A COMPARISON OF ANALGESIC EFFICACY OF KETOROLAC AND PIROXICAM FOR POSTOPERATIVE PAIN RELIEF AFTER CHOLECYSTECTOMY

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ABSTRACT

A Randomized Control Trials (RCT) single blinded study was designed to evaluate the analgesic efficacy of ketorolac and compare its effectiveness with the analgesic efficacy of piroxicam for postoperative pain management after cholecystectomy at Department of Anaesthesiology and intensive care, PNS Shifa Hospital, Karachi. In this study, fifty patients who had to undergo cholecystectomy were randomized in two groups. The patients were followed for 72 hours post operatively. All the patients were operated through a standard subcostal incision (3 to 4 inches in length). The patients were American Society of Anaesthesiology status (ASA) of I, II, of both the sexes, aged between 30 to 60 years. A balanced anaesthetic technique was used for all the patients during the conduct of procedure. First dose of both the drugs was given immediately after induction (30 mg Ketorolac I/V and 20 mg Piroxicam I/M). Postoperatively, group I patients received injection Ketorolac 30mg I/V 8 hourly, group II patients were given injection Piroxicam 20 mg I/M once daily. If pain persistently remained above 5 on visual analogue scale (VAS), injection Pethidine 50 mg I/V p.r.n. was used as rescue analgesia for both the groups. . In group I (ketorolac group) only 5 patients (20%) required rescue analgesia whereas in group II eight patients (32%) required it. The effect of both the drugs on pulse rate, blood pressure, respiratory rate and oxygen saturation were monitored and recorded. The frequency of postoperative complication was recorded. Relevant laboratory data (bleeding time, platelets count, serum urea and electrolytes and liver function tests) was monitored. Both the drugs were found effective in controlling postoperative pain. Both drugs Ketorolac and Piroxicam provided adequate pain relief.

Keywords: Pain, postoperative analgesia, ketorolac, piroxicam

INTRODUCTION

Postoperative pain remains a point of maximum concern to the patients undergoing surgery. Best postoperative pain management begins preoperatively or at least intra operatively. Numerous methods / techniques and a number of analgesics have so far been used for this purpose.

The severity of postoperative pain may remain under assessed due to various reasons, for example, a non conversant patient in immediate postoperative period, or an under treated patient due to fear of side effects of the drugs like traditional narcotic analgesics. The most important side effects of narcotics analgesics are respiratory depression, excessive sedation and higher incidence of nausea and vomiting.

A lot of work has been done in the past in management of postoperative pain and still, a

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lot needs to be done. Ketorolac (injection Toradal brand by Roche) and Piroxicam (Injection Feldene by Pfizer) are nonsteroidal anti-inflammatory drugs (NSAIDs) and being used as analgesics in the management of different types of pain. Piroxicam is an old NSAID but Ketorolac is relatively newer agent. These agents are devoid of side effects like respiratory depression etc that the narcotics analgesics have, though these drugs have their own pros and cons.

The objective of the study was to compare the analgesic efficacy of Ketorolac and Piroxicam on ASA-I and ASA-II patients coming for cholecystectomy, who fulfill the inclusion / exclusion criteria.

MATERIAL AND METHODS

This study of fifty patients, to compare the analgesic effect of Ketorolac (Toradal brand by Roche) and Piroxicam (Injection Feldene by Pfizer) for relief of postoperative pain, was approved by the ethical committee of PNS Shifa Hospital, Karachi. The study design was Randomized Control Trials (RCT). This is a single blinded study. These fifty patients who had to undergo cholecystectomy were randomized in two groups.

Informed consent was obtained from the patients. All the patients were operated through a standard subcostal incision (3 to 4 inches in length).

Following were the inclusion criteria:

- ASA-I and ASA-II patients (fig.1)
- Both male and females
- Age 30-60 years

Following were the exclusion criteria:

- History of gastrointestinal bleeding
- History of allergy to NSAIDs
- Bleeding disorders
- Renal insufficiency
- Morbid obesity
- Patients with fitness o ASA-III, ASA-IV and ASA-V
- Patients with history of bronchial asthma and chronic obstructive pulmonary diseases.
- Pregnancy
- History of jaundice

Pre anaesthetic assessment was made by taking detail history and clinical examination and all the patients were evaluated to fulfill inclusion / exclusion criteria.

Following investigations were performed on all the patients in addition to complete picture of blood and routine urinalysis.

