ORIGINAL ARTICLE

Preemptive analgesia with intravenous tramadol for postoperative pain management in patients undergoing inguinal hernioplasty: a randomized controlled trial

Muhammad Fahim, Sadia Ijaz Abbasi, Naveed Akhtar Malik, Jahangir Sarwar Khan, Hamid Hassan, Muhammad Mussadiq Khan

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Abstract:
Pain is recognized to be a major source of post-operative morbidity and pain intensity peaks during first post-operative hours and in adequate management leads to several pathophysiological changes in pulmonary and cardiovascular systems. A variety of post-operative analgesic strategies ranging from simple analgesic agents administered orally to nerve blocks to combat this pain has been sought. A simpler strategy of pre-emptive analgesic agent may be more acceptable for both surgeons and patients as a reliable pain relief technique. This is a prospective, randomized, placebo-controlled trial to assess the effectiveness of pre-emptive analgesia using tramadol in reducing post-operative pain following inguinal hernioplasty.
Objective:To compare the post-operativepain with and without administration of pre-emptive intravenous tramadol in patients undergoing inguinal hernioplasty.
Patients and Methods: It was a Randomized, double-blinded, placebo-controlled study conducted at Surgical Unit – I of Holy Family Hospital, Rawalpindi conducted from January 2011 to June 2012. Group I patients received 100 mg of tramadol intravenously while group II patients received 4ml of normal saline (placebo) before start of inguinal hernioplasty. VAS ratings of pain 6 hours following inguinal hernioplasty was measured in both groups.
Results: A total of 248 patients, 124 patients in each group were randomized. All patients were male. Mean age was 37.02 (SD=12.66) in group I, while it was 38.24 (SD=13.87) in Group II. VAS scores 6 hours after surgery range from 0 to 10. Mean VAS score 6 hours after surgery was 3.48, (SD=1.67) in patients who received Tramadol (Group I), while it was 6.40, (SD=1.68) in patients who received placebo i.e. normal Saline (Group II) and a p-value of less than 0.0001
Conclusion: This implies that the administration of tramadol before the start of the surgical procedures can produce effective post-operative analgesia

Key words: Pre-emptive, tramadol, inguinal hernioplasty, post-operative pain.

Holy Family Hospital, Rawalpindi, Pakistan
M Fahim
SI Abbasi
NA Malik
JS Khan
H Hassan
MM Khan

Correspondence:
Dr. Muhammad Fahim
email:
muhammadfahim92@gmail.com

Introduction:

When the area of the hernioplasty "wakes up" after the anesthesia, it can recover some of its senses, which can cause mild discomfort in the groin, and the pain increases slowly and can linger for a long time.[1] Post-operative pain is recognized to be a major source of post-operative morbidity.[2] Studies suggest that a painful stimulus can 'sensitize' the central somatosensory pathway and any stimulus that can prevent the original painful stimulus from activating this sensitization by blocking the transmission of noxious perioperative inputs to the spinal cord, thus can alleviate pain intensity, reduces analgesic consumption and delay time to first analgesic requirement after surgery.[2,3] Studies suggest that pain intensity peaks during first post-operative hours and inadequate management leads to several pathophysiological changes in pulmonary and cardiovascular systems.[4] Early post-operative pain can decrease early ambulation, decrease the return of bowel function and be a major problem in acceptance of early discharge by patients. Thus attenuation of early post-operative pain remains an important concern for every surgeon.[5]

A variety of post-operative anesthetic strategies ranging from simple analgesic agents adminis-

tered orally to nerve blocks to combat this pain has been sought.[6] A simpler strategy of preemptive analgesic agent may be more acceptable for both surgeons and patients as a reliable pain relief technique.[2,4,7]

Preemptive analgesia is defined as an anti-nociceptive treatment that prevents establishment of altered central processing of afferent input from injuries.[8] This can effectively prevent earlier onset of the pain than that of the preventive administration of the drugs after surgical procedures, but it was controversial whether preemptive or preventive analgesia should be used to describe the difference between the two analgesic techniques.[9-11] Generally, hernias are repaired under spinal anesthesia in the day-surgical department with less treatment of the pain from groin incision.

