COMPARISON OF EFFICACY OF INTRAVENOUS PARACETAMOL AND INTRAVENOUS DICLOFENAC FOR POST-OPERATIVE ANALGESIA IN LAPAROSCOPIC SURGERIES
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ABSTRACT

BACKGROUND
This was a double blind, prospective randomized clinical study. 105 patients scheduled to undergo elective laparoscopic surgery in a tertiary hospital between Jan 2014 to Aug 2015 were randomly selected by closed envelope method after obtaining the institute’s ethical committee approval.

METHODS
One hundred and five patients belonging to ASA-PS I & II, scheduled for elective laparoscopic surgery were included. The patients were randomly allocated to one of the three groups to receive one gram/100 ml IV paracetamol (group A), 75 mg of IV diclofenac in 100 ml saline (group B) and 100 ml of normal saline (group C) over 20 min before the completion of the skin closure. Analgesia was assessed postoperatively. VAS score was used to assess the efficacy of analgesia.

RESULTS
We found that HR was comparable between paracetamol and diclofenac. SBP, DBP and MAP were low in diclofenac group till the patient was given rescue analgesia which was statistically significant. The duration of analgesia was 317.14±55.549 min with paracetamol and 297.43±65.311 min with diclofenac which was comparable. There were no serious side effects noted with any of the groups.

CONCLUSIONS
Paracetamol appears to be equally safe and effective analgesic for postoperative pain like diclofenac. It is haemodynamically stable and does not cause respiratory depression. Paracetamol is devoid of any serious side effects and can be used for both intra and postoperative analgesia.

KEYWORDS
Paracetamol, Diclofenac, NSAIDs, Laparoscopic Surgery, Intravenous


BACKGROUND
The International Association for the Study of Pain (IASP) in 1986 defined pain as- “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of tissue damage, or both.”

Postoperative pain is a very important issue and its management is very necessary irrespective of the surgery type or method. Laparoscopic surgery causes less postoperative pain and smoother recovery than other surgeries but it can even cause intense pain sometimes. Pain in laparoscopic surgery is due to stretching of the peritoneum, residual gas, effect of surgery and the port-hole skin incisions. The major goal in the management of postoperative pain is minimizing the dose of medications while providing adequate analgesia.

Postoperative pain relief leads to early mobilization, less hospital stay, reduced stress response, sympathetic activity, reduced hospital cost and increases patient satisfaction.

Anaesthesiologists have a variety of drugs to treat pain: opioids, NSAIDs, local anaesthetics, cyclo-oxygenase inhibitors (coxibs) and adjuvant drugs like ketamine, anticonvulsants (example: gabapentin) and tricyclic antidepressants. Opioids are most widely used to relieve postoperative pain due to their efficacy and effectiveness and remain so today. However, opioids have many adverse effects like nausea, vomiting, respiratory depression and addiction on prolonged use. Therefore, non-opioid analgesics are favoured as they are devoid of opioid induced side effects and lesser postoperative monitoring is required. Paracetamol is a useful anti-pyretic and moderately potent analgesic with weak anti-inflammatory action. Studies and data concerning paracetamol are fewer in number. Hence, this study was undertaken to compare the effectiveness of paracetamol as an analgesic.
Paracetamol is de-ethylated active metabolite of phenacetin. Paracetamol inhibits both COX-1 and COX-2 where the concentration of arachidonic acid and peroxides are low. It suppresses inflammation and platelet activity where the concentration of these chemicals are high. In brain and spinal cord, paracetamol is conjugated with arachidonic acid to form N-Arachidonoylphenolamine (AM404). AM404 is an activator of capsaicin receptor and cannabinoid receptor both of which produce analgesia in the central nervous system.17,18 Diclofenac is the sodium salt of amino-phenylacetic acid. It was developed as an analgesic, but has anti-inflammatory and anti-pyretic properties also.19,20 Diclofenac exerts its action via inhibition of prostaglandin synthesis of COX-1 and COX-2 with slight selectivity for COX-2. Both diclofenac and paracetamol are widely available and used.

