EFFICACY OF PRE-EMPTIVE ETORICOXIB IN PATIENTS UNDERGOING HERNIOPLASTY UNDER GENERAL ANAESTHESIA- A PROSPECTIVE RANDOMISED-CONTROLLED TRIAL

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ABSTRACT

BACKGROUND

Obtaining adequate analgesia in the perioperative period is an enormous task. Studies show that etoricoxib, a selective COX-2 inhibitor given pre-emptively reduces the pain and thereby enhances recovery.

The aim of the study is to evaluate the effect of pre-emptive etoricoxib in reducing intraoperative requirements of anaesthetic agents, decreasing postoperative pain and improving functional outcome in patients undergoing inguinal hernioplasty.

MATERIALS AND METHODS

Two groups, each of thirty patients were formed- Group S and Group C. Group S received a single dose of etoricoxib two hours prior to anaesthesia, while Group C received a placebo. Sevoflurane used during the intraoperative period was calculated. The patient's pain, sleep and body language in the postoperative period was noted. The rescue analgesics were recorded.

Statistical Analysis- The data was analysed using Mann-Whitney U test, Wilcoxon test, independent two sample t-test, Pearson Chi-square test and Fischer's exact test.

Settings and Design- The study was performed in the Department of Anaesthesia in Jubilee Mission Medical College and Regional Institute, Thrissur, from January 2015 to March 2016. This was a prospective study.

RESULTS

Age, gender and duration of surgery were comparable in both groups. The amount of sevoflurane consumed was less in group S. The postoperative pain was also less in group S at all the time points. Patients in group S demanded less rescue analgesics. 83.3% of the patients in group S had good sleep versus 26.7% in the group C. Up to 93.3% of the patients in group S had a relaxed body language versus 36.7% in group C. No adverse effects were noted.

CONCLUSION

Pre-emptive etoricoxib is thus a safe, simple and cost-effective therapy in reducing the intraoperative anaesthetic and postoperative analgesic requirements.

KEYWORDS

Anti-Inflammatory Agents, Non-Steroidal, Cyclooxygenase-2 Inhibitors, Double-Blind Methods, Herniorrhaphy, Pain Management, Prospective Studies.

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BACKGROUND

Inadequate treatment of pain in the perioperative period predisposes to persistent pain in about 10-50% individuals and chronic pain in about 2-10% patients.[1,2] Thus, postoperative analgesia enhances patient recovery and rehabilitation, while reducing complications and hospital stay.

Most of the conventional analgesics are associated with undesirable side effects, which are often dose-related.[3] The nonselective NSAIDs, which act on both isoforms of cyclooxygenase (COX) enzymes. This implies that their analgesic effect is accompanied by gastric ulceration, platelet dysfunction and renal irritation.[4,5]

Etoricoxib, a selective COX-2 inhibitor provides analgesia with greater gastrointestinal safety and unimpaired platelet function.[6,7]

AIMS AND OBJECTIVES

Our study aims primarily to test the efficacy of etoricoxib in reducing the intraoperative anaesthetic and postoperative analgesic requirements.

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MATERIALS AND METHODS

After obtaining institutional ethical committee approval, eighty patients aged between 20 and 65 years of age posted for inguinal hernioplasty were recruited for the study. This was a prospective, double-blind study conducted in our hospital during the period from January 2015 to March 2016. Informed consent was obtained from all patients. Patients with ASA-PS class 3 or more, known allergy to NSAIDs, renal, hepatic or cardiac problems and coagulopathies were excluded from the study. The patients were randomly allocated to two groups using a computer generated number. Group S received a single dose of etoricoxib, whereas Group C received a placebo two hours prior to anaesthesia and surgery. The dose of etoricoxib was predetermined depending on the patient's body weight.

All the patients were premedicated with IV midazolam 1 mg, IV ondansetron 4 mg and IV glycopyrrolate 0.2 mg. They were hydrated with 10 mL/kg of lactated Ringer's solution through an 18-guage intravenous cannula. The non-invasive blood pressure, oxygen saturation (SpO2) and electrocardiogram (ECG) were monitored. The patients were induced with IV propofol 1.5 mg/kg. The airway was secured using a laryngeal mask airway. Intraoperative analgesia was attained with IV fentanyl. A bolus of 1 µ/kg followed by half-hourly supplements of 0.25 µ/kg were given. IV atracurium 0.5 mg/kg was used to facilitate muscle relaxation. The depth of anaesthesia was maintained with the help of sevoflurane. The concentration was adjusted so that the vitals remained within 20% of the baseline values. At the end of the surgical procedure, the patient was extubated after giving IV neostigmine 0.05 mg/kg. The patient was monitored for next 24 hours. Postoperative analgesia was provided by extended release paracetamol tablets given sixth hourly. IV tramadol 0.5 mg/kg was used as rescue analgesic.

