



Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com



Original Article

Pre emptive analgesia with iv paracetamol and iv diclofenac sodium in patients undergoing various surgical procedures: a comparative study

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ARTICLE INFO

Keywords:

Pre emptive analgesic
VAS
PSS paracetamol

ABSTRACT

To lay surgery is an every day 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 control post operative pain can lead to serious complications. Aim of this study is to asses intra and post operative analgesic effects of i.v. paracetamol and i.v. diclofenac sodium used pre-emptively also to compare there hemodynamic effects. Meterial and method: Sixty patients undergoing various surgical procedures were included in the study. Patients were randomized in to 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. To start with, written concent was obtained and the patients were explained about he 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. Anesthaesia 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 wuth O2 *n20-50:50, vecuronium as a muscle relaxant and intermittent halothane. Pulse rate, SBP, DBP and Spo2 were recorded every 15 minitus during the procedure. At the end of surgery residual neuromuscular blocked was reversed with inj. Neostigmine methyl sulfate 2.5 mg. and inj. Glycopyrollate 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 analogue score was between 7-10 at this point, these patients were excluded from the futher 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, respiration 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 4.27+ 1.26 hrs. in gp A while 4.86+1.55 hrs. in gp B. thus was stastistically significant. Conclusion: preemptive iv paracetamol is long acting and provides better analgesia than diclofenac with less sie effects.

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1. Introduction

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. The occurrence of these adverse events is now the major area of quality assessment and an area where improvement should be targeted.

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“ FOR ALL THE HAPPINESS THAT MAN CAN GAIN,
IT IS NOT IN PLEASURE BUT IN REST FROM PAIN .”

- John Dryden

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.” Post operative pain is a subject receiving an increasing amount of attention. Poorly controlled post operative pain can lead to serious complications like longer hospital stays, increased use of medications, slower recoveries. Lack of proper analgesia may cause the patient to hold respiration, thereby causing reduction in vital capacity and other lung functions . It also affects cough reflex. Post operative pain differs from patient to patient depending upon site and nature of operation. It is more in thoracic surgeries followed by those in abdomen . Fear and anxiety may aggravate post operative suffering by causing rigid muscle contraction in an attempt to splint the operative site .

The strategic management of post operative pain :

- Ensures smooth post –operative course with earlier discharge from hospital
- Reduces the onset of chronic pain syndrome
- Reduces recuperation period
- Helps faster mobilization , return of full activities and work status

Anaesthesiologist is a logical choice to provide pain relief in immediate post – operative period, since,

- They are aware of pharmacology of analgesia,
- They are aware of the short and long term effect of drugs given intra-operatively,
- Have knowledge about pain pathways and their interruption
- They are skilled in the techniques to perform multiple forms of pain control

Both of the peripheral and the central nervous system are involved in the perception of pain , with the spinal and supraspinal components of the CNS, playing key roles.

The transduction of the noxious stimuli begins with the peripheral nociceptors . Signals from these nociceptors travel primarily along small myelinated A and C fibres with soma lying in the dorsal root ganglion . Their axons synapse in the dorsal horn of the spinal cord, where the neurons of laminae I , II and V are most involved in the perception of pain .

The signals travel along the spinothalamic tract of the spinal cord to the thalamus and the cortex. Large fiber inputs from other sensory modalities and descending pathways may provide a physiologic explanation for the increased pain experience by the patients who have high level of depression and anxiety .

Any analgesic used during various surgical procedures should possess the following features .

- Adequate analgesia efficacy
- Minimal hemodynamic effects .
- Short lasting sedative effect.
- Minimal abuse potential
- Long duration of action .
- Patient compliance
- Rapid onset.

2. Material And Method

60 patients undergoing various surgical procedures were enrolled into the study. Patients were randomized into three groups:

In Group I, iv paracetamol, 1 g (100ml infusion , over 15-20 mins) was given 30 minutes prior to induction.

In Group II, iv diclofenac sodium (75mg), (in 100ml saline, over 15 -20 mins) , was given 30 minutes prior to induction .

Postoperatively, rest and activity pain scores, sedation scores, hemodynamic parameters, postoperative analgesic consumption, side effects, patient satisfaction, and total hospital stay were recorded.

The criteria for exclusion from the study was :

1. American Society of Anesthesiologists (ASA) scores III and IV.
2. History of allergic reactions to paracetamol or diclofenac sodium.
3. History of usage of paracetamol, opioids, or nsais in the 48 hours (h) before requiring chronic analgesic treatment.
4. Chronic alcoholism, deficiency of liver and kidney, deranged LFT & KFT
5. Cardiovascular system illness.
6. Bleeding diathesis.