We wanted to compare the efficacy of IV paracetamol and diclofenac in terms of postoperative analgesia, haemodynamic stability and side effects in laparoscopic surgeries.

METHODS
After obtaining Ethical committee approval and informed consent of the patients, this study was conducted to compare the efficacy of IV paracetamol and diclofenac for postoperative analgesia in laparoscopic surgeries. This was a double blind, randomized clinical study, 105 patients scheduled to undergo elective laparoscopic surgery in K.S. Hegde Medical Academy, Deralakatte, Mangalore between January 2014 to August 2015 were randomly selected by closed envelope method.

Inclusion Criteria
- Patients belonging to ASA physical status I AND II.
- Patients between 18-65 years of age.
- Patients undergoing elective laparoscopic surgeries.

Exclusion Criteria
- Patients with known hypersensitivity to paracetamol or diclofenac.
- Patient refusal.
- Patients with liver or renal disease.
- Patients with history of gastric or duodenal ulcer.
- Patients with blood dyscrasias or haemorrhagic diathesis.
- Patients with a known history of bronchial asthma.
- Patients with a history of gastric or duodenal ulcer.
- Patients undergoing major surgery.
- Patients with history of gastrointestinal disorder.
- Patients with a history of peptic ulcer disease.
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METHODS
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RESULTS

| B. | GROUPS | N | Mean | Std. Deviation | Vas0/Mean | P value
|----|--------|---|-----|---------------|-----------|--------
| HR Basal | Group A | 35 | 78.74 | 8.15 | 47.208 | 0.537 | 0.575
| HR Basal | Group B | 35 | 78.05 | 8.41 | 47.208 | 0.537 | 0.575
| HR Basal | Group C | 35 | 77.50 | 8.33 | 47.208 | 0.537 | 0.575

The statistical analysis has been done using statistical software SPSS 20.0 version. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (inter group analysis) on metric parameters and ANOVA has been used to find the significance of study parameters between three groups.

Table 1. HR Trends Among Groups A, B and C

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Table 2. SBP Trends Among Groups A, B and C

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Table 3. DBP Trends Among Groups A, B and C

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Table 4. MAP Trends Among Groups A, B and C

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The groups were comparable in terms of age, weight, gender, ASA physical status and type of surgery. We found that demographic variables in our study were comparable in the groups. HR was comparable between paracetamol and diclofenac at all time intervals. SBP, DBP and MAP were on the lower side in diclofenac group which was statistically significant (Table III, IV, V).

Statistical analysis
The statistical analysis has been done using statistical software SSPS 20.0 version. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (intergroup analysis) on metric parameters and ANOVA has been used to find the significance of study parameters between three groups. (Table 1). SpO2 was comparable in both the groups at all time intervals. The VAS score was also comparable in both paracetamol and diclofenac groups. The duration of analgesia was 317.14±55.549 min and 291.43±65.311 min in both paracetamol and diclofenac groups respectively. (Table VI). There were no serious side effects in either of the groups.

DISCUSSION
Postoperative pain is associated with emotional and mental trauma with unpleasant sensory experience. It is precipitated by surgery and causes endocrine-metabolic, physiological and behavioural response. Inadequate pain relief causes complications like atelectasis, deep vein thrombosis, delayed recovery of bowel function, myocardial ischaemia, urinary retention and psychological trauma. Effective postoperative pain management reduces postoperative complications and reduces the hospital stay by enabling early mobilization. Opioids are the most potent analgesics used for pain relief both and intra and post-operatively. The adverse effects associated with opioids like constipation, nausea, vomiting, excessive sedation and respiratory depression limits their use under all circumstances. NSAIDs are commonly used due to their potent analgesic, anti-pyretic and anti-inflammatory properties. Paracetamol is a potent analgesic and anti-pyretic with little anti-inflammatory properties. This study was done as IV paracetamol as an analgesic is widely being used in many countries and studies and data concerning it are few in number. While analysing the demographic variables in our study, we found that there were no statistically significant variations for age (p value= 0.899), sex (p value= 0.972), weight (p value= 0.751) and ASA classification (p value= 0.215). One patient was excluded from group C (placebo) due to accidental administration of IV diclofenac immediately after shifting the patient to PACU.

