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A Study on Haemodynamic and Adverse Effects of Intramuscular Parecoxib in Adults for Postoperative Pain Relief

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Abstract

Background: Postoperative pain control is generally best managed by anaesthesiologists since they offer regional anaesthetic techniques as well as pharmacological expertise in analgesics.Various postoperative analgesic modalities are offered in day to day practise such as oral or parenteral analgesics, peripheral nerve blocks, neuraxial blocks with local anaesthetics, intraspinalopioids TENS and others. Use of traditional NSAIDs have many side effects like gastritis, pepticulceration, bleeding from upper G I tract, delayed platelet inhibition, headache, vertigo, insomnia, bronchospasm, allergic reaction, anaemia, nephrotoxicity, salt and water retention.In contrast to NSAIDs, cox-2 inhibitors like Parecoxib are free from adverse effects and drug dependence.Hence we thought it is appropriate to study the haemodynamic and adverse effects of intramuscular Parecoxib for post operative pain relief. *Materials and Methods:* This study comprised of 100 postoperative patients of both sexes betweenage group of 18-70 years who were scheduled for various elective surgical proceduresand all thosewho satisfied inclusion and exclusion criteria. All patients are visited preoperatively, written consent was taken and premedicatedwith diazepam 0.2 mg/kg body weight at night. Parecoxib sodium 40 mg given in the recovery room, when patient complained of pain. Heart rate and blood pressure were recorded at intervals. Adverse effects were noted. The observation were recorded, tabulated and subjected to statistical analysis. *Results:* Inthe study group, 45 were males and 55 were females. There was no significant change in blood pressure or heart rate for 2-8 hours after intramuscular administration. There were 9% of patients with nausea and vomiting, 4% with headache and 3% with pruritus. *Conclusion:* Intramuscular Parecoxib provides good postoperative analgesia with no haemodynamic variations and minimal adverse effects.

Keywords: Parecoxib; Intramuscular; Haemodynamic Changes; Adverse Effects; Postoperative Analgesia.

Introduction

Effective pain control is an important aspect of optimal care of surgical patients. Despite advances in knowledge of pathophysiology, pharmacology of analgesics and development of more effective techniques for post-operative pain control many patients continue to experience appreciable discomfort [1].

Newer developments in nerve physiological techniques are providing insights into effect of pharmacologically active agents upon the specific areas of CNS[2]. In recent years information has been accumulating about specific sites within the CNS that are likely to be involved with modification of physiology and pharmacology of pain.

There are different methods of postoperative pain management like systemic opioids, intraspinal opioids, epidural anaesthesia, non-opioid analgesics, transcutaneous electrical nerve stimulation (TENS), psychological and other methods [2].

Use of traditional NSAIDs have many side effects like gastritis, peptic ulceration, bleeding from upper GI tract, delayed platelet inhibition, headache, vertigo, insomnia, bronchospasm, allergic reaction, anaemia, nephrotoxicity, salt and water retention [4,5].

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Parecoxib is the first selective cox-2 inhibitor for parenteral administration. Parecoxib is 28,000 times more selective to cox-2 than cox-1. It has faster onset of action, analgesic efficacy superior to intravenous morphine. It does not interfere with platelet function, no dose adjustments required in elderly and in mild hepatic and renal impairment. It is free from adverse effects like respiratory depression. It has superior gastrointestinal tolerability, free from drug dependence and therapeutic tolerance.Commonest side effects in short term use include dyspepsia, peripheral edema, pruritis and oliguria.

Parecoxib is an attractive alternative to parenteral Ketorolac in the treatment of postoperative pain because of lower gastrointestinal events and it is not contraindicated in patients on Heparin.

The present study seeks to evaluate the haemodynamic and adverse effects of intramuscular Parecoxib used in postoperative pain relief in adult patients.

Materials and Methods

This study was conducted in the Department of Anaesthesiology, Kempegowda Institute of Medical Sciences and Research Centre, Bangalore from June 2003 to 2005 after obtaining ethical committee clearance.