- Bleeding / clotting time
- Liver function test (Serum bilirubin, ALP and ALT)
- Serum creatinine
- Prothrombin time

All the above-mentioned investigations were repeated once after 48 hours postoperatively for comparison with preoperative values.

All the patients were explained about the method of assessment on a horizontal 10cm Visual Analogue Scale (fig.2).

Drugs used:

Ketorolac (Toradol brand by Roche)

Piroxicam (Feldene brand by Pfizer)

Grouping of patients:

Patients on ketorolac were placed in group-I and those on piroxicam were placed in group-II.

First dose of both the drugs was given immediately after induction (30mg Ketorolac I/V and 20mg Piroxicam I/M).

Anaesthetic Technique

After securing I/V line, all the patients were anaesthetized to using balanced anaesthetic induction technique. Injection

Pethidine 50mg was administered as a part of induction agent along with thiopentone sodium (5mg/kg) and suxamethonium (1.5mg/kg). The patients were intubated and Atracurium Besylate (0.5mg/kg) was used as a long acting muscle relaxant. Anaesthesia was maintained on oxygen, nitrous oxide and supplemental doses of muscle relaxant along with inhalational agent (halothane or isoflurane).

All most all the procedures were concluded in an averaged time of 70 ± 10 minutes.

The patients were extubated fully awake and after spending about 30 minutes in recovery room, were shifted to postoperative wards.

Non-invasive blood pressure, pulse rate, respiratory rate, oxygen saturation and urine output were monitored during and after surgery (Table-2,3). Intravenous fluids were replaced by calculating the fasting period and duration of surgery.

Postoperatively, group-I patients received injection Ketorolac 30mg I/V 8 hourly, group-II patients were given injection Piroxicam 20mg I/M once daily. Injection Pethidine 50mg I/V p.r.n. was used as rescue analgesia for both the groups. The number of demand boluses of Pethidine used was documented.

The intensity of pain was estimated by using horizontal visual analogue scale (VAS) (fig.2). The assessment of pain was done every hour for initial six hours, and 2 hourly for the next 12 hours. Thereafter, the assessment was made every four hourly. The frequency of postoperative complication was recorded.

The entire data was recorded on a proforma and at the end of study the results were analyzed. Using SPSS version 10.0. T test and chisquare test was applied and P-value calculated to compare both the groups.

RESULTS

Since the patients in both these groups were comparable as regards their age, physical status, ASA grade, the type and duration of surgery (Table-1), the assessment of postoperative pain was made objectively.

Group-I (Ketorolac group)

- 1-4 hours: The assessment of pain with horizontal VAS scale showed VAS score zero for the first four hours (same as group II patients).
- After 5th hour: Five patients had VAS score 1-2 (Mild pain), 2 patients had a VAS score of 3-5 (moderate pain), and one patient had VAS score of 6-7 (severe pain) in this group. None of the patients had VAS score beyond 7 in this hour.
- After 6th hour: Three patients had VAS score 1-2 (mild pain), one had VAS score 3-5 (moderate pain) and another one had VAS score 6-7 (severe pain).
- After 8th hour: Two patients had VAS score of 1-2 (mild pain), another two had VAS score 3-5 (moderate pain). No patient had VAS score more than 5 during this period.
- After 12 hours: Only two patients had a VAS score of 1-2 (mild pain) and no patient had VAS score more than 2 during this period.
- After 14 hours: Only one patient had VAS score of 1-2 (mild pain).
- After 16 hours: Only one patient had VAS score of 1-2 (mild pain).
- After 18 hours: Only one patient had VAS score of 1-2 (mild pain).
- After 20 hours: VAS score of all the patients remained zero.
- After 24 hours: VAS score of all the patients remained zero.

Group-II (Piroxicam group)

- 1-12 hours: The assessment of pain with horizontal VAS scale showed VAS score zero for the first twelve hours.
- After 12 hours: Four patients had VAS score 1-2 mild pain, 2 patients had VAS score 3-5 (moderate pain), 2 patients had VAS score 6-7 (severe pain).
- After 14 hours: Three patients had VAS score 1-2 (mild pain), 2 patients had VAS score 3-5 (moderate pain), one patient had VAS score 6-7 (severe pain).
- After 16 hours: Two patients had VAS score of 1-2 (mild pain), one patient had VAS score of 3-5 (moderate pain).
- After 18 hours: One patient had VAS score of 1-2 (mild pain), one patient had VAS score of 3-5 (moderate pain).
- After 20 hours: One patient had VAS score of 1-2 (mild pain).
- After 22 hours: One patient had VAS score of 1-2 (mild pain).
- After 24 hours: VAS score of all the patients remained zero.

