

Comparison of the Efficacy of Intravenous Paracetamol and Diclofenac for Post-Operative Analgesia

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Abstract: To compare the efficacy of Paracetamol and Diclofenac administered intravenously for post-operative analgesia and to assess the safety of intravenous Paracetamol. Pain, a biological phenomenon, is easy to comprehend but difficult to define. Pain inflicted intra operatively continues in post-operative period, and could lead to myocardial ischemia, altered pulmonary functions and cause thromboembolic complications if pain persists. Effective pain management is hence an important component of postsurgical care. After approval from Institutional ethical committee, this study was conducted in 100 ASA I and II patients, posted for tubectomy. Patients were randomly allocated to four groups, 25 patients each, Group I S/I C who were given IV Paracetamol and allowed to breathe spontaneously/whole ventilation was controlled and Group II S/II C who were given IV Diclofenac and allowed to breathe spontaneously/whole ventilation was controlled. The technique of induction and maintenance was similar in all groups. In the post-operative period the following parameters were monitored at time interval 0-4 hours, 5-12 hours, and 24 hours Systolic & Diastolic blood pressure, Pulse rate, VAS, FRS & BRS, Need of rescue analgesic, (Tramadol), Side effects, Patient's satisfaction. Administration of analgesics Paracetamol and Diclofenac towards end of surgery and repeated at frequent intervals in the post-operative first 24 hours is effective. We also found that in IV Paracetamol groups and in spontaneously breathing groups, hemodynamic variables, VAS, FRS and patient's satisfaction were better than in Diclofenac and in controlled ventilation group. This study indicates the analgesic effects of newly introduced IV Paracetamol are better than those of the established inj. Diclofenac but larger studies would be needed to firmly conclude the same.

Keywords: Pain, Analgesia, Visual analogue scale, Paracetamol, Diclofenac

INTRODUCTION

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [1].

Pain can be divided into two categories:

- Acute pain, which is primarily due to nociception.
- Chronic pain, which may be due to nociception but in which psychological and behavioral factors often play a major role.

Most surgical procedures inflict pain during the procedure and this also continues in the post-operative period as post-operative pain. Adequate pain relief should be considered as basic human right.

Failure to relieve pain is morally and ethically unacceptable [3]. Providing rapid and effective relief of pain remains a humanitarian issue, whereas allowing patients to suffer as a result of analgesic under medication may be considered a breach of fundamental human rights [2-4].

Post-operative pain is one of the worst types of pain a patient may suffer. The goal for the post-operative pain management is to reduce an individual patient's pain considerably with minimal or no associated suffering or distress [5]. Adverse sequelae of surgical trauma and unrelieved pain include [6]:

- Cardiovascular stress (tachycardia, hypertension etc.).
- Autonomic hyperactivity
- Pulmonary dysfunction

- Hypercoagulability and deep vein thrombosis.
- Dysfunction of immune system.
- Delayed return of bowel function.

In the early 1900's George Crile suggested, "Control of Post-operative pain could favorably influence the results of surgery" [7]. Study has shown that post-operative pain is maximum during initial 48-72 hours & it declines thereafter. Therefore, post-operative pain relief is also a major concern for an anesthesiologist. Recommended approach for postoperative pain management is to initiate treatment with analgesics such as Paracetamol, NSAIDs followed by adjunctive use of opioids to treat more acute pain symptoms.

Paracetamol

Is effective for mild to moderate pain and an effective component in multimodal analgesia in combination with morphine, [8] weak opioids and NSAIDs [9]. Intravenous Paracetamol was first used at Christchurch Hospital in New Zealand in 2006. Paracetamol IV preparation is a good alternative with more advantages over IM and oral. IV administration of drugs is gaining more popularity because of lesser pain on administration, ease of administration, better patient acceptance, faster onset of action and more predictable bio-availability. IV Paracetamol recently introduced in India has a good safety profile and is used to provide effective analgesia for acute postoperative pain. The preemptive use of IV Paracetamol can give rise to a subsiding pain pattern and decrease in analgesic requirements during the postoperative period [10].