Most of the surgeries the patients underwent in all the three groups were laparoscopic appendicectomy and cholecystectomy followed by laparoscopic ovarian cystectomy and hysterectomy. The baseline haemodynamic characteristics like HR (p value= 0.575) and SBP (p value= 0.162) were comparable in all the groups. Baseline HR was 75.74±8.151 in group A (paracetamol), 78.03±8.41 in group B (diclofenac) and 77.32±11.045 in group C (placebo). There was no statistically significant difference in the HR between the three groups starting from baseline till the patient was given rescue analgesia. The HR between group A (paracetamol) and B (diclofenac) was also comparable at all time intervals. Baseline SBP was 123.34±8.775, 119.83±7.755 and 119.79±9.887 mmHg in group A (paracetamol), group B (diclofenac) and group C (placebo) respectively (p value= 0.162). The baseline SBP was comparable between the three groups. There was a significant rise in SBP in group C (placebo) at 60 min (p value <0.001) and 120 min (p value <0.001). On comparing group A (paracetamol) and B (diclofenac), the SBP was statistically significant from 15 min to 360 min in PACU but was clinically insignificant. The DBP was statistically significant at all time intervals till the time to rescue analgesia but was highly significant from 15 min till 120 min (p value <0.005) in PACU. This was clinically insignificant. On comparison of group A (paracetamol) and B (diclofenac), the DBP was low in group B at all time intervals till the administration of rescue analgesia which was statistically significant (p value <0.005). The MAP showed variable significance at different time intervals being statistically significant from 15 min to 120 min (p value <0.005) in PACU. It was consistently on the lower side till 120 min but this was clinically insignificant. On comparing group A (paracetamol) and B (diclofenac), the MAP was low in group B at all time intervals till the patient was given rescue analgesia (p value <0.005). The baseline SpO2 was comparable in all the three groups at all time intervals which was statistically insignificant.

The VAS score was statistically significant (p value <0.005) till 180 min among the three groups in PACU. The VAS score was consistently high in group C (placebo) as compared to the other two. The VAS score in group A (paracetamol) and group B (diclofenac) was comparable at all time intervals. The time to rescue analgesia was 317.14±55.549 min, 291.43±65.311 min and 72.79±47.597 in group A (paracetamol), group B (diclofenac) and group C (placebo) respectively which was statistically significant (p value <0.005). The time to rescue analgesia was shortest for group C (placebo) and longest for group A (paracetamol) among the three groups. The time to rescue analgesia in group A (paracetamol) and B (diclofenac) was comparable (p value=0.880).
Sinan S et al (2010) conducted a study to compare the analgesic efficacy of parenteral paracetamol and diclofenac after septoplasty. 54 patients included in the study were divided into two groups. Group paracetamol received 1g/100ml paracetamol over 15 min and the dose was repeated every six hours till 24th hour. Group diclofenac received 75 mg diclofenac IM and the dose was repeated every 12 hours till 24th hour. There were no serious side effects in either of the groups similar to our study. There was no statistical difference between males and females for postoperative scores in either groups similar to our study.18 Yoganarasimha N et al (2012) conducted a study on 60 ASA I and II patients for comparison of paracetamol infusion with diclofenac infusion for perioperative analgesia in patients undergoing lower abdominal surgeries. The patients were divided in two groups- group P received one-gram paracetamol infusion and group D received diclofenac infusion at the time of rectus abdominis muscle closure. The VAS score in group P increased after 6 hrs of surgery compared to group D where VAS score increased after 2 hrs. The time to rescue analgesia was three times longer in paracetamol group which was statistically significant whereas the time to rescue analgesia in both group A (paracetamol) and B (diclofenac) in our study was comparable. There were no serious complications in either of the groups similar to our study.9

CONCLUSIONS
Paracetamol appears to be equally safe and effective analgesic as diclofenac for postoperative pain. It is haemodynamically stable and does not cause respiratory depression. Paracetamol is devoid of any serious side effects and can be used for both intra and postoperative analgesia.

REFERENCES