and length of hospital stay in the postoperative period are reduced. D&E is a brief procedure, but it is associated with mild to moderate pain.

Short-acting narcotics are commonly used for perioperative pain relief in brief surgical procedures as these drugs provides good analgesia.[14,15] However, resource variability is a major problem in developing countries, and working conditions may vary from excellent to poor. One of the working challenges in these places is the nonavailability or sudden shortages of opioids/narcotic drugs forcing anesthetist to look for safe alternatives. Fentanyl unlike other opioids has fewer side-effects, but still can cause dose-dependent respiratory depression, which may contribute in delayed awakening, bradycardia, and hypotension, etc.[10] These effects can delay discharge in day care procedures.

Paracetamol is a safe and effective analgesic agent for mild-to-moderate pain. The IV form of this agent has the theoretical advantage of greater predictability and acceptability compared with oral or rectal routes of delivery. It passes easily through the blood-brain barrier and shows its central analgesic effects within 15-20 min, which starts to decline after 4-h of administration. It is preferred in most surgical patients because it is does not affect

Table 1: Demographic and anesthetic measurements of the study patients

Variables	Group P (n = 30)	Group F (n = 30)	*P* value
Age (years)	28.70±4.37	27.47±4.17	0.95
Weight (kg)	67.43±9.03	67.30±8.56	0.95
Height (cm)	154.4±5.09	155.2±5.81	0.57
ASA (%)			
I	20 (66.7)	20 (66.7)	0.99
II	10 (33.3)	10 (33.3)	

Data are presented as mean and standard deviation. Independent sample t-test applied for quantitative data and Chi-square test used for ASA status, ASA = American Society of Anesthesiologists

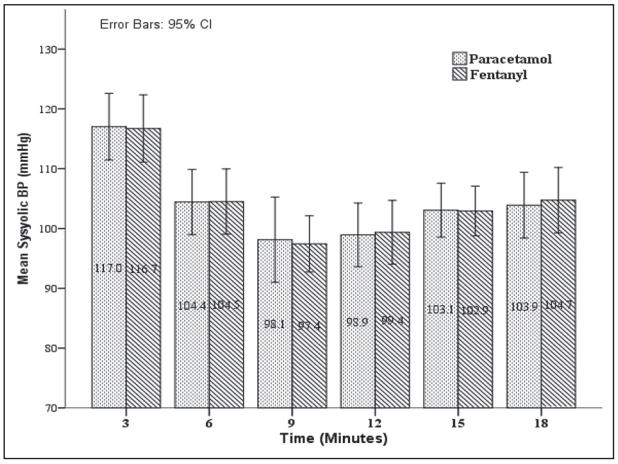

Figure 1: Comparison of mean systolic blood pressure between groups. Error bars shows 95% confidence interval, which also indicate insignificant difference between groups at each point time

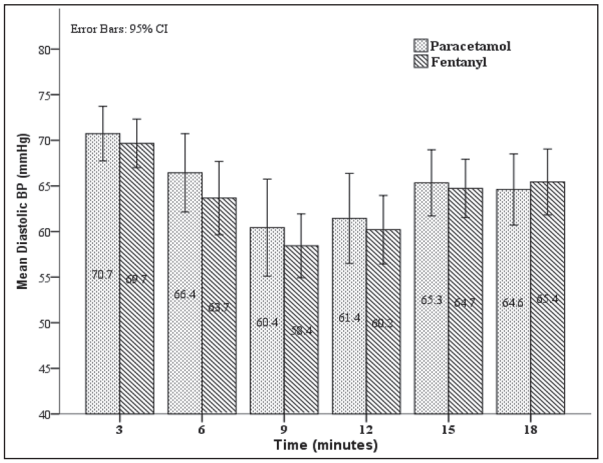

Figure 2: Comparison of mean diastolic blood pressure between groups. Error bars shows 95% confidence interval, which also indicate insignificant difference between groups at each point time

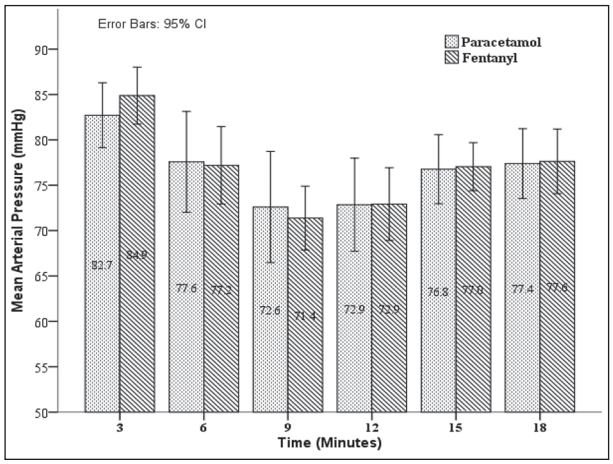

Figure 3: Comparison of mean arterial pressure between groups. Error bars shows 95% confidence interval, which also indicate insignificant difference between groups at each point time