To start with, written consent was obtained . the patients were explained about the Visual analogue score and pain severity score . The baseline vital parameters like pulse rate , systolic B.P , diastolic B.P, SpO2 of all the patients were recorded . The recommended drugs were then given to patients 30 minutes prior to the induction of anaesthesia . Paracetamol and Diclofenac sodium were given i.v. as infusion over 20 minutes.

After 20 minutes vital parameters were noted again. Then premedication with 0.2 mg of glycopyrrolate and injection midazolam 1 mg i.v. was given to all patients. After oxygenation for 3 minutes, anaesthesia was induced with injection thiopentone for 5mg/kg i.v. and injection succinylcholine 2 mg/kg i.v. IPPV was given for one minute, laryngoscopy was done and airway secured with an appropriately sized cuffed endotracheal tube.

Maintenance of anaesthesia was done with O₂ & N₂O, intermittent halothane inhalation and long acting muscle relaxant were given and the patients were ventilated manually. Pulse rate, SBP, DBP and SpO₂ were noted every 15 minutes during the procedure. At the end of surgery residual neuromuscular blockade was reversed with injection neostigmine methyl sulphate 0.06mg/kg and injection glycopyrrolate 0.2mg per mg of neostigmine methyl sulphate and extubation was done after thorough oral suction and onset of spontaneous respiration and adequate muscle power, judged by head lift for 5 seconds.

Subsequently patients were assessed for pain relief . The assessment of post operative pain, in immediate post operative period i.e 1 minutes after the reversal when the patients were oriented and conscious enough to answer the question asked and the further at 1 hour, 2 hour , 4 hour and 6 hour was made.

The changes in B.P, pulse rate and respiratory rate at different time periods were noted.

For postoperative pain assessment, VAS and Pain Severity Score were used.

The patients were given rescue drug when their pain severity score was 2 i.e when they themselves complained for pain and their visual analogue 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, respiration depression, itching, allergic reaction, stomach irritation, diarrhoea, and constipation, were cross-examined and recorded.

3.Results

•TABLE-(1)

There was no great intergroup difference as regards age, weight of the patients and duration of surgery.

Table - 1: Mean ± sd of Various parameters of the patents

Parameters	Group	
	A	B
Age (Years)	38.27 ± 6.34	37.27 ± 6.56
Wt. (Kgs.)	53.93 ± 3.65	55.30 ± 3.28
Duration of Surgery (Min.)	73.83 ± 7.68	73.20 ± 7.08

• TABLE-(6)

On observing the mean change in base line pre- operative values of vital parameters and 20 min after the analgesic administration, in group A (diclofenac sodium) there was highly significant rise in pulse rate from mean of 82.27+7.55 to 85.60+ 6.54 with P value <.001 ,

while in group B (Paracetamol) it was 80.10 + 8.70, 20 min after with a P value >.05 that is not significant.

In SBP in group A, there was no significant change. It was mean of 124.20 + 8.49 before analgesic and 125.67 + 8.08 with mean change of 1.47 + 5.60 and P value >.05.

In group B, SBP dropped from mean of 127.27+ 2.09 to 121.67+ 10.88 with mean change of decrease 5.60 + 4.18 and P value < .001 that is highly significant.

Similarly DBP raised from 80.00 +6.49 to 82.47+ 6.58 in group A and in group B fall to 76.33 + 7.17 from pre analgesic value mean of 79.07+ 7.64 with a mean of 2.73 + 2.49 and P value <.001 that is highly significant.

In respiratory rate and spO₂ there was not significant change in group A, while in group B respiratory rate fall from mean of 15.60 + 1.47 to 14.63 + 1.17 with P value <.001 and spO₂ from mean of 99.27+ 0.44 to 99.00 + 0.52 with P value <.01.

• TABLE-(7)

In comparison of the mean change in vital parameters 20 min after administration of analgesic in between the two groups it was observed that there was no significant difference in pulse rate, as it was 3.33 + 4.16 in group A and 0.97 + 5.29 in group with P value >.05 that is not significant.

There was highly significant fall in SBP in group B in compare to group A. It mean change was 1.47 + 5.60 in group A and 5.60 + 4.18 in group B with P value < .001 that is highly significant. In DBP there was no significant difference in between the two groups as P value was >.05.