The study comprised of 100 patients of both sexes in the age group of 18 to 70 years, who are scheduled for various elective surgical procedures and all those who satisfied inclusion and exclusion criteria.

Inclusion Criteria

1. Males and/or females between 18-70 years.
2. Postoperative patients in the recovery room who have undergone various procedures like gynaecological, orthopaedic, general or dental surgery.

Exclusion Criteria

1. Pregnant or lactating women.
2. Patients with history of hypersensitivity to NSAIDs.
3. Patients with conditions predisposing to gastrointestinal dysfunction (e.g. history of peptic ulcers, upper gastrointestinal disease, ulcerative colitis, smoking, advanced age, concurrent corticoids, alcohol abuse, etc).
4. Patients with a history of bleeding tendencies, cirrhosis and oesophageal varices.
5. Patients who may require concomitant therapy with lowdose aspirin, Warfarin, antiepileptics, oral hypoglycaemic drugs, fluconazole, ketoconazole, etc.
6. Patients with severe cardiac, hepatic, renal or cerebrovascular disease, malignancy, chronic uncontrolled systemic disease e.g. diabetes, hypertension, asthma, collagen disorders, etc.

Procedure

All patients were visited preoperatively. Detailed history was taken and general physical examination and systemic examination was done and relevant investigation was done to check whether patients satisfied inclusion and exclusion criteria. Written informed consent was taken from all the patients who satisfied inclusion and exclusion criteria. Advantages and consequences explained to them in their own language.

Premedication

All patients were premedicated with oral dose of diazepam 0.2 mg/kg at night.

Postoperative Analgesia

After surgical procedure patients were shifted to recovery room and injection Parecoxib sodium 40 mg IM was given at first complaint of pain by the patient.

Heart rate and blood pressure were recorded at intervals. Adverse effects like nausea, vomiting, abdominal fullness, abdominal pain, pruritus, bleeding were observed. The observations were recorded, tabulated and subjected to statistical analysis.

Statistical Analysis

The data collected in this study is analysed statistically through SPSS 11.0 by computing descriptive statistics like mean, standard deviation, standard error of mean and 95% confidence interval for mean. Mean of the statistical inference is obtained by comparing the difference in means through the independent sample student's t test (under the assumptions that the population's variances are not known). The difference is considered statistically significant whenever p value is 0.05.

Results

In the present study, it was observed that of the 100 subjects studied 45 (45.0%) were male, 55 (55.0%) were female, and between 21-50 years of age both male and female constituted about 84.0%. Further, of the 45 males, majority i.e., 35 (77.8%) were in the age group of 21-50 years whereas among the 55 females 49 (89.1%) were belonging to 21-50 years.

In this study, the mean weight of male was 56.09 with a SD of 5.116 whereas for female it was 54.45 with a SD of 4.992. The overall mean weight was 55.19 and SD of 5.008. However, between male and female, there was no significant difference.

This study shows that (Table 1), at base the mean ± SD of pulse rate was 80.32±7.67 beats/minutes, which has increased to 81.68±7.65 beats/minutes at 15 minutes. From here onwards, gradually it has decreased from 79.28±6.914 beats/minutes at 30 minutes to 77.71±7.747 beats/minutes at 4 hours. After 4 hourstill 24 hours, the pulse rate was increased gradually from 78.61±6.075 beats/minutes to 83.38±5.5 beats/minutes respectively. It was also noticed furtherthat, the changes in the mean pulse rate from baseline to 1 hour was statistically highly significant ($p<0.0001$). But from 1-2 hours, it was not significant,whereasfrom 2-4 hours and 4-6 hours ($p<0.015$ and $p<0.017$ respectively) was significant. A similar significance was seen during 10-12 hours whereas from 6-10 hours as well as from 12-24 hours the difference in mean was not seen to be significant.

