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ABSTRACT

Today surgery is an everyday occurrence. Although the mortality due to surgical procedures have come down significantly, adverse effects such as pain, post operative nausea and vomiting are still common. Poorly controlled post operative pain can lead to serious complications. Aim of this study is to assess intra and post operative analgesic effects of i.v. paracetamol and i.v. fentanyl used pre-emptively also to compare their hemodynamic effects.

Material and method: Sixty patients undergoing various surgical procedures were included in the study. Patients were randomized into two groups. In group I - i.v. paracetamol 1 gm. In 100 ml saline infusion was given over 15-20 mins, 30 min prior to induction of anesthesia. In group 2 iv fentanyl 100ug was given in 100 cc NS. To start with, written consent was obtained and the patients were explained about the visual analogues score and pain severity score. Base line vital parameters like pulse rate, systolic and diastolic B.P. and Spo2 were recorded. The recommended drugs were given 30 min. prior to induction of anesthesia. 30 min. after giving the study drugs pre medication was given as inj. Glycol pyrolate 2mg. with inj. Midazolam 1 mg. i.v. to all the patients. Anesthesia was induced with inj. Thiopentone sodium 5 mg/kg and inj. succinyl choline 2mg/kg, after IPPV, airway was secured with appropriate sized cuffed endotracheal tube. Anesthesia was maintained with O2 *N2O-50:50, vecuronium as a muscle relaxant and intermittent halothane. Pulse rate, SBP, DBP and Spo2 were recorded every 15 minuets during the procedure. At the end of surgery residual neuromuscular blocked was reversed with inj. Neostigmime methyl sulfate 2.5 mg. and inj. Glycopyrrolate 5mg. After through oral suction and onset of spontaneous respiration with adequate muscle power, judged by head lift for 5 secs, subsequently patients were assessed for pain relief. The assessment of post operative pain, in immediate post operative period i.e. in immediate post operative period, after the reversal when the patient was fully oriented and conscious enough to answer the question asked and further at 1 hour, 2 hours, 4 hours and 6 hours was made. The changes in pulse rate, SBP, DBP and respiratory rate, Spo2 at different time periods were noted. For postoperative pain assessment, VAS and Pain Severity Score were used. The patient were given rescue drug when their pain severity score was 2 i.e when they themselves complained for pain and their visual analog score was between 7-10 at this point, these patients were excluded from the further comparison in the study. The duration of analgesia was taken as the time between administration of analgesic drug and administration of rescue drug. Side effects, such as nausea, vomiting, respiratory depression, itching, allergic reaction, stomach irritation, diarrhoea, and constipation, were cross-examined and recorded. Results: pain severity score should no significant difference among the two group while VAS also was similar in both the gps. Duration of analgesia was statistically significant in group 1. Conclusion: preemptive iv paracetamol is long acting and provides better analgesia than fentanyl with less side effects.

1. Introduction

- Pain is the most compelling reason that brings a patient to the physician and whatever the cause, it demands relief. Pain has been defined by international association for study of pain, as, “unpleasant sensory and emotional experience associated with actual or potential tissue damage.”

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• Various methods to relieve intra-operative and post operative pain are
  • SYSTEMIC ANALGESIA
  • SYSTEMIC OPIOIDS ADMINISTRATION : such as natural opium alkaloids (morphine), semi synthetic opioids (oxycodone) and synthetic opioids (pethidine hydrochloride, fentanyl citrate, tramadol hydrochloride, butorphenol tartrate, buprenorphine hydrochloride).
  • NSAIDS : such as non selective salicylates (asprin), propionic acid derivatives (ibuprofen, ketoprofen), anthranilic acid derivatives (mephenamic acid), arylacetic aci derivative (ketorolac) sulphonamide derivative (nimesulide) and para amino phenol derivative (paracetamol). Cox-2 selective - paracoxib sodium, Valdecoxib, celcoxib.
  • LOCAL ANAESTHETICS:
    • Regional blocks
    • Continuous infusion with or without opioid – intrathecal, epidural or in patient controlled analgesia.
  • Wound infiltration.
  • NON PHARMACOLOGICAL APPROACH LIKE TRANSCUTANEOUS ELECTRIC NERVE STIMULATION

METHOD:
• 60 patients undergoing open cholecystectomy were enrolled into the study. Patients were divided into 2 groups:
  • In Group A, iv paracetamol 1 g (100ml infusion, over 15-20 mins) was given 30 minutes prior to induction.
  • In Group B, iv fentanyl (1 microg/kg), (in 100ml saline, over 15-20 mins), was given 30 minutes prior to induction and 1 microg/kg/hr as continuous infusion intraoperatively.

