Original Article

A study of the analgesic efficacy of Intravenous paracetamol versus intravenous diclofenac for the postoperative pain following modified radical mastectomy

Namrata Ranganath[1*], Khushbu Goel[2], Sumitha C S[3], Arathi B H[4], V B Gowda[5], Rashmi Satheesh[6]

Department of Anaesthesia and Pain relief, Kidwai Memorial Institute of Oncology, Bangalore, Karnataka, INDIA.
Email: namrang@gmail.com

Abstract

Background and aims: Post operative pain relief is important for decreased morbidity and mortality. It would be easy to compare analgesic efficacy of iv Paracetamol and iv Diclofenac postoperatively in two groups of patients undergoing similar surgeries Modified Radical Mastectomy experiencing similar pain. **Methods:** After Ethical committee approval, 70 patients undergoing modified radical mastectomy were randomly allocated to one of the two groups, each receiving IV Diclofenac and IV Paracetamol. Each group received the respective analgesic after axillary dissection, 30 minutes prior to reversal. IV Paracetamol 1 Gm. was administered as 100mL (10 mg/mL) proprietary solution over 20 minutes. IV Diclofenac 75 mg was administered in 100 mL saline as an infusion over 20 minutes.After surgery patients were shifted to Post-operative ICU. Analgesia was assessed postoperatively at the following intervals – immediate postop (time 0), 30 minutes, 1 hour, 2 hour from extubation and then at 2 hourly interval for first ten hours after surgery. Fentanyl was administered when the VAS scores crossed 4 and/ or the patient demanded the rescue analgesic. The time when the patient demanded the dosage of rescue analgesic was noted. **Results:** Pain scores changes during a 6 hour period between two groups were similar, 6 hours after surgery, pain scores were significantly higher with Paracetamol compared to Diclofenac ($p<0.05$),At 8hrs, 10hrs post extubation pain scores were significantly higher with Diclofenac. Group P patients received rescue analgesic 60-90 minutes prior to the group D (± minutes).The total number of patients demanding rescue analgesic in each of the groups was found to be statistically similar. **Conclusion**: Both Intravenous Paracetamol and Intravenous Diclofenac have equal efficacy for post operative analgesia following Modified radical mastectomy except duration of analgesia which is longer for Intravenous Diclofenac, as inferred from VAS scores and time of need for rescue analgesic. It appears from our study that IV Paracetamol is good alternative to IV diclofenac for post operative analgesia following Modified radical mastectomy.

Keywords: Pain, Analgesia, Visual analogue scale, Paracetamol, Modified radical mastectomy.

[*]**Address for Correspondence:**
Dr. Namrata Ranganath, Department of Anaesthesia and Pain relief, Kidwai Memorial Institute of Oncology, Bangalore, Karnataka, INDIA.
Email: namrang@gmail.com

Received Date: 05/12/2016 Revised Date: 10/01/2016 Accepted Date: 02/02/2016

Access this article online	
Quick Response Code:	Website: www.statperson.com
	Volume 6 Issue 1

INTRODUCTION

Pain is defined as an unpleasant sensory and emotional experience, associated with actual or potential tissue damage or described in terms of such damage. This definition of pain according to "International Association for Study of Pain" (IASP) by itself speaks so much about pain and how important it is to relieve pain. In our search for freedom from pain, we quickly realized that there are multiple mechanisms of its causation. Some being classified based on the onset like 'acute' or 'chronic'. While acute pain indicates to a tissue injury/ damage, a disease process, or the abnormal function of muscle or viscera; 'chronic' pain may persist after the injury or noxious stimulus is withdrawn and sufficient time has