The systolic blood pressure in the present study at baseline was 122.12±1.25 mmHg and from there on it has gradually decreased to 119.23±9.009 mmHg at 8 hours. However, there was a slight gradual increase from 10 hours (120.40±10.396 mmHg) to 24 hours (123.50±11.605 mmHg). The overall mean systolic blood pressure was 120.91±11.158 mmHg. Nevertheless, the fluctuation of systolic blood pressure was observed to be statistically significant (Table 2) at baseline-15 minutes ($p<0.048$), 1-2 hours ($p<0.072$) and 10-12 hours ($p<0.017$). At all other time points, the variationwas not statistically significant. The overall combination of time intervals was seen to be statistically highly significant.

Table 1: Descriptive statistics of pulse rate (beats/minute)

Time interval	No. of subjects	Min (beats/min)	Max (beats/min)	Mean (beats/min)	Std. Deviation	Std. Error
Baseline	100	60	90	80.32	7.674	0.767
15 minutes	100	62	96	81.68	7.653	0.765
30 minutes	100	60	90	79.28	6.914	0.691
1 hour	100	58	86	77.88	6.756	0.676
2 hours	100	60	88	77.80	6.645	0.665
4 hours	98	62	88	77.71	6.747	0.682
6hours	92	66	86	78.61	6.075	0.633
8 hours	78	68	86	80.77	5.006	0.567
10 hours	50	70	90	80.96	5.051	0.714
12 hours	16	74	88	82.75	5.459	1.365
24 hours	16	72	88	83.38	5.500	1.375
Total	850	58	96	79.47	6.798	0.233

Table 2: Changes in systolic blood pressure (mmHg)

Time interval	No. of subjects	Min (mmHg)	Max (mmHg)	Mean (mmHg)	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
							Lower Bound	Upper Bound
Baseline	100	100	160	122.12	12.497	1.250	119.64	124.60
15 minutes	100	100	160	123.20	12.475	1.248	120.72	125.68
30 minutes	100	100	160	121.84	11.405	1.141	119.58	124.10
1 hour	100	100	154	120.48	10.844	1.084	118.33	122.63
2 hours	100	102	156	119.88	10.563	1.056	117.78	121.98
4 hours	98	104	160	119.80	11.005	1.112	117.59	122.00
6hours	92	100	160	119.65	10.726	1.118	117.43	121.87
8 hours	78	100	144	119.23	9.009	1.020	117.20	121.26
10 hours	50	100	148	120.40	10.396	1.470	117.45	123.35
12 hours	16	110	140	123.50	11.207	2.802	117.53	129.47
24 hours	16	100	140	123.50	11.605	2.901	117.32	129.68
Total	850	100	160	120.91	11.158	0.383	120.16	121.66

In case of diastolic blood pressure, the mean±SD at baseline (Table 3) was 79.98±9.174 mmHg and had increased to 81.52±9.364 mmHg at 15 minutes. But from 30 minutes it has gradually deceased from 78.90±7.808 mmHg to 77.51±7.949 mmHg at 4 hours. Further, it has gradually increased from 78.37±7.691 mmHg at 6 hours to 84.00±8.733 hours at 24 hours. The statistical analysis shows that the variationin mean difference at different time intervals (0-15 min, 15-30 min, 30 min-1 hour) was statistically significant at various levels viz. $p< 0.021$, $p<0.01$, $p<0.006$ respectively. However, from 1-8 hours and 10-12 hours, the mean difference was observed to be statistically significant, whereas the overall combination of intervals wasto be statistically highly significant $p<0.0001$).

Inthe present study of 100 patients, the adverse events like nausea, vomiting, headache, pruritis, pain abdomen, dryness of mouth were seen in 19 subjects of which 9 (47.37%) were males and 10 (52.63%) were females. Between males and females, the distribution of adverse events was almost similar (Table 4).