Diclofenac sodium

Primary mechanism responsible for its anti-inflammatory, antipyretic, and analgesic action is thought to be inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX). It also appears to exhibit bacteriostatic activity by inhibiting bacterial DNA synthesis [11]. The action of one single dose is much longer (6 to 8 hr) than the very short half-life of the drug indicates. This could be partly because it persists for over 11 hours in synovial fluids [12].

Paracetamol has been recently added to the armamentarium of anaesthesiologists for intra-operative and post-operative analgesia. Moreover this drug is not yet routinely used in clinical anaesthesia, therefore it was decided to study this drug in respect of its efficacy in relieving postoperative pain of mild to moderate severity in patients undergoing abdominal tubectomy and compare it with Diclofenac sodium, a drug which has been in use for providing intra-operative and post-operative analgesia.

METHODOLOGY

A clinical study was conducted to evaluate the efficacy of intravenous Paracetamol for postoperative pain relief in comparison with intravenous Diclofenac in patients scheduled for elective surgeries (tubectomy) under general anaesthesia.

After approval from the Institutional ethical committee, this study was carried out in 100 randomly selected, uncomplicated ASA grade I and II patients, in the age group between 16-40 years, posted for tubectomy (a relative short duration procedure) which is known to be associated with moderate degree of postoperative pain. Pre anaesthetic check-up was done one day prior to the surgery and a written informed consent was taken from the patients.

Inclusion criteria

Normal, healthy patients posted for tubectomy in the age group between 16-40 years in ASA. Grade I and II and those who were willing to participate in the study.

Exclusion criteria

- History of allergic reactions (bronchospasm, shock, rhinitis, urticarial) following the use of Aspirin or any NSAID's
- Hypersensitivity to Paracetamol, Diclofenac and other NSAIDs.
- Active stomach and/or duodenal ulceration or gastrointestinal bleeding
- Inflammatory intestinal disorders such as Crohn's disease or ulcerative colitis
- Severe Difficulty in Breathing or Exertion related chest pain.
- Severe liver disease like jaundice, Ascitis or Altered liver function tests.
- Severe renal diseases (creatinine clearance <30 ml/min, Altered renal function tests)
- Patients with severe, active bleeding

During the visit to the patient one day before the operation, a thorough physical examination was done after getting detailed history and the patient was informed about the anesthetic procedure and given training about usage of visual analog scale (VAS).

All patients were randomly, equally allocated into four groups as under:

Group is - paracetamol (spontaneous)

Patients in this group were allowed to breathe spontaneously during the intraoperative maintenance period and were administered intravenous Paracetamol in infusion form 15mg/kg towards the end of surgery which was repeated later every 6 hours till 24 hours after surgery.

Group i c - paracetamol (controlled)

Patients in this group were kept under controlled ventilation during the intraoperative maintenance period and were administered intravenous Paracetamol in infusion form (15mg/kg) towards the end of surgery which was repeated after every 6 hours till 24 hours after surgery.

Group ii s - diclofenac (spontaneous)

Patients in this group were allowed to breathe spontaneously during the intraoperative maintenance period and were administered intravenous Diclofenac in infusion form (1.5mg/kg) towards the end of surgery which was repeated after every 8 hours till 24 hours after the surgery.

Group ii c - diclofenac (controlled)

Patients in this group were kept under controlled ventilation during the intraoperative maintenance period and were administered intravenous Diclofenac in infusion form (1.5mg/kg) towards the end of surgery which was repeated after every 8 hours till 24 hours after the surgery.

Primary outcome measures

- Haemodynamic status- Effects/ Alterations in systolic blood pressure, diastolic blood pressure and pulse rate at the interval 1/2, 1, 2,4,6,8 and 24 hours postoperatively.
- Efficacy- visual analog score and face rating scale after deep inspiration measured at 1/2, 1, 2,4,6,8 and 24 hours after the surgery.
- At 0-4 hours' time period, VAS & FRS values were calculated by taking the mean of the VAS and FRS values at 1/2, 1, 2 and 4 hours after the surgery.
- At 5-12 hour time period, VAS and FRS are calculated by taking the mean of the VAS and FRS values at 6 and 8 hours after the surgery.
- At 24 hours' time period, the value at 24th hour after surgery of VAS and FRS are taken for this period.