When compared between group A and B respiratory rate fall significantly in group B with P value <.001. spO₂ was comparable with slight fall (0.27+ 0.47) in group B.

TABLE-11,12,13

On comparison of mean changes with pulse rate from base line values, intra operatively, immediate post operative, 1, 2, 4, 6 hrs post operatively in group A it was increase 3.70 + 6.44 and in group B decrease 0.67 + 2.87 with P value > .05 that is not significant. In immediate post op period group A patient showed mean rise of 0.67 + 3.38 and group B increase 5.10+ 9.38 that was significantly higher in group B as comparison group B . Similarly 1, 2 & 4 hrs later also there was significantly higher pulse rate in paracetamol group.

Systolic bp showed significant fall in intraoperatively and 1 hr post operatively in paracetamol group, that was decrease 3.00 + 2.39 intra operatively and 0.07 + 9.8 immediate post op. P value show significant fall on comparison to diclofenac group. After 1 hr there was no significant difference among two groups. Diastolic BP changes were almost similar in both groups. Similarly rise or fall was visible.

Respiratory rate was significantly higher in group A as compare to group B 1, 2 and 4 post operatively.

TABLE 16 TABLE 2

Pain severity score showed no significant difference among the two groups while VAS also was similar in both the groups. Duration of analgesia was 4.27 + 1.26 hrs in group A while 4.86 + 1.55 hrs in group B.

**Table – 6. Mean Change in Baseline pre-operative values 20 minutes after analgesic administration
Group-A (Diclofenac Sodium)**

Parameters	Mean ± SD		↑ / ↓	Mean change ± SD	P Value	Significance
	Before anal.	After Anal				
Pulse (/min)	82.27±7.55	85.60±6.54	↑	3.33±4.16	≤.001	HS
SBP (mmHg)	124.20±8.49	125.67±8.08	↑	1.47±5.60	>.05	NS
DBP (mmHg)	80.00±6.49	82.47±6.58	↑	2.47±5.16	<.05	Sig
RR (/min)	15.87±1.17	15.70±1.19	↓	0.17±0.95	>.05	NS
SPO ₂	99.37±0.48	99.37±0.48	↓	0.00±0.00	>.05	NS

Group-B (Paracetamol)

Parameters	Mean ± SD		↑ / ↓	Mean change ± SD	P Value	Significance
	Before anal.	After Anal				
Pulse (/min)	80.10±7.67	81.07±8.70	↑	0.97±5.29	>.05	NS
SBP (mmHg)	127.27±2.09	121.67±10.88	↑	5.60±4.18	<.001	HS
DBP (mmHg)	79.07±7.64	76.33±7.17	↑	2.73±2.49	<.001	HS
RR (/min)	15.60±1.47	14.63±1.17	↓	0.97±0.81	<.001	HS
SPO ₂	99.27±0.44	99.00±0.52	↓	0.27±0.45	<.01	Sig

SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure
RR = Respiratory Rate, HS = Highly Significant, Sig = Significant
NS = Not Significant, SD = Standard Deviation

**Table – 7. Comparison of the mean change in vital parameters 20 min. after administration of analgesics between various group
Group – A v/s Group B**

Parameters	Group		P Value	Significance
	Group A	Group B		
Pulse (/min)	3.33±4.16	0.97±5.29	>.05	NS
SBP (mmHg)	1.47±5.60	5.60±4.18	<.001	HS
DBP (mmHg)	2.47±5.16	2.73±2.49	>.05	NS
RR (/min)	0.17±0.95	0.97±0.81	<.001	HS
SPO ₂	0.00±0.00	0.27±0.45		

**Table – 11. Comparison of Mean Change ± SD in Pulse Rate (/min.) from baseline values between various groups
Group – A Vs Group – B (Diclofenac Sodium Vs Paracetamol)**

Parameters	Intra Op	Immediate Post Op	1 Hrs. After	2 Hrs. After	4 Hrs. After	6 Hrs. After
	Group A	Group B				
Group A	↑	↑	↑	↑	↑	
	3.70±6.44	0.67±3.38	2.23±4.15	4.14±5.20	7.29±7.99	
Group B	↓	↑	↑	↑	↑	
	0.67±2.87	5.10±9.38	7.23±10.17	10.54±11.71	12.75±11.31	
P – Value	>.05	<.001	<.001	<.001	<.001	
Significance	NS	HS	HS	HS	HS	