Table 3: Changes in diastolic blood pressure (mmHg)

Time interval	No. of subjects	Min (mmHg)	Max (mmHg)	Mean (mmHg)	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
							Lower Bound	Upper Bound
Baseline	100	70	100	79.98	9.174	0.917	78.16	81.80
15 minutes	100	70	100	81.52	9.364	0.936	79.66	83.38
30 minutes	100	68	98	78.90	7.808	0.781	77.35	80.45
1 hour	100	66	98	77.50	8.012	0.801	75.91	79.09
2 hours	100	64	96	77.18	7.817	0.782	75.63	78.73
4 hours	98	64	96	77.51	7.949	0.803	75.92	79.10
6hours	92	66	100	78.37	7.691	0.802	76.78	79.96
8 hours	78	68	92	78.23	6.566	0.743	76.75	79.71
10 hours	50	70	100	79.60	7.407	1.047	77.50	81.70
12 hours	16	74	100	84.00	8.944	2.236	79.23	88.77
24 hours	16	74	100	84.00	8.733	2.183	79.35	88.65
Total	850	64	100	78.92	8.245	0.283	78.37	79.48

Table 4: Adverse events

Adverse events	Sex		Total number of patients
	Male	Female	
Nausea	3 (33.3)	2 (20.0)	5(26.31)
Vomiting	2 (22.22)	2 (20.0)	4(21.05)
Headache	2 (22.22)	2 (20.0)	4(21.05)
Pruritis	1 (11.11)	2 (20.0)	3 (15.78)
Pain abdomen	1(11.11)	1 (10.0)	2 (10.52)
Dryness of month	-	1 (10.0)	1 (5.26)
Total	9	10	19(100)

Discussion

Pain is not just a sensory modality but is an experience.The International Association for the study of pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage."This definition recognizes the interplay between the objective, physiological sensory aspects of pain and its subjective, emotional and psychological components [6].

The aim of postoperative pain treatment is to provide subjective comfort, in addition to inhibiting trauma induced nociceptive impulses in order to blunt autonomic and somatic reflex responses to pain and subsequently to enhance restoration of function by allowing the patient to breathe, cough and move more easily. One of the primary aims of anaesthesia is to provide analgesia during the surgical procedure. However, pain during postoperative period is a cause of concern not only for the patient but also for the surgeon and anaesthesiologists. Anaesthesiologists with their knowledge of and familiarity with pharmacology, various regional techniques and the neurobiology of nociception, are continually in the forefront of clinical and research advances in acute postoperative pain management.

Pharmacological interventions in pain management include COX inhibitors, opioids, antidepressants, neuroleptic agents, anticonvulsants, corticosteroids and systemic administration of local

anaesthetics, but these are associated with various adverse effects also like pruritus, nausea, vomiting, urinary retention, gastritis,peptic ulceration,salt and water retention etc. Parecoxib in contrast to opioids and NSAIDs has less adverse effects. Parecoxib is the first selective cox-2 inhibitor for parenteral administration. Parecoxib is 28,000 times more selective to cox-2 than cox-1. It has faster onset of action, analgesic efficacy superior to intravenous morphine.

It does not interfere with platelet function, no dose adjustments required in elderly and in mild hepatic and renal impairment. It is free from adverse effects like respiratory depression. It has superior gastrointestinal tolerability, free from drug dependence and therapeutic tolerance.

Cheer. S.M et al [7] reported that the most common adverse events irrespective of treatment (Parecoxib, Ketorolac or placebo) after dental surgery was nausea, dizziness, alveolar ostitis and headache.

In our study with 40mg of Parecoxib Sodium intramuscularly for 100 patients, we encountered nausea and vomiting 9%, pruritus 3%, headache 4% occurred between 3 and 4 hours after the drug administration, no cardiovascular adverse effects were noted in given study and all patients remained haemodynamically stable throughout the study period.

Conclusion

It is concluded that intramuscular Parecoxib used for postoperative analgesia has less adverse effects.The main adverse effects being nausea and vomiting (9%), pruritus (3%), headache (4%) with no haemodynamic instability.

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