Efficacy of Diclofenac Sodium for Post Op Pain Relief in Patients undergoing Laparoscopic Sterilization

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Citation

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Abstract

In this double blinded, randomized, placebo controlled study the analgesic efficacy of a Preoperative dose of Diclofenac sodium IM in treating postoperative pain associated
With Laparoscopic Sterilization was evaluated. Patients were randomized to receive a single IM dose of Inj. Diclofenac Sodium 75mg (n = 30) (G1) ½ (A); 1 (B); 1 ½ (C); and 2 (D) hrs before surgery or placebo (n = 30) (G2). The Intensity of post op pain was measured on Numerical Analogue Scale. Incidence of adverse effects was documented. It was found that patients who had received Diclofenac sodium 2 hrs prior had significantly lower incidence of pain during the immediate as well as the early post op period. At 1 hr mean of pain score in G1 (A) = 5.6 +/- 2.03; G1(B) = 4.9+/- 2.23; G1 (C) = 3.7+/- 2.38; G1(D) = 2.8 +/- 1.54, G2 = 6.23 +/- 2.35, at 2 hrs G1(A) = 3.6 +/- 1.32; G1(B) = 3.0 +/- 1.12; G1 (C) = 2.4 +/- 1.34; G1(D) = 1.6 +/- 1.54, G2 = 4.5 +/- 2.44 and at 3 hr G1(A) = 1.30 +/- 0.74; G1(B) = 0.89 +/- 0.76; G1 (C) = 0.52 +/- 0.69 G1(D) = 0.26 +/- 0.58, G2= 2.8 +/-2.04, with a P value of (>.05)
We conclude that in patients presenting for laparoscopic tubal ligation, preoperative administration of Diclofenac 75 mg i.m. 2 hrs prior, conferred additional analgesic benefits compared with a similar dose given after operation.

INTRODUCTION

After Laparoscopic Surgeries, pain is the most frequent complaint and most common cause for post op morbidity ([1], [2]). Pain associated with Out- patient Laparoscopic surgeries are usually managed with opioid analgesics or nonsteroidal anti-inflammatory analgesics.

Laparoscopic tubal ligation is associated with increase in release of prostaglandins in circulation which leads to intense pain at the time of ligation and in the post operation period as well. Also associated are low back ache, lower abdominal pain and post operation nausea and vomiting.

NSAID inhibit prostaglandin production thereby decreasing peripheral stimulation of nociceptors ([3],[4],[5]). Moreover, there is evidence suggesting a central action for these drugs ([6]). Several studies investigating NSAID premedication have shown an analgesic, but not a pre-emptive effect for these agents ([7],[8]). Diclofenac sodium is a phenylactic acid derivative which is formulated for oral, i.m. and rectal use ([4]). It is an effective analgesic given after operation ([5]), but there are few studies which compared its pre-emptive analgesic efficacy. Therefore, we have compared the preoperative and postoperative analgesic effects of i.m. Diclofenac 75 mg in a randomized, double-blind, double blind study.

Diclofenac sodium is an analgesic, antipyretic, anti-inflammatory drug ([9]) which specifically inhibits prostaglandins. It is 99% protein bound, with a t 1/2 of ~2 hrs. It has good tissue permeability. Also it is one of the most cost effective analgesics available in hospital setup.

This study was performed to evaluate the analgesic efficacy of a single preoperative dose of i.m. Diclofenac sodium 75mg, for treating immediate post op pain in patients undergoing elective laparoscopic ligation. The principal hypothesis was that pts receiving these analgesics would experience less pain and post-op discomfort.

METHODS

This double blinded, randomized, placebo controlled study was conducted after approval by the ethics committee of the Institute. Written informed consent was obtained from each patient. Patients aged 25 to 44 yrs (mean age 30.73+/- 3.9) of different gravid status were selected at random in the Dept. of Obstetrics and Gynecology, Post Partum Center, who was to undergo laparoscopic tubal ligation with or with out D&C. Patients were asked for any significant medical

and surgical history. Patients underwent complete physical examination and lab tests prior to operation. Patients were excluded if they had any clinically significant condition which required chronic pain management.

On the day of surgery, during the study, each patient received two identical, coded, 3-ml injections, patients were randomized to receive Diclofenac sodium or placebo. After assessing baseline pain score using numerical analogue scale and establishing IV line access patients were administered 3 ml (75 mg) of Diclofenac sodium or normal saline 3 ml I.M. ½, 1, 1 ½ and 2 hrs before surgery in a double blinded method. Side effects like pain on Inj. administration, nausea and vomiting were documented. Patients were after 2 hrs administered Inj. Pethidine hydrochloride 75-100 mg; Inj. Phenergan 25mg and Atropine sulphate 0.6mg were given I.M. 1/2 hr prior to operation. Under all aseptic precautions 10ml of 1% lignocaine hydrochloride was infiltrated in the puncture site up to the peritoneum ($_{10}$).

The three hour period beginning at time T0 was considered "early post op period". T0 was when the patient was transferred to recovery and had been arousable on verbal command. At times T1, T2 and T3 (one hr intervals), pain intensity (PI) at rest was assessed using a numerical analogue scale where 0 represents "no pain" and 10 represents "worst possible pain". Ambulation and other patient activities were restricted for 10 min before any pain assessment. After a minimal stay of 4 hrs patients were discharged. During the stay of the patient in the surgical facility, all adverse events including excessive bleeding were documented.

RESULTS

A total of 150 patients were randomized in this study, 30 of group 1 (G1)(A),(B),(C) and (D) each were given Diclofenac sodium 75 mg /3cc and 30 of group 2 (G2) were given normal saline 3cc intramuscular each. The mean age (G1 (A) = 31.2 +/- 4.2; G1 (B) = 30.2 +/- 3.9; G1 (C) = 31.6 +/- 4.0; G1 (D) = 32.2 +/- 3.28 and in G2 = 30.73 +/- 3.92). Procedure conducted and weight of patient in both the groups were comparable. (Table 1)

Figure 1

Groups → Variables ↓	G1(A)	G1(B)	G1(C)	G1(D)	G2
Age (years) (mean+/- SD)	31.2 +/- 4.2	30.2 +/- 3.9	31.6 +/- 4.0	32.2 +/- 3.28	30.73+/- 3.92
Weight(Kgs) (mean+/- SD)	58 +/- 10	56 +/- 11	58 +/- 10	60 +/- 9	57 +/- 11
No. of LL	18	19	20	19	17
No. of MTP + LL	12	11	10	11	13

At all post operative time points pain scores were numerically smaller in Diclofenac groups (G1) than placebo (G2) group. At 1 hr mean of pain score in G1 (A) = 5.6 +/- 2.03; G1(B) = 4.9+/- 2.23; G1 (C) = 3.7+/- 2.38; G1(D) = 2.8 +/- 1.54, G2 = 6.23 +/- 2.35,

at 2 hrs G1(A) = 3.6 +/- 1.32; G1(B) = 3.0 +/- 1.12; G1 (C) = 2.4 +/- 1.34; G1(D) = 1.6 +/- 1.54, G2 = 4.5 +/- 2.44 and at 3 hr G1(A) = 1.30 +/- 0.74; G1(B) = 0.89 +/- 0.76; G1 (C) = 0.52 +/- 0.69 G1(D) = 0.26 +/- 0.58, G2= 2.8 +/-2.04, with a P value of (>.05)

In G1 (A) at T1 number of patients having no pain was 2 (B) = 3; (C) =3; (D) =5; whereas in G2 it was 0, number of patients having mild pain (numerical analogue scale NAS 1-3) in G1 (A) = 14; (B) = 15 ; (C) =16; (D) = 19; and G2 was 7, moderate pain (NAS 4-6) in G1 was 3 (B) = 3; (C) =5; (D) =7; and in G2 was 6 and severe pain (NAS 7-9) was 3 in G1 (B) = 2; (C) =2; (D) =0; and 17 in G2.

The mean for pain scale at different time interval is documented in table 2.

Figure 2

Groups→ Pain scores at different timings↓	G1(A)	G1(B)	G1(C)	G1(D)	G2
T1 (1 hr)	5.6 +/- 2.03	4.9+/- 2.23	3.7+/- 2.38	2.8 +/- 1.54	6.23 +/- 2.35
T2 (2 hr)	3.6 +/- 1.32	3.0 +/- 1.12	2.4 +/- 1.34	1.6 +/- 1.54	4.5 +/- 2.44
T3 (3 hr)	1.30 +/- 0.74	0.89 +/- 0.76	0.52 +/- 0.69	0.26 +/- 0.58	2.8 +/-2.04

The total number of patients who experienced incidences of nausea, vomiting, pain on injection and postoperative bleeding in excess are documented in table 3.

Figure 3

Groups → Complications ↓	G1(A)	G1(B)	G1(C)	G1(D)	G2
Pain on inj.	9	8	8	7	11
Vomiting	1	1	0	0	0
Nausea	6	6	5	7	5
Excessive bleeding	0	0	0	0	0

DISCUSSION

Experimental studies on nociception (the response to a noxious stimulus) have suggested that tissue injury and trauma lead to facilitation of processing of painful stimuli, with amplification and prolongation of pain ([11,12,13,14,15,16,17,18]). Human studies on pain also suggest functional alteration of the central nervous system ([20, 21]). Nociception has been unequivocally attenuated by pre-emptive analgesia ([18, 19]), but similar human studies have yielded conflicting results ([14, 22,23,24,25,26,27,28,29,30,31]).

This study demonstrated that a single preoperative dose of Diclofenac sodium is a cost effective analgesic which reduced the incidence of post operative pain in patients undergoing laparoscopic sterilization. At any given time during the assessment in the post op period the group G1 (D) shows a significant decrease in pain. Also the incidence of severe pain at any given time was 0 in G1(D). In a similar study conducted by Desjardins et al ([32]) found that "pain peaked with in 2-4 hrs after laparoscopic surgeries" thereby providing a single dose of Diclofenac sodium which has a t1/2 of 2 hrs would greatly benefit in reducing the intensity of pain in the immediate post op period.

In acutely injured tissues, maximal concentrations of prostaglandins occur 3-4 h after injury and this correlates with peak intensity of postoperative pain ([31]). NSAID such as Diclofenac decrease production of peripheral tissue prostaglandins in response to injury, rather than providing afferent block, although there is some evidence suggesting a central role for NSAID in the reduction of afferent input.

Also another study by Joshi et al ([33]) concluded that "a rational approach would be to include preoperative analgesic to the regular post operative analgesic regime as a preoperative dose produced significant benefits as early as 2-4 hrs. Further more it significantly reduced the "opioid intake" in laparoscopic surgeries. Opioid are known to have side effects like nausea, vomiting, somnolence, and respiratory depression limiting their use ([34]).

The results of our study are not In accordance with a study conducted by D. J. Buggy et al ([35]) who found no advantage conferred no additional

analgesic benefit compared with a similar dose given after operation.

NSAIDS have opioid sparing effect ([36, 37]) but have adverse effects like acid peptic disease, nausea, and gastric discomfort.

During the monitoring of these patients in the early post op period no significant incidences of excessive bleeding thru skin incision or post MTP were documented. Diclofenac sodium is a potent inhibitor of the enzyme Cyclo-oxygenase present in platelets, essential for formation of thromboxane A2, which is essential for platelet aggregation and vasoconstriction thereby prolonging bleeding ([38]). Of the short lasting antiplatelet action which may lead to slight increase in bleeding time though of no clinical significance ([39]). A study conducted by Power et al ([40]) concluded that "although the increase of bleeding time was seen one hour after a single dose of 75 mg of Diclofenac sodium given intramuscular was statistically significant, none of the BT was above the upper limit of 600 sec". Therefore although Diclofenac does effect platelets it does not produce abnormal homeostatic state in a previously normal individual.

In conclusion Diclofenac is a cost effective and potent preemptive analgesic for a economically growing country like ours which can be incorporated for relief of pain in laparoscopic tubal ligation.

References

1. Bisgaard T, Klarskov B, Rosenberg J, et al. Characteristics and prediction of early pain after Laparoscopic Cholecystectomy. Pain 2001;90;261-9.
2. Hession MC. Factors influencing successful discharge after outpatient laparoscopic Cholecystectomy. J Perianeasth Nurs 1998;13;11-5.
3. Ferreira SH. Peripheral analgesia: Mechanisms of the analgesic action of aspirin-like drugs and opiate antagonists. British Journal of Clinical Pharmacology 1980; 10: 237.
4. Code W. NSAIDs and balanced analgesia. Canadian Journal of Anaesthesia 1993; 40: 401^05. 24.
5. Murphy DF. NSAIDs and postoperative pain: sooner is better than later. British Medical Journal 1993; 306: 1493-1494.
6. Malmgrem AB, Yaksh TL. Hyperalgesia mediated by spinal glutamate or substance P receptor blocked by spinal cyclooxygenase inhibition. Science 1992; 257: 1276-1279.
7. Hill CM, Carroll MJ, Giles AD, Pickvance N. Ibuprofen given pre-and post-operatively for the relief of pain. International Journal of Oral and Maxillofacial Surgery 1987;16: 420-424.
8. Depuis R, Lemay H, Bushnelle MC, Duncan GH. Preoperative flurbiprofen in oral surgery: A method of choice in controlling postoperative pain. Pharmacotherapy

