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Oral Paracetamol Based Post-Operative Analgesia in Adult Off Pump Coronary Artery Bypass Grafting Surgery Patients Post Extubation A Safe Effective and Low-Cost Practice

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ABSTRACT

To assess effectiveness and other benefits of oral paracetamol-based post-operative analgesia for adult off pump Coronary Artery Bypass Grafting surgery patients post extubation in the ICU. The study was to assess the efficacy of the regular departmental analgesic protocol of regular Enteral paracetamol with small dose (30 microgram) IV boluses of Inj. Fentanyl for breakthrough pain. 100 (both male and female) adult patients undergoing Off-Pump Coronary Artery Bypass Grafting (CABG) surgery were studied. All had Total Intravenous Anaesthesia without inhalational agents and after surgery, were shifted to Post Operative ICU for overnight ventilation as per usual hospital protocol. All patients were administered 2 suppositories of Paracetamol 250 mg at the time of sponging of body early morning next day of surgery at about 5 am while on ventilator. Extubation was done between 8.30 AM to 9 AM. All were given 650 mg paracetamol 6 hourly by mouth, starting from noon. 30micrograms of Fentanyl was given IV whenever the patients complained of pain in spite of oral paracetamol. Effectiveness of Analgesia was assessed using NRS (Neumeric Rating Scale for pain) of 0-10 with 0 meaning no pain, 1 minimum pain and 10 maximum pain. Side effects if any were also noted. The mean weight was 68.4 kgs and mean age 61.4 years. 72 patients were men and 28 patients were women. The mean height was 161.6 cm. The Mean ejection fraction was 48%. Mean Duration of anesthesia was 310.4 minutes (Time from Induction to shifting to ICU). The mean pain score (NRS) at 12 hours (from extubation) was 3, at 24 hours was 2, at 48 hours was 1 and at 72 hours was 1. Number of Rescue doses of Fentanyl needed were 3-6 doses in 91 patients while 9 patients needed 8 doses. Post Operative Nausea/Vomiting (PONV) was seen in 2 patients. Patients had very good analgesia and were comfortable with the technique. This simple protocol for post-op analgesia is very easy to practice, had no major side effects and is very economical. This is like the WHO stepladder principle of analgesia for chronic pain, where the base advised is regular, by-the-clock oral paracetamol with the addition of other analgesic drugs later.

INTRODUCTION

Patients who have heart surgery may have pain around the incisions from sternotomy, chest tube insertion and incisions for harvesting leg veins. Numerous unfavourable outcomes, including cardiac ischemia, respiratory failure and thromboembolic problems, might be brought on by postoperative discomfort^[1]. In order to reduce such discomfort in the early postoperative phase, parenterally administered analgesics such as opioids and nonsteroidal anti-inflammatory medications (NSAIDs) are widely used. However, these analgesic medications' side effects limit their effectiveness by making it more difficult for patients to recover from surgery^[2]. Parenteral as well as oral NSAIDs, like Ketorolac and Diclofenac, may be linked to gastrointestinal lesions including ulceration, renal dysfunction and bleeding from platelet dysfunction. Opioids, like morphine, may be linked to respiratory depression, excessive sedation, biliary spasm, depression of gastrointestinal motility, Post Operative Nausea and Vomiting (PONV) and for older patients, confusion^[3].

Aspirin and acetaminophen (Paracetamol) are two examples of Non opioid analgesics with antipyretic effects. Aspirin belongs to nonsteroidal anti-inflammatory drugs that are in use for very long time and has anti inflammatory effects as well. The main way the NSAID medications work is by blocking the production of prostaglandins and cyclooxygenase, which are thought to be significant environmental factors in the prevention of pain and hypersensitivity^[4]. There had been two well known forms of cyclooxygenase (COX): cyclooxygenase 1 (COX-1), which is involved in hemostasis, platelet aggregation and gastric mucosa protection and cyclooxygenase 2 (COX-2), which is useful in treating fever, pain and inflammation^[5]. The analgesic effect of acetaminophen has been proposed to be mediated mostly by COX-3, a recently identified protein^[6]. The reduction of the COX pathway activity by Paracetamol is thought to inhibit the synthesis of prostaglandins in the central nervous system, leading to its analgesic and antipyretic effects. The analgesic properties may be due to a stimulating effect on the descending serotonergic pathways in the central nervous system (CNS). The word "paracetamol" is an abbreviated form of para-acetyl-amino-phenol, which was coined by Frederick Stearns *et al.* in 1956. Present study was conducted to assess the effectiveness and other benefits of oral paracetamol-based post-operative analgesia for adult post-cardiac surgery patients post extubation in the ICU.