Comparison of Mean Change \pm SD in Systolic BP (mmHg) from baseline values between various groups Group - A Vs Group - B (Diclofenac Sodium Vs Paracetamol)

	Intra Op	Immediate Post Op	1 Hrs. After	2 Hrs. After	4 Hrs. After	6 Hrs. After
Group A	↑	↓	↓	↓	↓	
	0.53 \pm 5.80	2.33 \pm 3.05	1.00 \pm 5.00	1.53 \pm 6.18	2.47 \pm 5.16	
Group B	↓	↓	↑	↑	↑	
	3.00 \pm 2.39	0.07 \pm 9.81	0.80 \pm 10.94	1.77 \pm 14.11	2.30 \pm 13.80	
P-Value	>.01	<.05	<.05	<.05	<.05	
Significance	Sig.	NS	NS	NS	NS	

Table - 13. Comparison of Mean Change \pm SD in Diastolic BP (mmHg) from baseline values between various groups Group - A Vs Group - B (Diclofenac Sodium Vs Paracetamol)

	Intra Op	Immediate Post Op	1 Hrs. After	2 Hrs. After	4 Hrs. After	6 Hrs. After
Group A	↑	↓	↓	↓	↓	
	1.53 \pm 5.23	2.87 \pm 3.13	1.40 \pm 4.11	1.25 \pm 4.85	0.35 \pm 6.45	
Group B	↓	↑	↑	↑	↑	
	1.73 \pm 1.46	0.53 \pm 7.18	2.13 \pm 8.24	3.31 \pm 9.68	3.70 \pm 9.09	
P-Value	>.05	<.05	<.05	<.05	<.05	
Significance	NS	NS	NS	NS	NS	

Table - 16. Comparison of Mean Change \pm SD in Pain Severity Score from immediate post operative values between various groups Group - A Vs Group - B (Diclofenac Sodium Vs Paracetamol)

	1 Hrs. After	2 Hrs. After	4 Hrs. After	6 Hrs. After
Group A	↑	↑	↑	
	0.43 \pm 0.56	1.08 \pm 0.93	2.23 \pm 0.44	
Group B	↑	↑	↑	
	0.27 \pm 0.45	1.00 \pm 0.69	1.95 \pm 0.67	
P-Value	<.05	<.05	<.05	
Significance	NS	NS	NS	

Table - 2. Mean \pm sd of Duration of Analgesia (Hrs.) in Various Groups in patients

Group A	Group B
4.27 \pm 1.26	4.86 \pm 1.55

4. Discussion:

Pain is a subjective sensation varying from person to person depending upon psychosomatic personality, age and nature of operation.

Relief of pain is of paramount importance to the patient as it causes discomfort and also increase the risk of pulmonary complications. The relief of post operative pain helps in effective coughing and adequate ventilation.

It is also the basic duty of an anaesthesiologist to provide pain relief not only intra-operatively but also in immediate post operative period. Numbers of pharmacological and non pharmacological approaches are being used for the relief of post operative pain and investigations are still under way to find out the best method or pharmacological agent for post operative analgesia.

Preemptive analgesia although not a new concept is gaining increasing attention in the recent years. Preemptive analgesia has been defined as an antinociceptive treatment starting before surgery that prevents establishment of altered central processing of afferent input from injuries. The nociceptive input is blocked, well into the post operative period, and cover the period of tissue injury associated with post operative inflammation.

In this study, the preemptive analgesic efficacy of two drugs, Diclofenac sodium, and Paracetamol was compared with regard to their duration of action, degree of analgesia and side effects.

Pre operative: Groups A and B showed increase in pulse rate after administration of analgesic. The SBP as well as DBP showed increase in Group A and decrease in group B. Group B showed significant decrease in SBP in comparison to Group A. The change in DBP between various groups was not significant. Respiratory Rate decreased in all the two groups after administration of analgesic. Oxygen saturation remained same in group A after administration of analgesic, while in group B, it showed a decrease.

Intra Operative: Mean values of Pulse Rate, SBP and DBP showed increase in group A and decrease in group B. The comparison of pulse rate between groups A and B was significant. The comparison of DBP between various groups was not significant. Oxygen saturation increased in the two groups intraoperatively due to positive ventilation by mixture of O₂ + N₂O.

Arici et al in 2009 found similar results with decrease in mean values of pulse rate, SBP, DBP, intraoperatively after paracetamol administration.

Immediate Post operative Period:

Insignificant mean changes were observed in Pain Severity Score and visual Analogue Scale.