Tramadol is a synthetic, centrally acting opioid analgesic with a potent opioid metabolite.[1,12] It produces less respiratory depression than other opioids and has no significant cardiac effects.[1,12] It can be used to provide prolong perioperative pain relief thereby accelerating recovery.[12,13] This type of management pharmacologically induces an effective analgesic state prior to the surgical trauma.[14]

Problem Statement:
Currently a wide variety of literature exists on the treatment of patients in need of postoperative pain. Despite wide variety of treatment regimens used for post-operative pain control, a debate still is going on within the literature on the best analgesic agent, timing of administration and route of administration etc. Without adequate guidelines or consistent standards the patient is placed at risk of too much, too little, or inappropriate analgesic agent to meet their analgesic demands. Since opioid are among the common analgesic agents to control post-operative pain, it is valuable to have an understanding of the analgesic effects of tramadol, an opioid analgesic agent on patient response to treatment. In keeping with an evidence based approach to patient care it is important to understand the effect of timing of administration of the drug in controlling post-operative pain.

The purpose of this study is to evaluate the effectiveness of preemptive analgesia using tramadol in reducing post-operative pain following inguinal hernioplasty.

Objective:
The objective of the study was to compare the post-operativepain with and without administration of pre-emptive intravenous tramadol in patients undergoing inguinal hernioplasty.

Operational Definitions:

Preemptive analgesia:
It is defined as an anti-nociceptive treatment that prevents establishment of altered central processing of afferent input from injuries.

Tramadol:
It is a centrally acting opioidanalgesic, used in treating moderate to severe pain.

Hernioplasty:
It is the surgical repair of hernial defect using prolene mesh.

Pain:
The VAS ratings of pain will be measured 6 hours post operatively with the 10-cm chiroscience gauge as the primary outcome, i.e. subjective pain intensity score will be established based on a 0–10 cm linear VAS (0 = no pain; 10 = worst pain imaginable). It will be noted at 6 hours following surgery.

Hypothesis:
Mean post-operative pain with Pre-emptive intravenous tramadol is less as compared to placebo in patients undergoing inguinal hernioplasty.

Patients and Methods:
It was a randomized, double-blinded, placebo-controlled study conducted in Surgical Unit-I of Holy Family Hospital, Rawalpindi from January, 2011 to June, 2012.

Sample Technique:
Non probability consecutive sampling.

Sample Selection:

Inclusion criteria:

- Scheduled for hernioplasty for inguinal hernia
- Age 20-70 years
- American Society of Anesthesiologists (ASA) I or II physical status

Exclusion criteria:

- Known allergy to tramadol.
- Analgesics abuse
- Operative complication necessitating any procedure more than hernioplasty.
- Any physical or psychological problem that may influence pain response or ability to comply study.
- Patients requiring post-operative intensive care / ventilator support.

Data Collection Procedure:
After approval of the study by the Institutional Research Ethics Committee and obtaining the written informed consent, the patients scheduled for inguinal hernioplasty meeting inclusion criteria were enrolled in the study. Patients were explained to understand that one end of the scale represent no impact of pain at all and the other end is representative of extreme or severe impact of it. All patients were kept blinded to the group allocated throughout the study.

Each individual was randomly assigned to one of two groups by lottery method. The envelope was opened in the operating room by the anesthetist 15minutes before induction of anesthesia to indicate which patient is to receive intravenous tramadol, 4ml equivalent to 100mg (Group I) or 4ml of 0.9% NaCl (Group II, placebo).

Severity of pain was assessed in post anesthesia care unit (PACU) by trainee doctor at 6hours by using VAS. Standard post-operative regimen for all patients was a tablet containing a mixture of paracetamol with dextroproxyphene given on 'as required' basis.

All the data was recorded in the specially designed Performa.

Data Analysis Procedure:
Data was analyzed on SPSS version 12. Categorical variables such as gender and ASA class were expressed as frequencies. Pain scores and age were expressed as mean and standard deviation. Independent sample t- test was used to compare pain scores between two groups. P value <0.05 was considered significant.

Outcome Measure:
VAS pain score 6 hours after surgery was the primary outcome measure. Pain score was compared between the two groups and independent sample t-test compared the pain scores between two groups.

Results:

Frequency:
From January 2011 to June 2012, 248 consecutive outpatientswere enrolled on a convenient sampling bases; 124 patients received preemptive analgesia with intravenous tramadol 100mg (Group I), and 124 patients received 4ml of Normal saline intravenously (Group II). The division of the patients is shown in the Table I.

Age:
Our study population was in age group of 20 to 70 years.Mean age of patients in our study was 37.65 years.

Mean age was 37.02 (SD=12.66) in group I, while it was 38.24(SD=13.87) in Group II.