Paracetamol is available in different forms for administration. Oral Tablets, IV infusions and Suppositories are the most widely used in adults. Oral tablets of Paracetamol are one of the most easily available, Cheap, easily administered and most widely

used analgesic-antipyretic medicines in the world and is available OTC (Over The Counter) without prescription in many countries including USA. Cost of a 650mg tablet that has been used in the study is 2 Indian Rupees (INR) only making a total of 8 rupees for a whole day. Many centers use Intravenous paracetamol which is also very effective analgesic but costs 350-550 rupees per 1000mg dose and need syringes, infusion tubes, intense nursing care etc and will practically cost at least INR 750 per dose, that is INR 3000 per day for paracetamol alone, which very many patients may not be able to afford. Single 250mg Paracetamol suppository costs INR 20 (20 x 2= 40 INR per adult dose) and needs a pair of disposable gloves and one time nursing attention for administration. In 1996, WHO published the Second Edition of its book "Cancer Pain Relief"^[7] in which the concept of Step Ladder pattern of Analgesia for Cancer pain was introduced, where the initial step in pain management is Paracetamol with other drugs added in next steps. Our analgesic protocol use here also is based on WHO stepladder principle of analgesia for chronic pain.

MATERIALS AND METHODS

This prospective study was conducted in the Cardio Thoracic-ICU (CT ICU) and 100 adult (both male and female) patients undergoing Off-Pump Coronary Artery Bypass Grafting (CABG) surgery. The following criteria was used for selection of study subjects:

Inclusion Criteria:

- Age group between 40-70 years of both male and female gender. Females-non pregnant
- Patients undergoing elective open-heart surgeries- Coronary artery bypass grafting on Off-pump technique. Stable post-operatively

Exclusion Criteria:

- Patients with known allergy to Paracetamol or Fentanyl.
- Patients with expected prolonged ventilation like those taken up as emergency, unstable patients on IABP support and patients on heavy inotropic support.
- Patients with known renal/hepatic problems and those with blow 40% LV Ejection Fraction
- Patients who were on Anti-platelet drugs within 5 days of surgery

For the surgery, all patients were anesthetized in the OT with an intravenous technique using Midazolam, Fentanyl, Propofol, Morphine and Pancuronium and ventilated in the OT with oxygen and medical air with 40% FIO₂. Patients were shifted to

CT-ITU after surgery and were ventilated overnight with 40% FIO₂ and were given 30 ug of Fentanyl and 1 mg of Midazolam as intermittent boluses for sedation. Total dose of Morphine used during anaesthesia was 10-20mg per patient. Patients were administered 2 suppositories of Paracetamol 250 mg at the time of sponging of body early morning next day at about 5 am while on ventilator. Patients were extubated in the morning between 8.30 am to 9 am and oral feeds started 45 minutes later. 650 mg tab Paracetamol was started orally by noon and given 6 hourly irrespective of the absence of pain as a pre-emptive technique. 30ug of Fentanyl was given IV if anybody had breakthrough pain. Pain control was assessed in all patients using a Numeric Rating Scale (NRS) of 0-10 with 0 meaning no pain, 1 minimum pain and 10 maximum pain. Data thus obtained were subjected to statistical analysis for significant pain >4NRS. $p < 0.05$ was considered significant.

Patients were mobilised on the 2nd postoperative day after removing the chest drainage tubes. 50ug of Fentanyl was given IV to all patients 10 minutes before removal of tubes on 2nd post operative day. Patients were shifted from ICU to postoperative ward on the 3rd postoperative day. They were assessed for pain for 72 hours from time of extubation. None of the patients required Inj Fentanyl after shifting from ICU/reaching ward (Table 1 and 2).

RESULTS AND DISCUSSIONS

The mean pain score (NRS) at 12 hours was 3, at 24 hours was 2, at 48 hours was 1 and at 72 hours was 1, which shows that the patients were having adequate control of pain. Rescue doses of Fentanyl needed was 3-6 doses for 93 patients while 7 (out of 100 patients) needed 8 doses and PONV was seen in 2 patients. Pain is defined as an unpleasant emotional and sensory experience linked to prospective or existing tissue injury^[8]. Postoperative pain after medical therapy (such as surgery) might occur and this sets off physiological and biochemical stress reactions^[9]. Pain is a significant clinical, social and economic issue as well as a global public health concern^[10]. Most people experience post-surgical pain as nociceptive discomfort^[11]. It is well-recognized that surgical trauma can cause hyperalgesia and central and peripheral sensitization, which, if left untreated, can result in persistent postoperative pain following surgery^[12]. The present study was conducted to assess the effectiveness and other benefits of oral paracetamol-based post-operative analgesia for adult post-cardiac surgery patients post extubation in the ICU (Fig 1).