Intra operatively vital parameters & Postoperatively, pain scores, hemodynamic parameters, postoperative analgesic consumption, side effects, patient satisfaction were recorded.

Patients who were given rescue analgesia at any point in the study were further excluded from the study.

PAIN SEVERITY SCORE:
• No pain
• Slight pain (complains on asking)
• Moderate pain (self complaining)
• Severe pain

VAS:
• 0-10; 0: no pain
• 10: worst pain imaginable
• Criteria for Exclusion
• The criteria for exclusion from the study were:
  1. American Society of Anesthesiologists (ASA) scores III and IV.
  2. History of allergic reactions to paracetamol or fentanyl.
  3. Chronic alcoholism, deficiency of liver and kidney, deranged LFT & KFT.
  4. Cardiovascular system illness.
  5. Bleeding diathesis.

Results
• It was observed that there was no great variation between the groups with respect to age, weight and duration of surgery.

So to say, they were comparable demographically.

In group A, 2 patients were given rescue analgesic at the end of 1 hour. So these patients were excluded from further study. At the end of 2 hours, 3 more patients demanded rescue drug. So these patients were also excluded from further study. At the end of four hours, remaining all patients demanded rescue drug.

The rise in pulse from base line value from 82.27±5.55 per min to 85.60±6.54 per minute was noticed after 20 minutes of paracetamol administration. The mean change 3.33 ± 4.16 was significant.

During intraoperative period the mean pulse rate was 82.97±5.85 per min. the mean change was 0.70 ± 3.44 which was not significant.

The mean pulse rate in immediate post operative period was 82.93±5.97 per min. mean change of 0.67 ±3.38 was not significant.

After 1 hour post operatively, the pulse rate was 84.90±5.49 per min, with mean change of 2.63 ±4.13 which was significant.

After 2 hours post operatively 28 patients remained in the study. The mean pulse rate was 85.97±3.5 per min with mean change of 3.70 ±4.20 which was significant. The increase in pulse rate in post operative period may be due to feeling of pain by the patient.

After 4 hours post operatively 25 patients remained. The mean pulse rate was 88.58±3.28 per min. the mean change was 6.29±7.99 which was significant.

After 5 hrs all the remaining patients demanded rescue analgesic, so no further study was conducted.

SYSTOLIC BLOOD PRESSURE (SBP)
• The mean systolic BP before administration of analgesic was 124.2 ± 8.49 mm Hg which increased to 125.67 ± 8.08 mmHg after paracetamol administration. The mean change was of 1.47 ± 5.60 which was not significant.

Intraoperatively, the mean systolic BP was 124.73± 7.27 mm Hg which was almost equal to baseline value. The mean change of 0.53± 5.80 was not significant.

During immediate post operative period, the systolic BP was 121.87±7.46 mmHg with mean change of 2.33±3.02. This decrease was significant.