Gender:
In this study, all 248 patients were male and none of the female patient was female, in either of the group.

Table I: *No. of patients in each group*

Groups	No. of Patients	Lost in Follow-up	Total (n)
Tramadol (group I)	124	0	124
Normal Saline (Group II)	124	0	124
Total	248	0	248

Table II: *Gender Distribution of the trail population*

Groups	Female	Male	Total
Tramadol (group I)	0	124	124
Normal Saline (group II)	0	124	124
Total	0	248	248

Table III: *Visual Analog Scale 6 Hours after Surgery for Both Groups*

	Treatment Group	Frequency	Percent (%)
Tramadol	0	5	4.0
	1	8	6.5
	2	26	21.0
	3	26	21.0
	4	19	15.3
	5	22	17.7
	6	18	14.5
	Total	**126**	**100**
Placebo	4	18	14.5
	5	26	21.0
	6	24	19.4
	7	19	15.3
	8	22	17.7
	9	11	8.9
	10	4	3.2
	Total	**126**	**100**

Table IV: *Visual Analog Scale 6 Hours after Surgery for Both Groups*

Treatment Group	N	Mean	Std. Deviation	P value
Tramadol	124	3.48	1.670	0.000
Placebo	124	6.40	1.682	

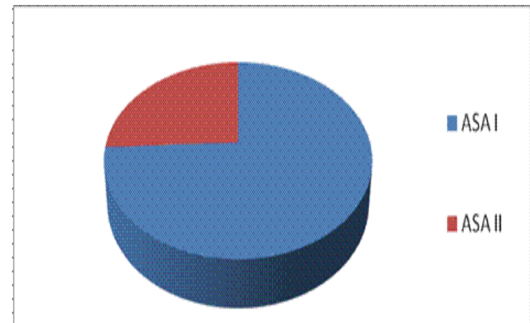

Fig.2: *Percentage of ASA class*

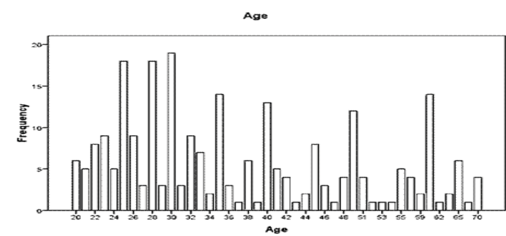

Fig.3: *Visual Analog Scale 6 Hours after Surgery for Both Groups*

ASA Class:

There were 184(74.2%) patients who were in ASA Class I, while there were 64(25.8%) patients who were included in ASA Class II

VAS 6 hours After Surgery:

VAS score 6 hours after surgery range from 0 to 6with mean of 3.48 (SD=1.67) in patients who received Tramadol (Group I), while it range from 4 to 10 and a mean of 6.40 (SD=1.68) in patients who received placebo i.e. normal Saline (Group II) and a p-value of 0.000

In group I, there were 5 patients (4%) had VAS score of 0, 8 patients (6.5%) had VAS score of 1, 26 patients (21%) had VAS score of 2, 26 patients (21%) had VAS score of 3, 19 patients (15.3%) had VAS score of 4, 22 patients (17.7%) had VAS score of 5 and 18 patients (14.5%) had VAS score of 6.

In group II, there were 18 patients (14.5%) had VAS score of 4, 26 patients (21%) had VAS score of 5, 24 patients (19.4%) had VAS score of 6, 19 patients (15.3%) had VAS score of 7, 22 patients (17.7%) had VAS score of 8, 11 patients (8.9%) had VAS score of 9 and 4 patients (3.2%) had VAS score of 10.

These results are shown in Fig 3, Table III and Table IV.

Discussion:

Crent clinical practice is designed to minimize pain in the perioperative period based on the scientific evidence from peer-reviewed medical literature. The data of this study demonstrate

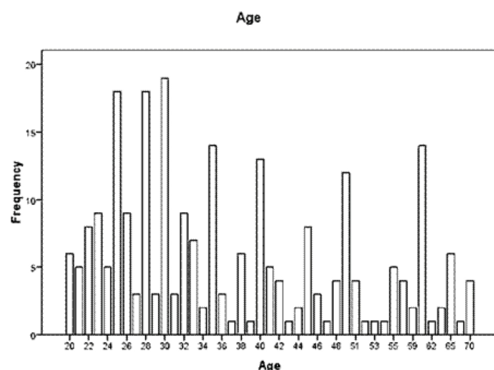

Fig.1: *The age distribution of the patients*

that intravenous preemptive analgesia with tramadol (100 mg) prior to inguinal hernioplasty produced superior analgesic effects when compared with the placebo group. There are statistically significant differences between groups in pain intensity measured by VAS at 6 hours post-surgery. The preoperative administration of tramadol provides anti-nociceptive treatment before the noxious stimulus, and it is effective in the postoperative period, when the inflammatory response at the site of surgery can generate noxious inputs.