The intraoperative requirements of sevoflurane were compared in both groups. Pain status, sleep and overall body language were assessed at 0 hours, 6 hours, 12 hours, 18 hours and 24 hours after completion of anaesthesia and surgery. Intensity of pain was assessed in both groups using the numeric pain rating scale. The pain was rated using the integers zero to ten where zero stood for no pain, while ten indicated worst imaginable pain. The total number of tramadol injections demanded by the patient was also compared. Quality of sleep was categorised as good, interrupted and no sleep. Body language was grouped into relaxed, tensed and unhappy.

All the data was assessed with the help of a biostatistician. Levene's test and t-test were used to compare the intraoperative sevoflurane requirements. The pain rating at 0 hour, 6 hours, 12 hours, 18 hours and 24 hours were analysed using Mann-Whitney U test and Wilcoxon test. The sleep and body language of the two groups were compared using the Pearson Chi-square test. A p-value of less than 0.05 was considered to be clinically significant.

RESULTS

The mean age, gender of the patients and duration of surgery were similar in both the study groups (p=0.137, p=0.688 and p=0.193, respectively) (Table 1 and 2).

	Group	Number of Patients	Mean	Standard Deviation	Standard Error Mean	Significance
Age (years)	Group S	30	53.267	10.5665	1.9292	0.137
	Group C	30	48.667	12.9491	2.3642	
Duration of Surgery (in min.)	Group S	30	58.167	14.8256	2.7068	0.193
	Group C	30	53.167	14.5912	2.6640	

Table 1. Comparison of Age and Duration of Surgery in the Two Groups

		Males		Females		Significance
	Group	Number	%	Number	%	
Gender Ratio	Group S	27	90.0	3	10.0	0.688
	Group C	26	86.7	4	13.3	

Table 2. Gender Distribution in the Two Groups

Intraoperative sevoflurane requirements (sevoflurane consumed per minute) was found to be less in Group S when compared to Group C (16.387±6.03 vs. 39.067±18.57) (Table 3).

Group	Number of Patients	Mean	Standard Deviation	Standard Error Mean	Significance
Group S	30	16.38750	6.031043	1.101113	0.000
Group C	30	39.067	18.565905	3.389655	

Table 3. Comparison of the Intraoperative Sevoflurane Consumption

Pain rating was lower in group S at all study points (Table 4). The patients in Group S also demanded less rescue analgesics (IV tramadol) compared to their counterparts in Group C (mean of 22.95 in Group S vs. 38.05 in Group C; p-value=0.000).

Study Point	Group	Number of Patients	Mean	Standard Deviation	Standard Error Mean	Significance
0 hour	Group S	30	2.167	1.4641	0.2673	0.000
	Group C	30	3.933	1.5522	0.2834	
6 hours	Group S	30	2.467	0.9371	0.1711	0.003
	Group C	30	3.233	1.0063	0.1837	
12 hours	Group S	30	2.667	0.8023	0.1465	0.033
	Group C	30	3.167	0.8743	0.1596	
18 hours	Group S	30	2.500	0.8200	0.1497	0.022
	Group C	30	3.067	0.9072	0.1656	
24 hours	Group S	30	1.733	0.7397	0.1350	0.000
	Group C	30	2.600	0.5632	0.1028	

Table 4. Pain Rating at 0 Hours, 6 Hours, 12 Hours, 18 Hours and 24 Hours in the Two Groups

93.3% of the patients in group S had a relaxed body language as against 36.7% in Group C. Only, 6.7% of the patients in group S had a tensed body language, whereas about 40% of the patients in Group C were tensed. None of the patients in Group S were unhappy versus 23.3% in Group C (Table 5).

Nature of Body Language	Group S		Group C	
	Number of Patients	Percentage	Number of Patients	Percentage
Relaxed	28	93.3	11	36.7
Tensed	2	6.7	12	40
Unhappy	0	0	7	23.3

Table 5. Comparison of the Body Language in the Two Groups

The quality of sleep was also found to be better in Group S (Table 6).