After one hour post operatively the mean systolic BP was 123.2±5.85 mmHg with mean change of 1.00 ± 5.00 which was not significant.
• After 2 hours post operatively the mean systolic BP was 123.17 ± 4.58 mmHg with mean change of 1.00 ± 5.00 which was not significant.
• After four hours post operatively the mean systolic BP of remaining patients was 124.12 ± 3.85 mmHg. The mean change of 2.47 ± 5.16 which was not significant.
• Upto intra operative period, there was not significant change in systolic BP. In the immediate post operative period SBP showed a decline, afterwards there was a gradual increase in mean SBP.
• DIASTOLIC BLOOD PRESSURE
• After analgesic administration, the DBP increased to 82.47 ± 6.58 mm Hg from baseline mean DBP of 80.00 ± 6.49 mmHg. The mean change was 2.47 ± 5.16 that was significant.
• The mean intra operative DBP was 81.53 ± 7.28 mm Hg with mean change of 1.53 ± 2.23 that was not significant.
• In immediate post operative period, the DBP decreased to 77.13 ± 5.92 mmHg from baseline value with a significant mean change of 2.87 ± 3.13.
• After 1 hour post operatively the mean DBP was 80.60 ± 5.68 mmHg with non significant mean change of 0.40 ± 4.11.
• After 2 hours post operatively the mean DBP of remaining patients was 78.08 ± 5.58 mmHg with non significant mean change of 1.25 ± 4.85.
• After four post operatively, the mean DBP was 79.53 ± 3.91 mm Hg, which was almost equal to base line value. The mean change was 0.35 ± 6.45 that was not significant.
• Upto intra operative period, there was no significant change in mean DBP. In immediate post operative period, the mean DBP decreased after that there was gradual increase in DBP, which became almost equal to baseline after four hours post operatively.
• PAIN SEVERITY SCORE (PSS) AND VISUAL ANALOGUE SCALE (VAS)
• The mean PSS and VSS immediately post operatively were 0.07 ± 0.25 and 0.33 ± 1.50 respectively.
• After 1 hour post operatively, PSS increased to 0.20 ± 0.54 with a mean change of 0.13 ± 0.35 and VAS increased to 0.66 ± 0.73 with a mean change of 0.33 ± 0.57. Hence both showed significant change.
• After 2 hours post operatively, the mean PSS of remaining patients was 0.32 ± 0.57 with a mean change of 0.25 ± 0.58 and the mean VAS of remaining patients was 0.78 ± 0.88 with a mean change of 0.45 ± 0.69. Hence both showed a significant increase from immediate post operative values, but not significant change compared to 1 hr post operatively.
• After four hour post operatively, the mean PSS of remaining patients was 1.07 ± 0.62 with a mean change of 1.00 ± 0.63 and the mean VAS of remaining patients was 2.63 ± 2.73 with a mean change of 1.73 ± 1.57. Hence both showed a highly significant increase.
• In group B, 5 patients were given rescue analgesic at the end of 1 hour; so these patients were excluded from further study. At the end of 2 hours, 12 more patients demanded rescue drug, so these patients were also excluded from further study. Before 6 hours post operatively, remaining 13 patients demanded rescue analgesic, leaving no scope for further study.
• PULSERATE
• The rise in pulse rate from baseline value of 80.10 ± 7.67 per min to 81.07 ± 8.70 per min was noticed after 20 minutes of analgesic administration. The mean change of 0.97 ± 5.29 was not significant.
• During intra operative period, the mean pulse rate was 79.43 ± 8.13 per min. The mean change was 0.67 ± 2.87 that was not significant.
• The mean pulse rate in immediate post operative period increased to 82.30 ± 5.41 per min. there was significant mean change of 2.10 ± 5.38.
• After 1 hour post operatively, the mean pulse rate was 84.90 ± 5.49 per min with significant mean change of 4.23 ± 8.17.
• After 2 hours post operatively, the mean pulse rate of remaining patients was 87.35 ± 9.46 per min with a highly significant mean change of 7.54 ± 8.88.
• After four hours post operatively, the mean pulse rate of remaining patients was 90.30 ± 10.15 per min with a highly significant mean change of 10.75 ± 10.30.
• The mean pulse rate before and after analgesic administration and during intra operative period was almost equal. From immediate post operative period afterwards there was a continuous increase in pulse rate. This increase may be due to feeling of pain by the patient.
• SYSTOLIC BLOOD PRESSURE
• The mean systolic BP before administraton of analgesic was 127.27 ± 2.09 mmHg which decreased to 121.67 ± 10.88 mmHg after fentanyl administration. The mean change was 5.60 ± 4.18 which was highly significant.
• Intra operatively, the mean SBP was 124.27 ± 11.30 mmHg which was less than the baseline mean SBP. The mean change of 3.00 ± 2.39 was not significant.
• During immediate post operative period, the mean SBP was 127.20 ± 9.06 mmHg which was almost equal to baseline value the mean change of 0.80 ± 10.94 was not significant.
• After 1 hour post operatively, the mean systolic BP was 128.07 ± 8.93 mmHg with mean change of 0.80 ± 10.94 which was not significant.
• After 2 hours post operatively, the mean systolic BP of remaining patients was 128.92 ± 8.88 mmHg. The mean change was 1.77 ± 4.11 which was not significant noticeably in comparision to immediate post operative period.
After four hours post operatively, the mean systolic BP of remaining patients was 129.90±8.42 mmHg. The mean change was 2.30±13.80 which was not significant.

The mean SBP after administration of analgesic showed a decline from baseline value. After that mean SBP increased continuously. It was almost equal to baseline value in immediate post operative period.