How to cite this article: Namrata Ranganath *et al.* A study of the analgesic efficacy of Intravenous paracetamol versus intravenous diclofenac for the postoperative pain following modified radical mastectomy. *International Journal of Recent Trends in Science and Technology* January to March 2016; 6(1): 111-115 http://www.statperson.com

elapsed for healing to occur. As anesthesiologists, we come across both varieties of pain but 'acute' pain draws most of our attention and energy. We also noted that acute pain could be of various kinds depending on the tissue of origin and/ or its nature viz. somatic, visceral, nociceptive, neurogenic, superficial, deep, referred, ischemic etc. The most pertinent of these are the nociceptive and inflammatory pain from superficial or deep, somatic or visceral structures. However, postoperative pain is not simple due to tissue injury alone but is the final result of various neurophysiological interactions. This makes efficient postoperative pain management much more difficult and an ideal pain management programme is still elusive. A step-up approach to post-operative pain management will provide adequate analgesia while minimizing exposure to adverse events. Paracetamol has been a useful antipyretic and moderately potent analgesic across various conditions, patient populations and circumstances. The remarkable tolerability and lack of serious side effects at clinical doses explain its popularity. However variable bioavailability of oral formulations and inability to use it in 'nil per oral' patients limited its use in perioperative conditions. With the introduction of a stable intravenous (IV) formulation of Paracetamol, it is now possible to use its analgesic effect in perioperative patients. In comparison to the oral route it has superior pharmacokinetics, efficacy and opiod sparing ability. NSAIDS an effective agent in postoperative setting but their usefulness may be limited due to their tendency to cause gastrointestinal and surgical site hemorrhage and renal failure in high risk patients. This study aims at comparing analgesic efficacy of IV Paracetamol with IV Diclofenac.

MATERIAL AND METHODS

Ethical clearance was sought from the Institutional Dissertation committee before commencing the study.70 adult Patients posted for modified radical mastectomy and confirming to inclusion criteria of ASA-PS grade I, II patients and Patients with known hypersensitivity to paracetamol, diclofenac or with hyper-reactive airway disorders, hepatic parenchymal diseases., renal disease and unable to rate their pain on VAS due to psychiatric or other reasons were excluded from the study. Preanesthetic check-up was done and All patients were explained regarding the surgical procedure, type of anaesthesia and drugs involved, and their effects in their vernacular. A written informed consent was obtained from the patients willing to be a part of the study. All the patients were familiarized with pain scoring. Demographic data was obtained and study population was randomly allocated to one of the two groups, each receiving IV Diclofenac and IV Paracetamol. Premedication, Induction and Maintenance of anesthesia was standardized.All patients were premedicated with ranitidine 150mg and alprazolam 0.5mg 12hr before surgery. After confirming NPO status, routine non-invasive monitoring with pulse oximetry, NIBP, ECG, was initiated in the operation theatre. 18 G iv cannula was put in all patients, and subsequently premedicated with Inj Midazolam (0.05mg/kg), Inj. Glycopyrollate (0.2mg), 4 mg of Ondansetron and Inj Fentanyl (1.5mcg/kg). After preoxygenation for 3 min General Anaesthesia was induced with Inj Thiopentone 5mg/kg and Inj Scoline (1.5mg/kg). Patient was intubated with appropriate cuffed Endotracheal Tube and tube position confirmed and connected to volume controlled mode of mechanical ventilation. Anaesthesia was maintained with Nitrous oxide, O2 and isoflurane.For maintenance of relaxation inj. Vecuronium bromide was given, an initial loading dose of 0.08 mg/kg followed by intermittent doses of Inj Vecuronium (0.1mg/kg). Intraoperative monitoring consisted of NIBP, continuous ECG, EtCO2 and SpO2. Each group received the respective analgesic after axillary dissection, 30 minutes prior to reversal. IV Paracetamol 1 Gm. was administered as 100mL (10 mg/mL) proprietary solution over 20 minutes. IV Diclofenac 75 mg was administered in 100 mL saline as an infusion over 20 minutes. At the end of surgery anaesthesia was reversed with Inj Neostigmine (0.05mg/kg) and Inj Glycopyrrolate (0.01mg/kg). Patients were extubated after complete neuromuscular recovery in deep inspiration after thorough suctioning in fully awake state. After surgery patients were shifted to Post-operative ICU. Analgesia was assessed postoperatively at the following intervals – immediate postop (time 0), after 30 minutes of extubation, at 1 hour from extubation, at 2 hour from extubation and then at 2 hourly interval for first ten hours after surgery. VAS scores was assessed by a person, who was not aware of the group allocation on a scale of 0-10 (0 mean no pain, 10 equals to worst imaginable pain). Fentanyl was administered when the VAS scores crossed 4 and/ or the patient demanded the rescue analgesic. The time when the patient demanded the required dosage of rescue analgesic was noted. Parameters noted were -Total duration of surgery, Pain scores – at 0 min, 30 mins, 1 hr, 2 hrs, 4 hrs, 6 hrs, 8hrs and 10 hrs according to VAS., Vital signs – pulse rate, and BP were recorded at 30 mins, 1 hr, 2 hrs, 4 hrs, 6 hrs,8 hrs and 10 hrs interval, Adverse effects – All patients were observed closely for any adverse effects such as nausea, vomiting, abdominal pain, Time at which VAS score crossed more than 4 and rescue analgesic was administered.