Quality of Sleep	Group S		Group C	
	Number of Patients	Percentage	Number of Patients	Percentage
Good	25	83.3	8	26.7
Interrupted	5	16.7	20	66.7
No sleep	0	0	2	6.7

Table 6. Comparison of Sleep Quality between the Two Groups

No undesirable effects attributable to etoricoxib was noted.

DISCUSSION

Unrelieved pain, prolonged recovery and minor anaesthetic complications after surgery often lead to delayed discharge resulting in increased healthcare costs and unnecessary patient dissatisfaction.[8] Recently, it was shown that multimodal analgesia was a rational approach to pain management and was in fact more effective.[9] A study by Kehlet and Dahl showed the important role of the anaesthetist in facilitating early postoperative recovery and preventing a transition from acute to chronic pain by ensuring optimal intraoperative anaesthetic management and adequate pain relief well into the postoperative period.[10] Watson et al revealed that the majority of the patients suffered inadequate pain relief and interference with sleep and daily living activities.[11]

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) constitute 10% of the non-opioid analgesics. Traditional NSAIDs and more recently COX-2 selective inhibitors have also been used for postoperative analgesia after daycare surgery. Etoricoxib is one of the newer available COX-2 inhibitors. It inhibits the enzyme COX, which catalyses the first step in the pathway of prostanoid synthesis. Some of these are implicated in the pathogenesis of inflammation and nociceptive pain.[12,13] It has got a rapid absorption after oral intake resulting in peak plasma concentration after one hour. It has also got the long duration of analgesic action lasting 22-24 hours.[14,15] Etoricoxib has got a definite clinical advantage in terms of gastrointestinal safety and unimpaired platelet function.[16] Dizziness is a less common side effect associated with this drug.[12,13]

Pre-emptive analgesia is an attractive strategy whereby the analgesics are administered before surgery in order to prevent the establishment of central sensitisation evoked by the incisional and inflammatory injuries occurring during surgery and in the early postoperative period.[17,18,19] Owing to this 'protective effect' on the nociceptive system, pre-emptive analgesia has the potential to be more effective than a similar analgesic treatment initiated after the surgery. Therefore, pre-emptive analgesia can reduce immediate postoperative pain and also prevent the development of chronic pain by decreasing the altered central sensory processing.[20,21]

Several studies have examined of the use of etoricoxib and have confirmed its efficacy in providing pain relief after gynaecological procedures (Liu et al, 2005,[22] Chau-in et al, 2008[23]), after laparoscopic surgery (Puura et al, 2006[6]), after thyroid surgery (Smirnov et al, 2008[12]), after orthopaedic surgery (Peter et al, 2012[24], Rasmussen et al, 2005,[25] Ibrahim et al, 2008,[26] Sowbhagya et al, 2014[27]) and after trauma surgery (Siddiqui et al, 2008).[28] Our work studies the efficacy of a single dose of etoricoxib administered preoperatively in reducing the intraoperative anaesthetic and postoperative analgesic requirements in patients undergoing open inguinal hernioplasty under general anaesthesia.

In our study, we found out that the amount of sevoflurane consumed during the intraoperative period was significantly less when a single dose of etoricoxib was administered two hours prior to the anaesthesia. The pain scores were also lower on the first postoperative day and subsequently demanded lesser rescue analgesics. Those who received etoricoxib were noted to be more comfortable and had a better sleep. None of the patients experienced any problems relating to the side effects of the analgesics.

CONCLUSION

Etoricoxib is COX-2 inhibitor by which it relieves pain, other non-steroid, non-anti-inflammatory drugs act by inhibiting enzyme cyclooxygenase inhibition. But, these drugs do have effects on thrombocytes, renal system and gastroenterology systems, which COX-2 inhibitors don't have, now multimodal analgesic therapy, one is usually fixed opiate derivative, next analgesic should be safe like etoricoxib as it reduces the need of general anaesthetics. It provides postoperative analgesia excellently and safely.

Limitations of our study was the relatively small sample size. A larger sample would perhaps have been more useful to assess the incidence of the adverse effects, which may occur due to intake of etoricoxib. Another limitation was that the rescue analgesic was given on demand by the patient without monitoring the pain score.

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