ANAESTHESIA TECHNIQUE

The patients were wheeled into operation theatre and all monitors such as NIBP, pulse oximeter, temperature, electrocardiogram (ECG) and end tidal CO₂ (EtCO₂) were connected to the patient. Base line vital parameters namely pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and SPO₂ were recorded.

All patients received the same anaesthetic agents except for the changes needed as per the group the patients were allocated.

Premedication - inj Fentanyl 1mcg/kg and inj Midazolam 0.05mg/kg.

Induction was done with inj Thiopentone 5mg/kg after 3 minutes of pre-oxygenation. Intubation was done with proper size of endotracheal tube facilitated by muscle relaxant inj Vecuronium 0.1mg/kg in the patients who were kept under controlled ventilation and inj Suxamethonium 1.5mg/kg in patients who were allowed to breathe spontaneously during the intraoperative maintenance period.

Maintenance of anaesthesia was with Oxygen (35%-40%) + Nitrous oxide (60%-65%) + Isoflurane (varying concentration with different vaporizer settings as per alterations in haemodynamic values and as per the group to which patient was allocated).

Intra-operatively signs of inadequate analgesia .i.e. Increase of pulse rate > 20% of base line, Increase in blood pressure >20% of base line, arrhythmias, sweating and tears were the indication to provide more doses of Fentanyl.

Intravascular fluid loss was promptly corrected by adequate and proper replacement by intravenous fluids. Patients were extubated after reversal of neuromuscular block with Inj Neostigmine 0.05mg/kg + inj Glycopyrrolate 0.008mg/kg in the controlled ventilation group after the operation, and they were sent to the recovery room after full recovery of neuromuscular functions.

Systolic, diastolic and mean arterial pressures, heart rate and oxygen saturation were recorded at 5 minute intervals during operation.

Intraoperative analgesia or rescue analgesia was provided according to the needs of the patient. Patients were administered IV Paracetamol/ IV Diclofenac in infusion form (keeping in mind the safe duration of infusion, for either of the drugs, as per manufacturer's instruction) towards the end of the surgery.

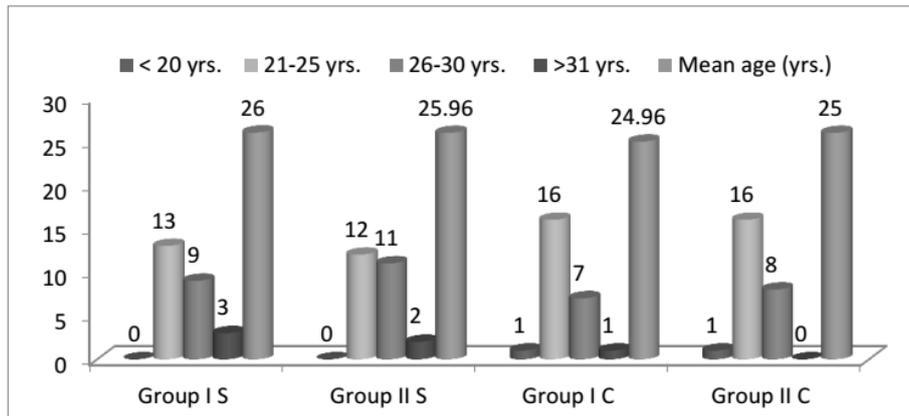
In the post-operative period the following parameters were monitored at the time intervals 0-4 hours, 5-12 hours and 24 hours:

- Systolic blood pressure, Diastolic blood pressure, Pulse rate
- Visual analogue scale, Face rating scale, Behavioural rating scale