RESULTS

70 patients were enrolled in the study, demographic characteristics such as age, weight and duration of surgery were comparable, surgeries performed were modified radical mastectomy Pain scores changes during a 6 hour period between two groups were similar, 6 hours after surgery, pain scores were significantly higher with Paracetamol compared to Diclofenac ($p<0.05$),At 8hrs, 10hrs post extubation pain scores were significantly higher with Diclofenac. Group P patients received rescue analgesic 60-90 minutes prior to the group D(± minutes). The total number of patients demanding rescue analgesic in each of the groups was found to be statistically similar.

Table 1: Comparison of VAS Score in two groups studied

VAS Score	Group D	Group P	P value
0 hour	2.37±0.59	2.23±0.88	0.719
0.5 hour	0.86±0.73	0.74±0.56	0.620
1hour	0.49±0.61	0.43±0.50	0.839
2hours	0.51±0.50	0.43±0.50	0.476
4 hours	0.57±0.56	0.66±0.99	0.772
6 hours	0.46±0.61	2.97±0.98	<0.001**
8 hours	2.69±0.96	1.40±1.68	<0.001**
10 hours	3.20±1.95	0.77±0.69	<0.001**

Pain scores was noted postoperatively using VAS, at 0 hr,30 min, 1 hr, 2hr, 4 hrs, 6 hrs, 8 hrs 10hr post extubation.

Table 2: Duration of analgesic effect

Duration post extubation (Hrs)	Group D		Group P	
	No (n=35)	%	No (n=35)	%
6-8	2	5.7	34	97.1
8-10	31	88.6	0	0.0
NA	2	5.7	1	2.9

No major differences in Pulse, Systolic BP, Diastolic BP in both the groups was found. The absolute number of cases complaining of epigastric pain was higher, 3 patients(8.6%) in Group-D compared to 1 patient (2.9%) in Group-P and the absolute number of cases having Nausea and Vomiting was comparable in group-D and group-P. None of the patients had liver or platelet dysfunction or bleeding tendencies. Over all Incidence of side effects are statistically similar.

DISCUSSION

Pain is a sensory experience that is subjective and individualised. It frequently exceeds its protective nature and makes postoperative period suffering. The knowledge of mechanism of production of acute pain has advanced sufficiently over the past decade so that rational rather than empirically derived therapy can be used by aiming specifically at interrupting the mechanisms responsible for generation of clinical pain. This concept is more relevant in the management of surgical pain than in any other scenario. In the postoperative period when the effect of the anaesthetic disappears, the tissue injury persists and pain producing substances which are liberated during the surgery greatly reduce the normally high threshold of the nocioceptors, so that noxious stimulation produces pain. More over there are cut ends of axons that further add to nociception. Pain relief after surgery has always been of great concern to the anaesthetists and although a large number of analgesic agents are available. Such unnecessary suffering take place because the doctors and nurses are concerned that repeated administration of narcotic drugs to control pain may lead to addiction. 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-steoridal anti-inflammatory drugs (NSAIDs) or paracetamol as adjunctive analgesics in order to reduce opioid related adverse effects and to improve the quality of analgesia. Despite the availability of a wide variety of analgesic drugs, routine management of post-operative pain remains a continuing challenge. Paracetamol has a proven record in the management of post-operative pain, alone and in combination, with other analgesics. At recommended dosages, paracetamol is devoid of serious unwanted side effects. Paracetamol is not associated with the increased incidence of nausea, vomiting and respiratory depression observed with opioids, or the deleterious gastrointestinal, haematological, renal and cardiovascular effects associated with NSAIDs, including selective COX-2 inhibitors. In this study, the effects of intravenous paracetamol are compared with intravenous diclofenac for post-operative pain relief. Diclofenac has been chosen for comparison because it is the most common standard analgesic used for post operative pain relief in our institution, obliging that the IV paracetamol is without side effects. MD Rawlins *et al* conducted a study on pharmacokinetics of paracetamol. He recommended dose of 15 mg/kg for those weighing between 10 kg and 50kg and adults weighing more than 50kg, one dosage of 1gm is to be administered as a 15 min IV infusion given 4 times a day.[44]The Dose of 1 Gm. of IV Paracetamol (equivalent to 2 Gm. of IV Propacetamol) has been found to provide effective analgesia.[21,27,28,29,30] Hence, we chose the same dosage for our study. The study population in this study was found to be comparable on various demographic parameters viz. age, sex and weight. The study groups were also comparable with respect to their ASA-PS status. There was no significant difference found in the type and