Clinical trials regarding the benefits of preemptive analgesia have been contradictory.[12] However certain groups of analgesics have shown the positive results in various clinical trials in humans. The topic of preemptive analgesia is controversial; there have been reports in favor as well those against. These agents include NSAIDs (non-steroidal anti-inflammatory drugs) like diclofenac, lornoxicam, ketorolac, tramadol, local anesthetic agents and nerve blocks etc.[15-17] depending upon the dose, route of administration and timings of administration in relation to surgery has shown variable result in controlling post-operative pain and post-operative analgesic demand. A meta-analysis by Ong et al[18] assessing the ability of preemptive analgesic interventions to attenuate postoperative pain scores, decrease postoperative analgesic requirements, and prolong the time to first rescue analgesia demonstrated an overall beneficial effect in selected analgesic regimens that was most pronounced after epidural analgesia, local wound infiltrations, and systemic NSAID administration.

There are conflicting results concerning preemptive and preventive administration of different groups of analgesics. Preemptive low-dose ketamine is able to produce an adequate postoperative analgesia and increases the analgesic effect of tramadol in patients who underwent laparoscopic cholecystectomy.[19] Premedication of meloxicam provided a better postoperative analgesia than placebo after abdominal hysterectomy.[20]

In addition, investigations of the effect of preemptive tramadol on postoperative pain were evaluated and showed interesting and meaningful results, no matter which delivery manner was used, either intramuscularly or intra-articularly or intravenously, the premedication of tramadol produced effective pain relief.[21-24]

In general, it is considered that preemptive analgesia is more effective than the preventive one. The main reasons for such recognition is based on the theories that preoperative medication could block the nociceptive input, increase threshold for nociception, and decrease nociceptor receptor activation before the incisional injuries.[25] On the other hand, the intraoperative medication could merely produce limited analgesic effect because it could not totally interrupt the ongoing nociceptive input, and this sometimes was used just an adjunctive manner to the anesthesia, thus its analgesic role after operation was narrow.[26] Although such contrasting viewpoints appeared, our data strongly advised that preemptive administration of analgesics, tramadol, was an effective way of treating pain from the inguinal hernioplasty.

While previous studies demonstrated effective analgesia with the premedication of tramadol and butorphanol, in general, such therapies were mainly based on the conditions that the preemptive delivery of the drugs was followed by continuous infusion plus PCA.[27] In this study, a single bolus injection of tramadol was

used to elucidate whether it would produce effective analgesia. The present data is expectedly interesting because it shows that it is an effective procedure in producing pain relief effect postoperatively.

Conclusion:

Pre-emptive delivery of tramadol expressed effective analgesia 6 hours after inguinal hernioplasty. VAS score was high in group who did not received preemptive tramadol. This implies that the administration of tramadol before the start of the surgical procedures can produce effective postoperative analgesia in the context of inguinal hernioplasty.

Conflict of Interest: None

Funding Sources: None

Role and contribution of authors:

Dr Muhammad Fahim, Post-graduate Resident, collected the data

Dr Sadia Ijaz Abbasi, Final Year Medical Student, collected the data and helped in discussion writing

Dr Naveed Akhtar Malik, Assistant Professor of Surgery, Surgical Unit-I, Holy Family Hospital, Rawalpindi, Pakistan, helped in analysis of data and result writing.

Dr Jahangir Sarwar Khan, Associate Professor of Surgery, Surgical Unit-I, Holy Family Hospital, Rawalpindi, Pakistan, helped in discussion writing, compiling the data and review the results.

Dr Hamid Hassan, Professor of Surgery, Surgical Unit-I, Holy Family Hospital, Rawalpindi, Pakistan, final lay out and re-analysis of the results.

Dr Muhammad Mussadiq Khan, Professor of Surgery, Surgical Unit-I, Holy Family Hospital, Rawalpindi, Pakistan, critically review the discussion, results, conclusion and final layout.

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