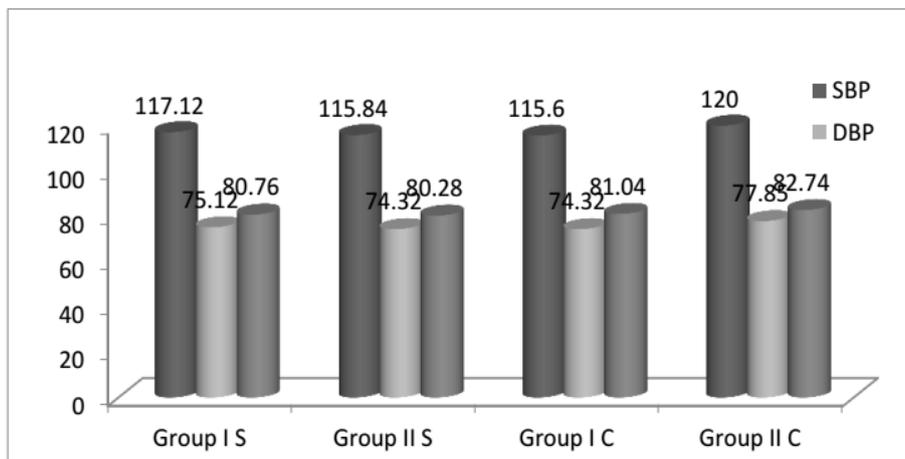
STATISTICAL ANALYSIS

Data analysis was done by descriptive statistics as mean, SD, percentage etc.

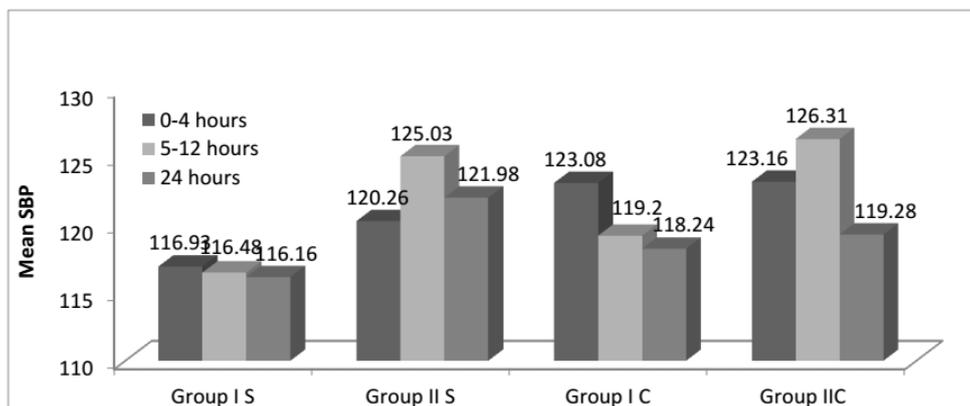
OBSERVATIONS AND RESULTS



Graph-1: Age distribution in the four study groups.



Graph-2: Comparison of preoperative SBP, DBP & Pulse rate of patients in the four study groups preoperatively



Graph-3: Comparison of postoperative mean values of Systolic blood pressure (SBP) at 0-4, 5-12 and 24 hours In the four study groups

I S v/s I C – In each time interval the mean SBP in group I S < I C, indicating postoperative pain is better controlled in spontaneously breathing patient who were managed with higher isoflurane concentration levels than patients who are under controlled ventilation.

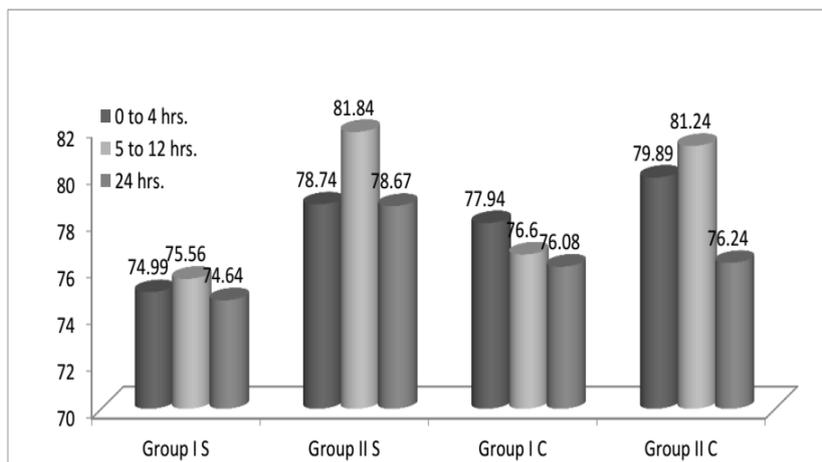
I C v/s II S – In the time interval 0-4 hrs, SBP is less in group II S than I C which may be due to delivery of higher Isoflurane concentration in spontaneously breathing group than in patients whose ventilation was controlled. But with passage of time the SBP gets reduced in group I C than in II

Showing Paracetamol is more effective as analgesic than Diclofenac.