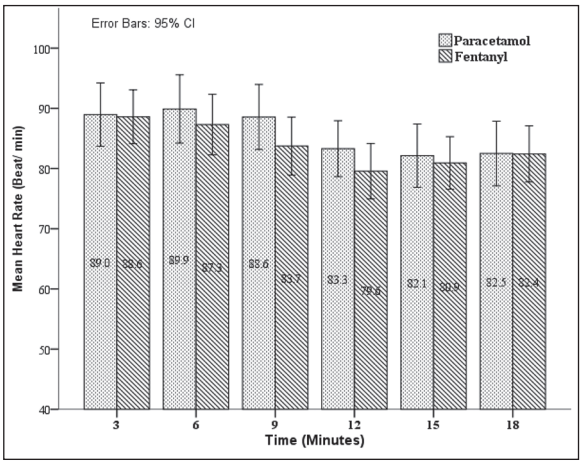

Figure 4: Comparison of mean heart rate between groups. Error bars shows 95% confidence interval, which also indicate insignificant difference between groups at each point time

Table 2: Comparison of pain relief between groups in dilation and evacuation (D&E) procedures

Pain (recovery room at 5 min)	Group P (n = 30) (%)	Group F (n = 30) (%)	*P* values
Mild	28 (93.3)	30 (100)	0.49
Moderate	2 (6.7)	0 (0)	
Severe	0 (0)	0 (0)	

Data are presented as n (%) and Fisher exact test used to compute P value for statistical significant

mental status, bleeding, respiratory drive, gastric mucosa integrity, or renal function.[16] We undertook this prospective randomized study to examine IV paracetamol as a suitable alternative to fentanyl for perioperative pain relief in dilation and curettage procedures.

Sinatra *et al.*[17] compared IV paracetamol with placebo after major orthopedic surgery. They found that IV paracetamol administered over a 24-h period in patients with moderate to severe pain after orthopedic surgery provided rapid and effective analgesia and was well-tolerated. A study in patients undergoing lower segment cesarean section, in which IV paracetamol was compared with oral Ibuprofen, as the analgesic supplementation agent to morphine, indicated that patients in IV paracetamol had better pain control compared to ibuprofen group.[18] Tsang *et al.*[19] did a study to see the opioids sparing effects of paracetamol in preoperative hip fracture patients, and they found that IV paracetamol had a significant opioid-sparing effect and satisfactory pain relief in preoperative hip fracture patients.

A randomized, double-blind study had compared IV paracetamol and IV morphine for acute limb trauma in an urban United Kingdom emergency department. Approximately, half in each group had a fracture, and the other half had soft tissue trauma. They received either 1000 mg IV paracetamol or 10 mg IV morphine. The outcome measures were: Pain score measured on a visual analog scale; requirement for rescue analgesia; and frequency of adverse reactions. There was no significant difference in the rescue medication, but there were significantly more adverse reactions in the morphine group. There were no significant differences between the groups in mean pain score and patient satisfaction.[20]

There was another randomized study of 84 patients undergoing out-patient knee arthroscopy comparing pain score and adverse reactions between 1000 mg IV paracetamol and IV morphine (0.1 mg/kg) given prior to awakening from general anesthesia. There was no difference in pain scores between those patients given the 2 medications, but there were more adverse reactions, dizziness, nausea, and vomiting, in the patients who received morphine. This study has important implications for discharge time from out-patient surgery centers.[21]

Our study did not indicate any statistically significant difference between the IV paracetamol and IV fentanyl groups in pain scores. Neither did we note any significant difference in physiological parameters and side-effect profiles clinically between the two groups. Limitations of our study were small sample size, lack of the placebo arm, single-blinded nature and short follow-up duration. All of these could have improved the results of our study, but due to technical reasons and limited availability it was not possible.

Conclusion

The study demonstrates the usefulness of IV paracetamol as it provides equivalent analgesia to fentanyl in dilation and curettage procedures.

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How to cite this article: Ali MA, Shamim F, Chughtai S. Comparison between intravenous paracetamol and fentanyl for intraoperative and postoperative pain relief in dilatation and evacuation: Prospective, randomized interventional trial. J Anaesthesiol Clin Pharmacol 2015;31:54-8.
Source of Support: Nil, **Conflict of Interest:** None declared.