**DIASTOLIC BLOOD PRESSURE**

After analgesic administration, the diastolic blood pressure (DBP) decreased to 76.33±7.17 mmHg from the mean baseline DBP of 79.07±7.64 mmHg. The mean change was 2.73±2.49 that was significant.

The mean intra operative DBP was 77.33±7.33 mmHg with mean change of 1.73±1.46 that was significant.

In the immediate post operative period, the mean DBP was 79.60±5.25 mmHg with the mean change of 0.53±7.18 that was not significant.

After 1 hour post operatively, the mean DBP was 81.20±5.88 mmHg with non significant mean change of 2.13±8.24.

After 2 hours post operatively, the mean DBP of the remaining patients was 82.23±5.69 mmHg with non significant mean change of 3.31±9.23.

After four hours post operatively, the mean DBP of the remaining patients was 82.10±5.00 mmHg with non significant mean change of 3.70±9.09.

After analgesic administration, the mean DBP decreased from baseline pre operative values. After that mean DBP increased continuously. In the immediate post operative period the mean DBP was almost equal to baseline values.

**PAIN SEVERITY SCORE (PSS) AND VISUAL ANALOGUE SCALE (VAS)**

The mean PSS and VAS immediately post operatively were 0.13±0.71 and 0.67±1.35 respectively.

After 1 hour post operatively, PSS increased to 0.40±1.21 with a mean change of 0.27±0.45 and VAS increased to 1.60±2.68 with a mean change of 0.93±1.46. Hence both showed a significant increase.

After 2 hours post operatively, the mean PSS of remaining patients was 1.13±0.68 with a mean change of 1.00±0.69 and the mean VAS of remaining patients was 4.08±2.16 with a mean change of 3.92±1.97 hence both showed a highly significant increase.

After four hours post operatively, the mean PSS of remaining patients was 1.95±0.67 with a mean change of 1.82±0.67 and the mean VAS of remaining patients was 8.57±1.80 with a mean change of 7.80±0.84 hence both showed a highly significant increase.

Post operatively PSS and VAS increased conti
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>70 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>120 ± 10/80 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td>98 ± 2</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Comparison of Mean Change ± SD in Stopping P. A.**

**Comparison of Mean Change ± SD in Pulse Rate**
Conclusion:

- Paracetamol (Group A) provided good analgesic efficacy intraoperatively and effect was comparable to fentanyl (Group B).
- Postoperatively, Group B patients showed greater increase in heart rate, Pss and Vas.
- The mean duration of analgesia with paracetamol was longer as compared to fentanyl.
- With paracetamol, 2 patients complained of nausea and 1 of vomiting.
- With fentanyl, 6 patients complained of nausea, 3 of vomiting, and 6 of drowsiness.
- As an intravenous pre-emptive analgesic, paracetamol provides good analgesia, intraoperatively, comparable to fentanyl. It also has a longer duration of analgesia postoperatively, prolongs first post-op analgesic demand, and has minimal side effects.

Discussion:

- As knowledge of the epidemiology and pathophysiology of postoperative pain increases, a new analgesic concept has been developed and applied for the prevention of pain whereby analgesic treatment is started prior to trauma and surgical intervention. Within this concept, referred to as pre-emptive analgesia, it is believed that through application of an analgesic medicine or technique, pain will either subside or be prevented prior to the painful stimulus. This effect is achieved by suppressing, either together or separately, central or peripheral sensitization.
- Paracetamol is a viable alternative to the NSAIDs, especially because of low incidence of adverse effects. It may be appropriate to combine paracetamol with NSAIDs.
- Opioids such as morphine may be associated with respiratory depression, excessive sedation, bilary spasm, depression of gastrointestinal motility, nausea, and vomiting (postoperative nausea and vomiting) and particularly in older patients - confusion.
- Paracetamol now also available for IV use, is not an NSAID and interferes neither with platelet nor kidney functions, nor does it present the unwanted effects of NSAIDs.
- Parenteral NSAIDs such as ketorolac may be associated with gastrointestinal lesion ulceration, renal dysfunction and bleeding caused by platelet inhibition.
- Paracetamol is not associated with the increased incidences of nausea, vomiting and respiratory depression observed with opioids and does not interfere with platelet or kidney function.
- Preincisional administration of either intravenous or epidural 2 mg/kg fentanyl lowers the postoperative analgesic use and prolongs the first analgesic requirement time.
- Preemptive IV paracetamol 1 g provided good quality postoperative analgesia, with decreased consumption of morphine and minimal side effects.
References:


