Int J Biol Med Res. 2013; 4(2) : 3037- 3040

BioMedSciDirect Publications

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Original Article

Comparison of efficacy and tolerability of Tramadol with Lornoxicam as post operative pain management by administering pre-emptively in patients undergoing elective gynecological surgery under regional subarachnoid block anesthesia

[a]Girija. B. S *, [b]Sahana G. N., [c]Chandrakumar, [d]Sudha T. R

[a]Associate Professor, Department of OBG,
[b]Assistant Professor, Department of Pharmacology
[c]Professor, Department of Anesthesia.
[d]Professor & HOD, Department of OBG , Hassan Institute of Medical Sciences, Hassan

ARTICLE INFO

Keywords:
Gynaecological surgeries
Lornoxicam
Pre-emptive analgesia
Tramadol

ABSTRACT

Objective: The purpose of the present study was to determine the pre-emptive analgesic effects of Tramadol and Lornoxicam. Materials and Methods: Fifty women of ASA (American society of anaesthesiologists) class I and II, who were undergoing gynaecological surgeries under Regional subarachinoid block anaesthesia, were assigned in a randomized manner into two groups. Group T received a single IV injection of Tramadol 50mg (1ml), Group L received a single IV injection of Lornoxicam 8mg(1ml) 1hour before surgery. Results: The post-operative pain scores were evaluated at 2, 4, 8, 12 and 24 hours by using a Visual Analogue Scale (VAS). The post operative VAS scores were significant ($p<0.001$) within the groups. The VAS score at 24hrs was significant between two groups ($p<0.0099$). The time taken to administer the first dose of rescue analgesic was significantly delayed in Lornoxicam group 194.96 ±103.94 minutes, when compared to Tramadol group 159.44 ±70.4minutes. The degree of satisfaction with post operative pain management in Tramadol group was good in 64% of women and 34% had fair scores, however none of them had excellent scores. Whereas in Lornoxicam group 16% of women had excellent scores, 66% had good scores and 18% had fair scores. The side effects like nausea and vomiting was seen in 15 women in Tramadol group and 3 women in Lornoxicam group. Conclusion: In our study Lornoxicam was found to be better pre-emptive analgesic when compared to Tramadol because the time taken for first rescue analgesic was significantly delayed, as well as the total rescue analgesic consumed was less compared to Tramadol. Hence Lornoxicam can be used in place of Tramadol as pre-emptive analgesic due to its above mentioned advantages as well as lesser side effects.

1. Introduction

Pain management remains a major concern in post operative period [1]. Postoperative analgesia is usually inadequate, perhaps because conventional approaches for pain relief do not take account of underlying mechanism [2]. The development of central sensitization and hyperexcitability after surgical incision lead to amplification of post operative pain. The importance of peripheral and central modulation in nociception has fostered the concept of "Pre-emptive analgesia" in patients undergoing surgery [3]. Pre-emptive analgesia is an evolving clinical concept which involves introduction of an analgesic regimen before the onset of noxious stimuli, with the goal of preventing post operative pain and improvement in quality of life [3].

Opioids are the traditionally used drugs in management of post operative pain. Their side effects such as respiratory depression, sedation, constipation, urinary retension limit their use[4]. On the other hand, Non steriodal anti-inflammatory drugs (NSAIDs) found a widespread use in post operative pain management. They have peripheral and central analgesic effects,

* Corresponding Author : **Dr. Girija. B. S.**
Associate Professor, Department of OBG
#48, 4th Floor HIMS Doctors Quarters
S.C.Hospital campus
Hassan, Karnataka- 573201
Mobile No: 9945462077
E mail Id: girijadotrada@yahoo.com

anti-inflammatory property and relatively more tolerability when compared to opioids. The drawback of Opioids has made Non steriodal anti-inflammatory drugs as drug of choice in post operative analgesia [5].

Lornoxicam is newer thienothiazineoxicam NSAIDs, belonging to Oxicam group with potent analgesic and anti-inflammatory activity [6]. Since there are less number of studies on pre-emptive administration of Lornoxicam to reduce post operative pain, we have taken up this study to prove that pre-emptive administration of Lornoxicam reduces post operative pain and analgesic requirement.

2. Material and methods

This is a randomized, single dose, double blind comparative study. Women aged 35 to 65 years belonging to ASA class I and II undergoing elective gynaecological surgery under regional subarachinoid block anaesthesia were enrolled in the study. They were randomised in to 2 groups of 50 each.

Women having received analgesic drugs within 2 weeks of surgery, taking anti-platelet drugs (drug interaction), alcohol abuse, H/o of allergy to NSAIDS, gastric ulcer and pregnant women , hepatic, renal and cardiac impairment were excluded from the study.

Preoperative examination:

The routine pre-anesthetic examinations and investigations of all the women were done on the previous day of the surgery. All of them received tablet Alprazolam 0.25 mg and Ranitidine 150 mg, the night before the operation. The women were randomized into two groups of 50 each. The randomization was done by random numbers table into 2 groups. Group T received a single IV injection of Tramadol 50 mg (1ml) Group L received a single IV injection of Lornoxicam 8mg (1ml). The test drugs were administered approximately one hour before the induction of the anesthesia. The women were explained about how to describe the pain intensity on a visual analog scale (VAS) of 0 to 10.

Anaesthetic technique:

Regional subarachinoid block anaesthesia technique was used which include administration of injection Bupivacaine/Lignocaine 2.5- 3 cc managed with fluids like Ringer lactate or Normal saline and oxygen. Women were administered rescue medication inj. Pentazocine 30mg/ml post operatively as and when required.

The primary measurements of efficacy will be pain intensity score measured on a Visual analog scale from 0 (no pain) to 10(severe pain) at 2, 4, 8, 12 and 24 hours. The total VAS score at the end of 24 hours was assessed to compare the analgesic efficacy of these drugs. The above parameters were assessed by interns who were unaware of the study medication. Neither the women nor the observer knew which drug was administered to them. The analgesic duration, which is the duration of the analgesia between the time of the end of the surgery and the time of the first rescue dose of analgesia which was given, was noted. In addition, the total amount of the rescue medication which was given was noted.

The Global efficacy was assessed at 24th hour by women on a 4-point Likert's scale, in which 1. Poor, 2. Fair, 3. Good and 4. Excellent. The women were withdrawn from the study if the requirement of Pentazocine was more than 3 doses during the first 4 hours, if they demanded analgesia more than 2 times during the 2 hours period following the initial 4hours or if they consumed the total daily dose allowance before the end of the 24 hours observation period.

Statistical and analysis method

The demographic data which included age, duration of the surgery and the time for the first rescue analgesic was analyzed by using descriptive statistics which was expressed as mean ± standard deviation. The VAS pain scores were analyzed by using ANOVA. A probability (p) value of <0.05 was considered as statistically significant.

3. Results

Figure 1. Flow diagram of patient progress through the present randomized trial.

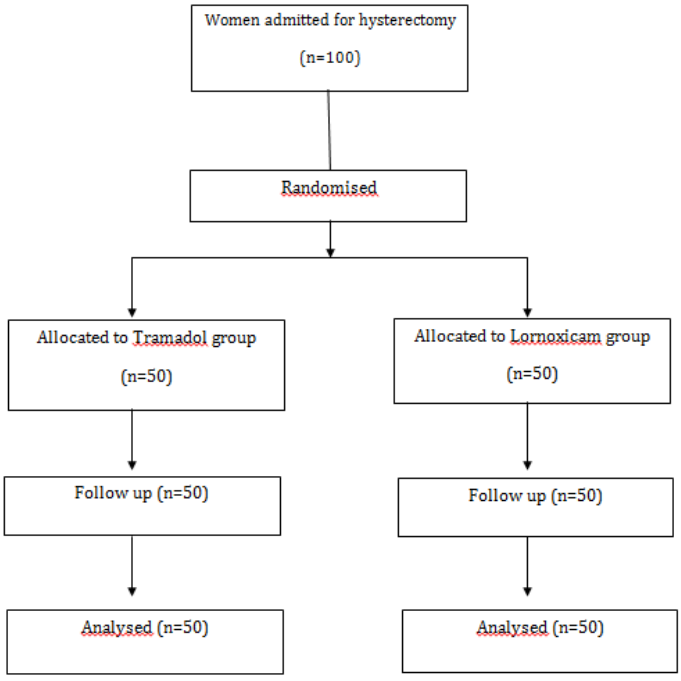

Table 1. Demographic characteristics and duration of surgery

There were no significant differences between the groups with regards to the demographic variables (age and ASA physical status) or the mean duration of the surgery in minutes (Table 1). The age of the women in Tramadol group was 44.8±8.1yrs and that of Lornoxicam group was 46.3±9.5yrs. The duration of surgery was 57.7±16.7mins in Tramadol group and 61.6±12.9mins in Lornoxicam group.

Table 2. Post-operative VAS values [median (min-max)]

The changes in the post-operative VAS pain scores are shown in (Table 2). The VAS pain scores which were recorded at 2, 4, 8, 12 and 24 hrs after the operation were almost similar in both the groups p<0.001. The VAS score at 24 hrs was significant p value < 0.0099 between the groups.

Table 1. Demographic characteristics and duration of surgery

Groups	Group T	Group L
Age	44.86±8.09	46.3±9.5
ASA (I/II)	(35-65yrs)40/10	(35-65yrs) 35/15
Duration of surgery(mins)	57.78±16.74	61.58±12.9

The changes in the post-operative VAS pain scores are shown in (Table 2). The VAS pain scores which were recorded at 2, 4, 8, 12 and 24 hrs after the operation were almost similar in both the groups p<0.001. The VAS score at 24 hrs was significant p value < 0.0099 between the groups.

Table 2. Post-operative VAS values [median (min-max)]

VAS	2 hrs	4 hrs	8 hrs	12 hrs	24 hrs
Group T	3(2-5)*	4(2-6)*	4.5(2-6)*	4(2-6)*	2.6(2-4)*#
Group L	3(2-4)♦	4.3(2-6)	4.6(2-6)♦	4(2-6)♦	3(2-6)♦#
ANOVA P value	<0.001	♦<0.001	<0.001	<0.001	<0.001

*, ♦ p value <0.001significant in each group. # p value <0.0099 significant at 24 hrs between the groups.

There was a significant difference observed with respect to the time for first rescue analgesic requirement between the two groups. The time taken for the first rescue analgesic requirement was longer in the Lornoxicam (194.96±103.94 min) than with Tramadol group (159.44±70.4 min) (Table 3). The amount of analgesic consumption was less in the Lornoxicam group (63.6±17.8) when compared to Tramadol group (64.2±21.86).

Table 3. Postoperative rescue analgesic requirements [median±SD]

VAS	Group T	Group L
Time for first pentazocine administration (mins)	159.44±70.4	194.96±103.94
Analgesic consumption(mg)	64.2±21.86	63.6±17.8 50
Number of women requiring pentazo	50	

Table 4. Patient satisfaction – Global efficacy

The patient satisfaction with the post-operative pain management in Lornoxicam group was excellent in 16% women and good in 66%, where as none of the Tramadol group scored excellent, but 64% showed good score (Table 4). The side effects like nausea and vomiting was seen in 15 women in Tramadol group and 3 women in Lornoxicam group.

Table 4. Patient satisfaction – Global efficacy

VAS	Group T	Group L
1.Poor	-	0.5% (1
2.Fair	18% (9)	34% (17)
3.Good	66% (33)	64% (32)
4.Excellent	16% (8)	-

4. Discussion

The mechanism pain can be divided into nociceptive, inflammatory and neurogenic pain. Nociceptive pain is often regarded as the key feature of the acute post-operative pain, the most common form of the acute pain symptoms. However, in addition to the incisional damage to the skin and various other tissues, the nociceptive barrage during surgery is followed by a protracted inflammatory state which is mediated by prostaglandins in the post-operative period. The transmission of the pain signals which are evoked by tissue damage during surgery leads to the sensitization of the peripheral and the central pain pathways. The only way to prevent the sensitization of the nociceptive system is to block completely any pain signal which originates from the surgical wound from the time of the incision until the final wound healing [3,7]. Thus the concept of preemptive analgesia was postulated.

The present study demonstrated that pre-emptive administration of the test drugs produced a significant decrease in the VAS score at 2, 4, 8, 12 and 24 hours. The findings of this study confirmed those of other studies, wherein the VAS score was significant at 12 and 24 hours in the active comparator groups (lumiracoxib, rofecoxib)[8,9]. The surgical damage produced the upregulation of PGE2, IL-6 and IL-8 in CSF and the surgical sites (upto 25 to 30 hours), that amplified the post-operative pain because of hyperalgesia [9] . Hence, it can be explained that the pre-operative administration of NSAIDs decreased the PGE2 and the IL-6 in the CSF and the surgical sites upto 30 hours, which was correlated with a decrease VAS score [10].

The 24 hours total opioid consumption was 64.2±21.86 in Tramadol and 63.6±17.8 in the Lornoxicam group and the time for the first pentazocine administration for the pain was more in the Lornoxicam when compared to Tramadol group. This indicated that NSAIDs had an opioid sparing effect and that they could be used for pre-emptive analgesia. The advantages of reducing the narcotic usage were evident as the patients were more alert and cooperative and as they could ambulate more rapidly. Besides their analgesic

Acknowledgements

effects, the anti-inflammatory properties of NSAIDs decrease the inflammatory mediators in the post-operative period, thus contributing significantly to the recovery of the patients as compared to opioids in the post-operative period.

Lornoxicam has been successfully used in the prevention and treatment of post-operative pain [11,12]. Lornoxicam provides an alternative to morphine and Tramadol for the treatment of post-operative pain, with fewer adverse events after hysterectomy[13]. Lornoxicam suppresses the inflammatory mediators like the prostaglandin production at the time of the surgical trauma. Thus pre-emptively, its administration improved the quality of the post-operative analgesia. Intravenous Lornoxicam 8 mg was found to be equianalgesic to 20 mg of morphine, 50 mg of pethidine and 50 mg of Tramadol[14]. The objective data from the present study revealed that the analgesic consumption was lower and that the time for first pentazocine use was more in the Lornoxicam than in Tramadol group.

The quality of the post-operative analgesia was excellent in 16% and 66% good in the Lornoxicam group as compared to 64% good in the Tramadol group. This indicated that Lornoxicam had an advantage over Tramadol. Studies have shown that Lornoxicam releases endogenous dynorphin and beta endorphin in the spinal cord, thus providing a central analgesic effect apart from the anti-inflammatory, peripheral analgesic action through prostaglandin synthesis inhibition at the site of the surgery[14]. Lornoxicam has a time-to-peak effect of approximately 20–30 min and an elimination half-time of 3–5 h in healthy young volunteers [15]. The 5′-hydroxy metabolite has a mean terminal elimination t 1/2 of about 11 hours with a range of 6 to 24 hours for a single 4mg dose, and a range of 8.5 to 9 hours after parenteral single or twice daily doses [6].

The most frequent side effects were nausea and vomiting in both the groups. Visceral and pelvic pains were the frequent causes of the post-operative nausea and vomiting. Studies reported the improvement of the nausea after the treatment of the pain[16]. NSAIDs are known for their tendency to cause bleeding, as a result of the inhibition of cyclooxygenase and thereby, platelet aggregation. But a meta-analysis of 1368 patients who were undergoing tonsillectomy reported that the incidence of the post-operative bleeding was not affected by the NSAID consumption [17]. In the present study, none of the patients had significant post-operative bleeding in the Lornoxicam

Thus pre-emptive analgesia may prevent the nociceptive input which is generated during surgery via sensitizing central neurons. Owing to this 'protective' effect on the nociceptive system, pre-emptive analgesia has the potential to be more effective than a similar analgesic treatment which is initiated after the surgery. It has been suggested that pre-emptive analgesia may reduce the risk of developing chronic post-operative pain[1].