II S v/s II C – In the time interval 0-4 hrs and 5-12 hrs the mean SBP is lesser in spontaneously breathing group then in controlled ventilation group, showing better analgesic effect in spontaneous breathing group then in controlled ventilation group. In both the groups in the time interval 5-12 hrs the SBP

increases compared to other interval indicating wearing off effect of Diclofenac in that period.

I C v/s II C – Initially there is no difference between the mean SBP in both the groups but with passage of time the mean SBP in group I C < II C showing Paracetamol is more effective as an analgesic than Diclofenac.



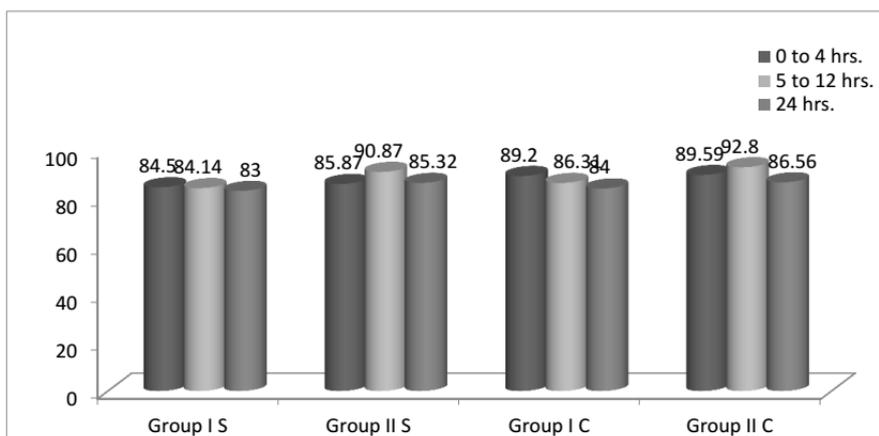
Graph-4: Comparison of postoperative mean values of Diastolic blood pressure (DBP) at 0-4, 5-12 and 24 hours Interval in the four study groups

I S v/s I C – In each time interval the mean DBP in group I S < I C, indicating postoperative pain is better controlled in spontaneously breathing patients who receive higher Isoflurane concentration level then in controlled ventilation group.

II S v/s II C – In each time interval there is not much change in the mean DBP between the two groups.

I C v/s II S – In each time interval the mean DBP in group I C < II S, showing Paracetamol is more effective as analgesic drug than Diclofenac.

I C v/s II C – In each time interval the mean DBP in group I C < II C indicating Paracetamol is more effective analgesic then Diclofenac. There is also increase in DBP in the time interval between 5-12 hrs then in the other intervals in the group II C showing wearing off effect of Diclofenac.



Graph-5: Comparison of postoperative mean values of Pulse Rate at 0-4, 5-12 and 24 hours interval in the four Study groups

I S v/s I C – In each time interval the mean Pulse rate in group I S < I C, indicating postoperative

pain is better controlled in spontaneously breathing group as patients who received higher Isoflurane

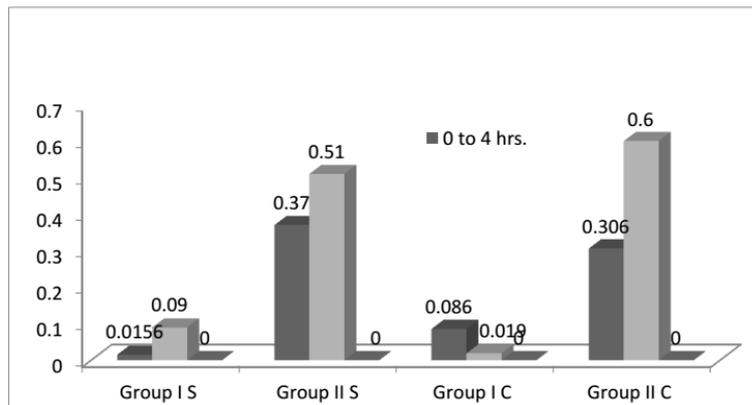
concentration then in patients whose ventilation was controlled.