1988; 8: 193-200.
9. Pharmacolologocal properties of Diclofenac sodium and its Metabolites. Scand j Rrheumatol 1978:22 (supplement : 5-16).
10. Bisgaard T, Klarskov B, Kristianson VB, et al. multiregional local anesthetic infiltration during Laparoscopic Cholecystectomy in patients receiving prophylactic multimodal analgesia. Anesthesia Analgesia 1999;89:1017-24.
11. Woolf CJ. Recent advances in the pathophysiology of acute pain. British Journal of Anaesthesia 1989; 63: 139-146.
12. Dubner R. Neuronal plasticity and pain following peripheral tissue inflammation or nerve injury. In: Bond MR, Charlton JE, Woolf CJ, eds. Proceedings on the Vth World Congress on Pain. Amsterdam: Elsevier, 1991; 263-276.
13. Dubner R, Ruda MA. Activity dependent neuronal plasticity following tissue injury and inflammation. Trends in Neuroscience 1992; IS: 96-103.
14. Dahl JB, Kehlet H. The value of pre-emptive analgesia in the treatment of postoperative pain. British Journal of Anaesthesia 1993; 70: 434-439.
15. Mendell LM. Physiological properties of unmyelinated fibre projection to the spinal cord. Experimental Neurology 1966; 16: 316-322.
16. Dickenson AH. A cure for wind-up: NMDA receptor antagonists as potential analgesics. Trends in Pharmacological Science 1990; 11: 307-309.
17. Munglani R, Jones JG. Pre-emptive analgesia-use of immediate early genes expression as markers of neuronal stimulation. British Journal of Anaesthesia 1993; 71: 458-464.
18. Codorre TJ, Vaccarino AL, Melzack R. Central nervous system plasticity in the tonic pain response to subcutaneous formalin injection. Brain Research 1990: 535: 155-158.
19. Woolfe CJ, Wall PD. Relative effectiveness of C primary afferent fibres of different origins in evoking a prolonged facilitation of the flexor reflex in the rat. Journal of Neuroscience 1986; 6: 1433-1442.
20. Dickenson AH, Sullivan AF. Subcutaneous formalin-induced activity of dorsal horn neurones in the rat: differential response to an intrathecal opiate administered pre or post formalin.Pain 1987; 30: 349-360.
21. La Motte RH, Londberg LER, Torebjork HE. Pain, hyperalgesia and activity in nociceptive C units in humans after intradermal injection of capsaicin. Journal of Physiology {London), 1992; 448: 749-764.
22. Raja SN, Campbell JN, Meyer RA. Evidence for different mechanisms of primary and secondary hyperalgesia following heat injury to the glabrous skin. Brain 1984; 107: 1179-1188.
23. Tverskoy M, Cozacov C, Ayache M, Bradley EL, Kissin I. Postoperative pain after inguinal hemiorrhaphy with different types of anesthesia Anesthesia and Analgesia 1990; 70: 29-35.
24. Ejlersen E, Bryde-Andersen H, Eliasen K, Mogensen T. A comparison between preincisional and postincisional lidocaine infiltration and postoperative pain. Anesthesia and Analgesia 1992; 74: 495-498.
25. Dierking GW, Dahl JB, Kanstrup J, Dahl A, Kehlet H. Effect of pre- versus postoperative inguinal field block on postoperative pain after hemiorrhaphy. British Journal of Anaesthesia1992; 68: 344-348.
26. Bugedo GJ, Garcamo CR, Mertens RA, Dagnino JA, Munoz HR. Preoperative percutaneous ilioinguinal and Iliohypogastric nerve block with 0.5 % bupivacaine for postherniorrhaphy pain management in adults. Regional Anaesthesia 1990; 15: 130-133.
27. Dahl JB, Hansen BL, Hjorrtso NC. Erichsen CJ, Moiniche S, Kehlet H. Influence of timing on the effect of continuous extradural analgesia with bupivacaine and morphine after major abdominal surgery. British Journal of Anaesthesia 1992; 69: 4-8.
28. Katz J, Kavanagh B, Sandier A, Nierenberg H, Boylan J, Friedlander M, Shaw B. Preemptive analgesia: clinical evidence of neuroplasticity contributing to postoperative pain. Anesthesiology 1992; 77: 439-446.
29. Gustafsson I, Nystrom E, Quilding H. Effect of preoperative paracetamol on pain after oral surgery. European Journal of Clinical Pharmacology 1983; 24: 63-65.
30. Murphy DF, Medley C. Preoperative indomethacin for pain relief after thoracotomy: comparison with postoperative indomethacin. British Journal of Anaesthesia 1993; 70: 298-300.
31. Sisk AL, Grover RJ. A comparison of preoperative and postoperative naproxen sodium for suppression of postoperative pain. Journal of Oral Maxillofacial Surgery 1990; 48: 674-678.
32. Desjardins P Joris, Grossman EH, Koss ME, et al. the injectable Parecoxib has analgesic efficacy when administered preoperatively. Anesthesia Analgesia 2001;93:721-7.
33. Cox-2 inhibitor for pain after Laparoscopic Cholecystectomy, Girish P Joshi, Eugene R Viscusi, et al; Anesthesia Analgesia 2004;98:336-42.
34. Kehlet H, Rung GW, Calleson T. Postoperative Opioid Analgesia: time for reconsideration? J of Clinical Anath. 1996;8:441-5.
35. D. J. Buggy, C. Wall and E. G. Carton Preoperative or postoperative diclofenac for laparoscopic tubal ligation British Journal of Anaesthesia 1994; 73: 767-770
36. Joshi GP. Pain Management after ambulatory surgery. Amblatory Surg 1999;7:3-12.
37. Johnson RC, Hedges AR, Morris R, et al. Ideal Pain relief following Laparoscopic Cholecystectomy. Int J Clin Pract 1999;53:16-8.
38. Weiss HJ, Aledort LM, Kochwa S. The effect of Salicylates on homeostatic properties of platelets in man. J of Clin Investigations 1968;47:2169-80.
39. Roraris M, Miralles J, Baer GA. Diclofenac vs Indomethacin given as IV infusion their effect on hemodynamics and beeding time. Annals of Clin Research 1985;17:308-9.
40. Platelet Function after IM Diclofenac Sodium. L Power, Chambers WA, Greer IA. Anesthesia 1990;45:916-19.

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