5. CONCLUSION

In our study Lornoxicam was found to be better pre-emptive analgesic when compared to Tramadol because the time taken for first rescue analgesic was significantly delayed, as well as the total rescue analgesic consumed was less compared to Tramadol. Hence Lornoxicam can be used in place of Tramadol as pre-emptive analgesic due to its above mentioned advantages as well as lesser side effects.

6. References

[1] Beilin B, Besler H et al. Effects of preemptive analgesia on pain and cytokine production in the post operative period. Anesthesiology 2003;98:151-5

[2] Bonica J : Poat operative pain. In: Bonica J eds: The management of pain. Philadelphia Lea and Febier 1990;461-80

[3] Kissin I. Preemptive Analgesia. Anesthesiology 2000;93:1138-43

[4] Austrup ML, Korean G: Analgesic agents for post operative periods. Opioids. Surg Clin North Am 1999;79:253-273

[5] Mc Crory CR, Sten G, Lindahl GE: Cyclooxygenase inhibition for post operative analgesia. Anesth Analg 2002;95:169-176

[6] Skodt NM, Davies NM. Clinical Pharmacokinetics of Lornoxicam. Clin Pharmacokinet 1998 Jun;34(6):421-428

[7] Dahl JB. The status of pre-emptive analgesia. Curr Opin Anaesthesiol. 1995; 8: 323–30.

[8] Grifka J, Enz R, Zink J, Hugot JL, Kreiss A, Arulmani U, et al. Preemptive versus post-operative lumiracoxib for analgesia in ambulatory arthroscopic knee surgery. Journal of Pain Research 2008:1 27–34.

[9] Buvanendran A, Kroin JS, Tuman JK, Lubenow TR, Elmofty D, Moric M, et al. Effects of the perioperative administration of a selective cyclooxygenase 2 inhibitor on the pain management and the recovery of function after knee replacement: A randomized controlled trial. JAMA November 12 2003;290(18): 2411-18.

[10] Buvanendran A, Kroin JS, Berger RA, Hallab NJ, Saha C, Negrescu C, et al. Upregulation of prostaglandin E2 and interleukins in the central nervous system and in peripheral tissues during and after surgery in humans. Anesthesiology 2006; 104:403–10.

[11] Zhao H, Ye TH, Gong ZY, Xue Y, Xue ZG, Huang WQ. Application of lornoxicam to patient-controlled analgesia in patients who were undergoing abdominal surgeries. Chin Med Sci J. 2005; 20: 59-62.

[12] Trampitsch E, Pipam W, Moertl M, et al. A preemptive, randomized, double-blind study with lornoxicam in gynecological surgery. Schmerz. 2003;17:4-10.

[13] Ilias W, Jansen M. Pain control after hysteroctomy: An observer-blind, randomised trial of lornoxicam versus tramadol. Br J Clin Pract. 1996; 50:197-202.

[14] Arslan M, Tuncer B, Babacan A, Taneri F, Karadenizli Y, Onuk E, et al. Post-operative analgesic effects of lornoxicam after thyroidectomy: a placebo controlled, randomized study. Exp and clinical studies.2006; 18: 27-33.

[15] Lorenz1 IH, Egger K, Schubert H, Schnu¨rer C, Tiefenthaler W, Hohlrieder M, et al. Lornoxicam characteristically modulates the cerebral pain-processing in human volunteers: a functional magnetic resonance imaging study. British Journal of Anaesthesia 2008; 100: 827–33.

[16] Keeny GMC. Risk factors for post-operative nausea and vomiting. Anaesthesia. 1994; 49: 6-10.

[17] Krishna S, Hughes LF, Lin SY. Post-operative hemorrhage with nonsteroidal anti-inflammatory drug use after tonsillectomy: a metaanalysis. Arch Otolaryngol Head Neck Surg 2003; 129: 1086-89.