I C v/s II S –In the time interval 0-4 hrs, Pulse rate is less in group II S than I C which may be due to higher Isoflurane concentration delivered in spontaneously breathing group than in patients whose ventilation was controlled. But with passage of time the Pulse rate reduced in group I C than in II S indicating Paracetamol is more effective analgesic than Diclofenac.

II S v/s II C - In each time interval the mean Pulse rate II S < II C, showing better analgesic effect in

spontaneously breathing group than in patients whose ventilation was controlled group, but in both the groups in the time interval between 5-12 hrs the Pulse Rate increases indicating wearing off effect of Diclofenac in this time interval.

I C v/s II C – In each time interval the mean Pulse rate in group I C < II C showing Paracetamol is more effective analgesic than Diclofenac. There is also increase in Pulse Rate in the time interval 5-12 hrs than in other intervals in the group II C showing the effect of Diclofenac wearing off in that period.



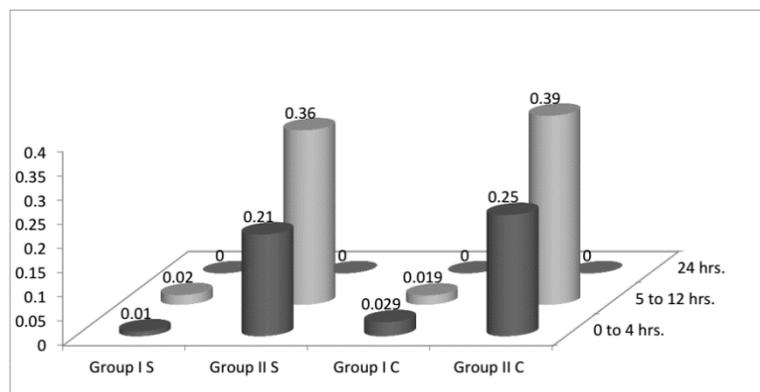
Graph-6: Comparison of mean values of Visual Analogue Scale (VAS) Postoperatively at 0-4, 5-12 and 24 hours duration in all four groups

I S v/s I C – There is not much difference in the mean VAS between the two groups in all time periods.

I C v/s II S –In the time interval 0-4 hrs and 5-12 hrs VAS in group I C < II S showing Paracetamol is more effective as analgesic than Diclofenac. There is increase in VAS in 5-12 hour interval in group II S compared to other two intervals, probably due to wearing off effect of Diclofenac between this period. But at 24 hours there is no pain in both the groups.

II S v/s II C – There is not much change in the mean VAS between the two groups.

I C v/s II C – In the time interval 0-4 hrs and 5-12 hrs, the mean VAS in group I C < II C showing Paracetamol is more effective analgesic than Diclofenac. There is also increase in VAS in the time interval 5-12 hrs compared to other two intervals in the group II C indicating wearing off effect of Diclofenac in that period.



Graph -7: Comparison of postoperative mean values of Face Rating Scale (FRS) at 0-4, 5-12 and 24 hours Interval in the four study groups

I S v/s I C – There is not much difference in the mean FRS between the two groups in all time periods.

I C v/s II S –In the time interval 0-4 hrs and 5-12 hrs FRS in group I C<II S, showing Paracetamol is more effective as analgesic than Diclofenac. There is increase in FRS in 5-12 hour interval in group II S compared to other two intervals probably due to wearing off effect of Diclofenac. But in 24 hours there is no pain in both the groups.

II S v/s II C – There is not much change in the mean FRS between the two groups.

I C v/s II C – In the time interval 0-4 hrs and 5-12 hrs, the mean FRS in group I C<II C showing Paracetamol is more effective than Diclofenac as analgesic. There is increase in FRS in the interval 5-12 hrs compared to other two intervals in the group II C probably due to wearing off effect of the drug Diclofenac in that period. There was no change in the BRS in each group as all the values were zero at each time interval.

DISCUSSION

Postoperative pain differs from other types of pain in that it is usually transitory with progressive improvement over a relatively short period of time. Transmission of pain signals evoked by tissue damage leads to sensitization at central and peripheral pain pathways. Pre-emptive analgesia is a treatment that is initiated before a surgical procedure in order to reduce the sensitization owing to its protective effect on nociceptive system.