Pulse Rate was almost equal to base line value in group A patients. It was increased in group B patients. Comparison of mean changes between group A & B was significant.

The mean changes in DBP did not differ in immediate post operative period.

Oxygen saturation decreased from base line value in two groups. This decrease in oxygen saturation was in comparison to base line values and no patient was in respiratory distress and no cyanosis was observed.

Similar results were found by Arici et al (2009) in studying paracetamol in balanced anaesthesia. They found that it did not produce nausea and vomiting.

Sinatra RS et al found that pain scores were lower in patients who received paracetamol, as were the cumulative numbers of patients withdrawn from the trial at each interval.

1 hour after Post-operatively: Mean PSS and mean VAS increased in all the groups. In group A rise in PSS and VAS was more as compared to group B. Similarly SBP, DBP, RR and Pulse rate also increased in comparison to immediate post operative period.

In group B all vital parameters were increased. Oxygen saturation decreased in all two groups. The comparison of decrease in oxygen saturation between various groups was not significant.

At the end of one hour post operatively, 6 patients in group A, 4 patients in group B demanded rescue drug, leaving 24 patients in group A, 26 patients in group B for further study.

Cakan T et al (2008) evaluated the analgesic efficacy, opioid-sparing effect and effects on opioid-related adverse effects of intravenous (IV) paracetamol in combination with IV morphine after lumbar laminectomy and discectomy. It demonstrated a significant opioid-sparing effect, it did decrease visual analog scale scores at certain evaluation times.

Gillberg LE et. al. (1993) found that pre operative diclofenac sodium reduces post laparoscopy pain and post operative analgesic requirements. Chan et al. (1996) evaluated the effect of diclofenac given before or after surgery and found that diclofenac given pre operatively provides better pain relief.

Campbell WI et. al. (1998) also studied intravenous diclofenac sodium administration before operation for suppressing post operative pain and found that patients who received intravenous diclofenac sodium had significantly less pain 30 minutes after operation.

2 hours after Post-operatively: Mean PSS and mean VAS increased in all the two groups. Pulse Rate, SBP, DBP, RR all increased in group B. In group A Pulse Rate and Respiratory Rate increased while SBP and DBP showed non significant change. Comparison of mean changes in oxygen saturation between groups A & B was not significant.

At the end of 2 hours post operatively, 7 more patients in group A, 6 more patients in group B demanded rescue analgesic leaving 17 patients in group A, 20 patients in group B and for further study.

Wilder-Smith CH et. al. (2003) investigated post operative pain and sensory sensitization in patients who had elective cesarean delivery. They found that the median time to first rescue analgesic was 113 minutes with diclofenac.

Arici et al (2009) found decrease consumption of morphine post operatively, after paracetamol usage preoperatively.

4 hours after post operatively: Pain Severity Score (PSS) and Visual Analogue Scale (VAS) increased in all two groups but the rise was more significant in group A. Similar trend was seen in all vital parameters.

At the end of 4 hours post operatively, all 17 patients in group A demanded rescue analgesic so this group was excluded from further study. At the end 4 hours post operatively, 15 more patients in group B demanded rescue drug leaving 5 patients in group B for further study.

Comparable results were also found by William Arici et al (2009) in studying the side effects and efficacy of paracetamol in patients undergoing total abdominal hysterectomy. They found that paracetamol provided good pain relief up to 4 hours duration.

Sunanda Gupta et. al. (1997) conducted randomized double blind study with diclofenac given as pre emptive intravenous analgesic in healthy patients undergoing elective orthopaedic surgery under general anaesthesia. They found that in the early hours post operatively (upto 3 hours), pain scores were less in experimental group as compared to the control group. The number of cases requiring post operative analgesic and the total dose of post operative rescue analgesic was significantly less in the experimental groups as compared to the control groups.

6 hours after post operatively: Remaining patients in groups B showed increase in PSS and VAS. Similar trend was also observed in vital parameters

Duration of Analgesia

The mean duration of analgesia in group A patients was 4.27 hours, in group B patients was 4.86 hours. So it was observed that the duration of analgesia in group B patients was slightly more than group A.

Side Effects Among 30 patients, 3 patients complained for nausea, 3 for vomiting and 1 patient complained for drowsiness in group A. In group B, 2 patients complained for nausea, 2 for vomiting. No cases of urinary retention were observed in either group. Cakan T et al (2008) found similar results with decrease incidence of vomiting with the use of i.v. paracetamol. Arici et al found no significant side effects with i.v paracetamol

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