In our study, the mean weight was 68.4 kgs. The mean height was 161.6 cm. The ejection fraction was 48% and mean duration of anesthesia was 310.4 minutes. Cattabriga *et al.*^[13] included 113 patients in which 56 patients received paracetamol and 57

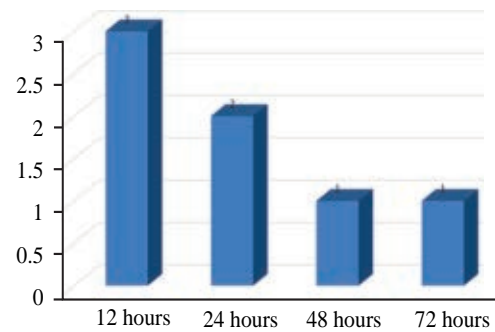


Fig. 1: Comparison of pain (NRS) with time from Extubation

Table 1: Baseline characteristics

Parameters	Mean value
Weight (Kgs)	72.4
Height (cm)	174.6
Ejection fraction (%)	48
Duration of anesthesia (minutes)	310.4
Age(Years)	61.4

Table 2: Comparison of pain (NRS)

Time	Rating of Pain	Pain Rating >4
12 hours	3	0
24 hours	2	0
48 hours	1	0
72 hours	1	0

placebo. Intravenous study drug (1 g) was administered 15 min before the end of surgery and every 6 hours for 72 hours. Baseline characteristics were equivalent between the two groups. At 12, 18, 24 hours after the end of operation, patients who received paracetamol had significantly less pain at rest after this time the two groups did not differ. During a deep breath the difference was significant only at 12 hours. Paracetamol group required less cumulative morphine than placebo group (48 mg vs 97 mg) even if the difference did not reach statistical significance.

The mean pain score (NRS) at 12 hours was 3, at 24 hours was 2 at 48 hours was 1 and at 72 hours was 1 in our study. Gousheh *et al*^[14] assessed whether paracetamol can provide effective analgesia as a sole analgesic at least in the first few hours postoperatively. 30 patients of ASA class I, aged 18-50 years, candidate for laparoscopic cholecystectomy were recruited and randomly divided into two equal groups. Group A (paracetamol group) received 1 gr paracetamol and group B received placebo ten minutes after the induction of anesthesia. 0.1 mg Kg⁻¹ Morphine was administered intravenously based on patient's complaint and pain score >3. Pain score and the opioids consumption were recorded in the first six hours postoperatively. Patient's pain was measured by the visual analogue scale(VAS). The pain score was lower in group A, but the morphine consumption showed no significant difference between the groups during the first 6 hours postoperatively.

Rescue doses of IV Fentanyl of 30ucg each was needed 3-6 times in the 3 days of study in 93 patients

while 8 doses were needed in 7 patients whereas PONV was seen in 2 out of 100 cases in our study. Petterson *et al.*^[15] studied eighty patients undergoing coronary artery bypass grafting with cardiopulmonary bypass. Patients were randomized to 2 groups: acetaminophen, 1g every sixth hour during the postoperative period, either as tablets or intravenously after extubation. The amount of opioids administered during the study period was measured starting with acetaminophen administration during the stay in the ICU until 9 o'clock the following morning. Incidence of postoperative nausea and vomiting (PONV) was noted. Pain was evaluated with a visual analog scale (VAS) from 0-10. Three patients, 2 in the oral and 1 in the intravenous group, were excluded because of incomplete data. The intravenous group received less opioids than the orally treated group, 17.4 +/- 7.9 mg compared with 22.1 +/- 8.6 mg. PONV incidence and VAS scores did not differ. During the first hours after extubation, 50 of 77 patients reported VAS scores >3 with no difference between groups.

CONCLUSIONS

Patients had very good analgesia and were comfortable with the technique. This simple protocol for post-op analgesia is very easy to practice had no major side effects and is very economical. This is like the WHO stepladder principle of analgesia for chronic pain, where the base advised is regular, by-the-clock paracetamol with the addition of NSAIDS and opioid drugs later.

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