Systemic opioid analgesics are regarded as gold standard in the treatment of severe postoperative pain. Unfortunately, their use is associated with frequent adverse effects, such as nausea, vomiting, pruritis and respiratory depression. It is therefore becoming increasingly common to administer non-steroidal anti-inflammatory drugs (NSAIDs) or Paracetamol as adjunctive analgesics in order to reduce opioid related adverse effects and to improve the quality of analgesia.

With this in mind a clinical study was conducted on 100 patients, randomly allocating them into 4 equal groups i.e into IS (IV Paracetamol in spontaneously breathing patients), IC (IV Paracetamol in patients whose ventilation was controlled), IIS (IV Diclofenac in spontaneously breathing patients) and IIC (IV Diclofenac in patients whose ventilation was controlled) groups to evaluate analgesic efficacy of IV Paracetamol to control post-operative pain and compare it with IV Diclofenac. The dose of IV Paracetamol

selected in this study was 15mg/kg body weight and dose of IV Diclofenac was 75 mg (adult).

Blood pressure

In Paracetamol groups i.e both in spontaneously breathing group and controlled ventilation group, mean SBP values are less in each time interval when compared with the Diclofenac groups. This shows the more effectiveness of Paracetamol when compared with Diclofenac for postoperative mild to moderate pain, seen clinically as well as proved statistically. With passage of each time interval there is decrease in the SBP in all the groups of Paracetamol and Diclofenac showing the effectiveness of both the drugs as analgesics, but there is increase in the SBP in both the groups of Diclofenac in the time interval of 5-12 hrs postoperatively because of wearing off effect of the drug during this period.

When comparing the spontaneously breathing group and controlled ventilation group with the same drug, the SBP is less in spontaneously breathing group than in controlled ventilation group with both the drugs. This shows that postoperative analgesic effect is better in spontaneously breathing group when compared to patients in controlled ventilation group, which is presumed to be due to the deeper level of anaesthesia administered by higher vaporizer settings and delivery of anaesthesia agent in spontaneously breathing group than in controlled ventilation group.

Similar findings are seen while comparing DBP and Pulse rate between different groups as discussed above with **SBP**. **VAS** – In spontaneously breathing and controlled ventilation group administered Paracetamol, mean VAS values are less in 0-4 hrs, 5-12 hrs time intervals when compared with groups administered Diclofenac. This shows Paracetamol is more effective when compared to Diclofenac for postoperative mild to moderate pain, seen clinically as well as proved statistically.

With passage of time there is decrease in the VAS in all the groups of Paracetamol and Diclofenac and at 24 hours the VAS values are zero in all the patient groups, showing the effectiveness of both the drugs as analgesics for mild to moderate pain, but there is increase in VAS values of both the groups of Diclofenac in the time interval of 5-12 hrs period postoperatively probably due to wearing off effect of the drug during this interval.

Comparison of spontaneously breathing group with the group under controlled ventilation using the same drug, there are no significant changes in the VAS values.

FRS - In Paracetamol groups i.e both in spontaneously breathing and controlled ventilation group, mean FRS values are less in 0-4 hrs, 5-12 hrs time intervals when compared with the Diclofenac groups. This shows Paracetamol has more effective analgesic effect when compared with Diclofenac for postoperative mild to moderate pain in patients undergoing tubectomy.

With passage of time there is decrease in the FRS in all the groups of Paracetamol and Diclofenac and at 24 hours the FRS values are zero in both the groups, showing the effectiveness of both the drugs as analgesics for mild to moderate pain, but there is higher FRS in both the groups of Diclofenac during the time interval of 5-12 hrs postoperatively showing the wearing off effect of the drug during this interval.

Comparison of spontaneously breathing group with controlled ventilation group with the same drug, shows no significant changes between the FRS values.

CONCLUSIONS

Administration of analgesics Paracetamol and Diclofenac towards end of surgery and repeated at frequent intervals in the postoperative first 24 hours provides good pain relief.

This study indicates the analgesic effects of newly introduced inj. Paracetamol are better than those of the established inj. Diclofenac but larger studies would be needed to firmly conclude the same.

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