duration of surgery in groups. Anaesthetic management for all patients were same. Thus it can be fairly presumed that the difference in various outcome variables may be attributed to the properties of the individual pharmacologic agents and not to various confounders. The first objective of our study was to determine the quality of post-operative analgesia achieved with IV Paracetamol in patients undergoing Modified radical mastectomy as compared to IV Diclofenac. VAS scores were used as the primary outcome variable for quality of analgesia.. Being aware of the fact that VAS is given to subjective variation, no attempt was made to derive a total score over the duration of observation. Instead the VAS scores were compared directly at various observation intervals between two groups. To further mitigate the effect of individual variation in the perception of pain (and hence the VAS scores), other outcome measures like the number of patients requiring rescue analgesia and the time of demand for rescue analgesic were also recorded and compared. As seen in Table 1,Pain scores changes during a 6 hour period between two groups were similar. But 6 hours after surgery, pain scores were significantly higher with paracetamol compared to diclofenac ($p<0.05$).At 8hrs, 10hrs post extubation pain scores were significantly higher with diclofenac as most patients in Group P had already received rescue analgesics before this time and patients in Group D given rescue analgesics. The time to administration of first dose of rescue analgesic is an indirect indication of the time up to which a particular analgesic is effective in curbing surgical pain. Here again we see that the Group P patients received rescue analgesic 60-90 minutes prior to the group D (± minutes) The total number of patients demanding rescue analgesic in each of the groups was found to be statistically similar. Vital signs: Pulse rate and BP: In our study there were no major differences in Pulse, Systolic BP, Diastolic BP in both the groups. Hence in our study it appears that after modified radical mastectomy IV Paracetamol provide analgesia as effective as Diclofenac. But IV Diclofenac appears to provide adequate analgesia for longer duration, comparable to that of paracetamol. Macario, A. and Royal, M. A. (2011) conducted a study with a objective to systematically review the literature to assess analgesic outcomes of intravenous (IV) acetaminophen for acute postoperative pain in adults. One study involved patients undergoing breast resection, or mastectomy with or without axillary resection, with a 1-g dose 20 minutes before the end of surgery and pain score followed for 24 hours. The authors found that 42% of IV acetaminophen patients did not receive any morphine, compared with 4% in placebo group[26]. The other objective of our study was to compare the side effect profile in the two arms of our study population. The absolute number of cases complaining of epigastric pain was higher, 3 patients (8.6%) in Group-D compared to 1 patient (2.9%) in Group-P. The absolute number of cases having Nausea and Vomiting was comparable in group-D and group-P. None of the patients had liver or platelet dysfunction or bleeding tendencies. Over all Incidence of side effects are statistically similar with P=0.690.This was similar to the results found by A. Hiller *et al*,[40] Cengizkara *et al*,[18] Further larger studies are required to determine maximum safe dose of intravenous paracetamol in renal failure and patients with liver disease, the efficacy of intravenous paracetamol in other surgeries having severe pain postoperatively and to know potential side effects of intravenous paracetamol in high risk patients like patients with bleeding disorders, gastric ulcers compared to intravenous diclofenac.

CONCLUSION

Both Intravenous Paracetamol and Intravenous Diclofenac have equal efficacy for post operative analgesia following Modified radical mastectomy except duration of analgesia which is longer for Intravenous Diclofenac, as inferred from VAS scores and time of need for rescue analgesic. Intravenous Paracetamol has comparable side effects like nausea, vomiting, and epigastric pain to Intravenous Diclofenac.It appears from our study that IV Paracetamol is good alternative to IV diclofenac for post operative analgesia following Modified radical mastectomy.

REFERENCES

1. S1. John J Bonica. History of pain concepts and therapies.In : The management of pain, 2nded. Philadelphia: Lea and Febiger; 1990. P.2-197.
2. Morgan GE, Mikhail MS, Murray MJ, editors. Clinical Anesthesiology. 4th ed. New Delhi; Tata McGraw-Hill Education Private Limited; 2006. p. 359-411.
3. Macres SM, Moore PG, Fishman SM. Acute Pain Management. In: Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, editors. Clinical Anesthesia.6th ed. Philadelphia; Lippincott Williams & Wilkins, a Wolters Kluwer Business; 2009. p. 1473-1504.
4. Stoelting RK, Hillier SC, editors.Pharmacology & Physiology in Anesthetic Practice.4th ed. Philadelphia; Lippincott Williams & Wilkins; 2006. p. 707-717.
5. Joshi M. Basic sciences and evaluations. In: Text book of pain management, 1st ed., Hyderabad: Paras Medical Publishers; 2005. p.1-61.
6. Collins VJ, editors, Mechanisms of pain and control. Chapter-46. In: Section II, regional anaesthesia. In: Principles of anaesthesiology – general and regional anaesthesia. 3rd ed., Philadelphia: Lea and Fabiger; 1993. p.1317-1349.
7. Guyton AC, Hall JE. Somatic Sensations, Chapter-48. In : Section II, pain, headache and thermal sensation. In:

Text book of medical physiology, Indian reprint. New Delhi: Reed Elseiver India Pvt. Ltd., 2007. P.598-609.
8. Chapman C Richard, Karen L, Syrjala. Measurement of Pain - The Management of Pain. John J, Bonica. 2nd Edn, Philadelphia. Lea and Fabiger 1990:580-594.
9. Wu CL. Acute postoperative pain. Chapter-72. In: Miller RD editor. Millers anaesthesia. 6th edition. Philadelphia: Elsevier Churchill Livingstone; 2005. p.2729-2762.
10. Sataslar RS, Bhandarkar SD, Rege NN, editors. Drugs acting on central neurons system. Chapter-10. In : Pharmacology and pharmacotherapeutics. 21st ed., Mumbai: Popular Prakashan; 2009. p.141-158.
11. Rang HP, Dall M, Reiter JM, FlowerRJ, editors. Analgesic drugs, Chapter-41. In: Flue neurons system, section 4. In : Rang and Dali's pharmacology, 6th edn., Reprint, Philadelphia : Churchill Livginstone, Elsevier; 2008. p.588-609.
12. Alan Boobis, Michael Rawlins, Simon Thomas, Mortin Wilkin. Analgesics. In: Therapeutic drugs, 2nd ed. Churchill Livingstone; p.D88-90, A19-21.
13. Sean C. Sweetman. Analgesics and anti-inflammatory drugs. In: Martindale – The complete drug reference. 36th ed. Pharmaceutical Press; p.44-46.
14. Robert W Hurley, Chistropher L Wu. Acute Post operative pain. Ronald D Miller. Miller's Anaesthesia, 7th ed. Philadephia, Churchill Livingstone, 2006; 2766.
15. G. Edward Morgan Jr, Maged S. Mikhail, Michael J Murray. Nonvolatile Anaesthetic agents. G. Edward Morgan, Jr, Maged S Mikhail, Michael J Murray. Clinical Anesthesiology, 4th edn.New Delhi, The McGraw-Hill edition, 2009; 196.
16. Barbara A Coda. Opiods. Paul G Barash, Bruce F Cullen, Robert K Stoelting, Michael K Cahalan, M Christine Stock. Clinical Anesthesia, 6th ed. Philadelphia, Lippincott Williams & Wilkins, 2009; 476-480.
17. D. Hynes, M. MeCarroland O. Hiesse-Provost. Analgesic efficacy of parenteral paracetamol (pro pacetamol) and diclofenac in postoperative orthopaedic pain. Acta Anaesthesiologica 2005 Mar; 50(3):374-381.
18. Cengiz Kara, Berkan Resorlu, Izzet Cicekbilek, Ali Unsal. Analgesic efficacy and safety of nonsteroidal anti-inflamatory drugs after transurethral resection of prostate. International Braz J Urol Vol. 36 (1): 49-54, January - February, 2010
19. Tuzuner Oncul AM, Yazicioglu D, Alanoglu Z, Demiralp S, Ozturk A, Ucok C. Postoperative analgesia in imparted third molar surgery: the role of preoperative diclofenac sodium, paracetamol and hornonicam. Med Princ Pract 2011; 20(5):470-6.
20. Oncül AM, Cimen E, Küçükyavuz Z, Cambazoğlu M. Postoperative analgesia in orthognathic surgery patients: diclofenac sodium or paracetamol? Br J Maxillofac Surg 2011 Mar; 49(2): 138-41.
21. Moller PL, Sindet-Pedersen S, Petersen CT, Juhl GI, Dillenschneider A, Skoglund LA. Onset of acetaminophen analgesia: comparison of oral and intravenous routes after third molar surgery. Br J Anaesth 2005 Mar; 94(5):642-8.
22. Silvanto M, Munsterhjelm E, Savolainen S, Tiainen P, Niemi T, Ylikorkala O, Scheinin H, Olkkola KT. Effect of 3 Gm. of intravenous parcetamol on post-operative analgesia, platelet function and liver enzymes in patients undergoing tonsillectomy under local anesthesia. Acta Anaesthesiol Scand. 2007 Oct; 51(9):1147-54.
23. E. Khoshraftar, H.M. Anvari, H.K. Assadi, A.S. Abdulamir and F. Abu Bakar, 2011.Comparative Study on the Effectiveness of Acetaminophen and Diclofenac Pretreatment in the Relief of Acute Pain after Out-Patient Surgery. European Journal of Dentistry and Medicine, 3: 23-27.
24. Durak P, Yağar S, Uzuner A, Kılıç M, Dilber E, Ozgök A. [Postoperative pain therapy after laparoscopic cholecystectomy: paracetamol versus diclofenac]. Agri. 2010 Jul; 22(3):117-20.
25. E. D. McNicol,A. Tzortzopoulou, M. S. Cepeda, M. B. D. Francia, T. Farhat and R. Schumann. Single-dose intravenous paracetamol or propacetamol for prevention or treatment of postoperative pain: a systematic review and meta-analysis. British Journal ofAnaesthesia106(6): 764–75 (2011)
26. Macario, A. and Royal, M. A. (2011), A Literature Review of Randomized Clinical Trials of Intravenous Acetaminophen (Paracetamol) for Acute Postoperative Pain. Pain Practice, 11: 290–296.
27. Gorocs TS, Lambert M, Rinne T, Krekler M, Modell S. Efficacy and tolerability of ready-to-use intravenous paracetamol solution as monotherapy or as an adjunct analgesic therapy for postoperative pain in patients undergoing elective ambulatory surgery: open, prospective study. Int J Clin Pract. 2009 Jan; 63(1):112-20.
28. Sinatra RS, Jahr JS, Reynolds LW, Viscusi ER, Groudine SB, Payen-Champenois C. Efficacy and safety of single and repeated administration of 1gm IV acetaminophen (paracetamol) for pain management after major orthopaedic surgery. Anaesthesiology 2005 Apr; 102(4):822-31.
29. TW.Hahn, T. Mogeusen, C. Lund, *et al*. Analgesic effect of IV paracetamol: possible ceiling effect of paracetamol in postoperative pain.Acta Anaesthesiol Scard 2003; 47:138-145.
30. Salonen A, Silvola J, Kokki H. Does1 or 2 gm paracetamol added to ketoprofen enhance analgesia in adult tonsillectomy patients? Acta Anaesthesiol Scan 2009 Oct; 53(9):1200-6.

Source of Support: None Declared
Conflict of Interest: None Declared