Rescue analgesia (Injection Pethidine 50mg I/V) was administered to 5 patients in-group I and to 8 patients in-group II. Furthermore, none of the patients demanded more than one dose of rescue analgesia (Table-2). In group-II the VAS score remained zero to a relatively longer duration, that is, up to 12th hour and after that the VAS score pattern remained comparable to group-I.

No clinically significant change in pulse rate and blood pressure was noted in both the groups (Table-3).

There was also no significant variation in respiratory rate and oxygen saturation in both the groups (Table-4). All the other

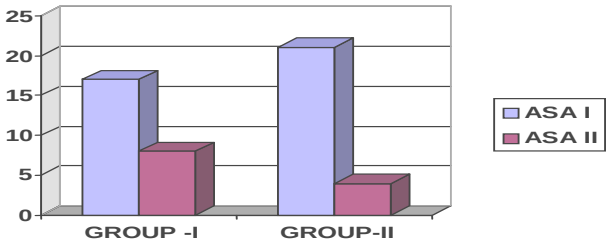

Fig.1: Distribution of patients according to ASA status

0	1 – 2	3 – 4 – 5	6 – 7	8 – 9	10
No pain	Mild Pain	Moderate Pain	Severe Pain	Very Severe Pain	Worst Pain

Fig.2: Visual analogue scale (with colour coding)

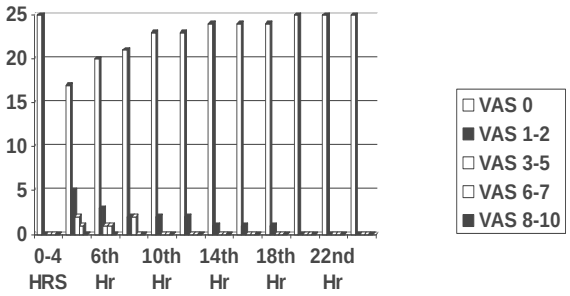

Fig.3: VAS score in post operative period group-I (ketorolac group)

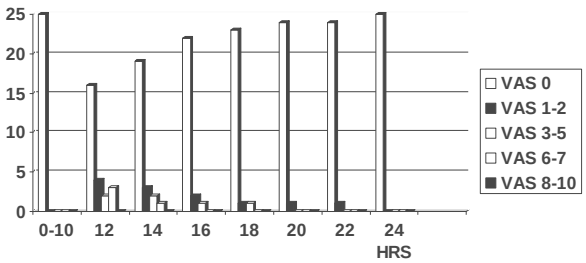

Fig.4: VAS score in post operative period group-II (piroxicam group)

Table-1: Demographic data

Description	Group-I	Group-II
Number of patients	25	25
Male and female ratio	4:19	3:22
Average age in years	38.13	39.99
Average weight in kg	60.9	63.7
Average duration of surgery (in minutes)	70 ± 10	70 ± 10
ASA-I	17	21
ASA-II	8	4
Analgesic	Ketorolac	Piroxicam
Education status (Under-matric / over-matric)	19/6	16/9

investigations were repeated after 48 hours and no significant derangements were found in liver function test and serum creatinine levels.

DISCUSSION

Like all types of pains, postoperative pain is also a subjective feeling. The intensity of postoperative pain varies with the individual patient and largely depends upon the site and nature of operation and constitution of the patient. Upper abdominal pain, for example, is more severe than lower abdominal pain and is aggravated by movements or cough. Adequate analgesic administration can

Table-2: Comparison of different parameters in group-I and group-II patients

	Group-I	Group-II
PONV#	4	3
Rescue analgesia	5	8
Hypersensitivity reaction	Nil	Nil
Increase in bleeding time*	5	0

#Post operative nausea and vomiting.
** Bleeding time still remained in normal range.*
**No significant postoperative bleeding observed.*

Table-5: Comparison of rescue analgesia

Injection Pethidine	Group-I	Group-II
Required	5	8
Not required	20	17

P-Value >0.05 using x^2-test

Table-3: Comparison of mean arterial blood pressure (MAP) and heart rate (HR)

Time in hours	MAP			HR		
	Group-I	Group-II	P-value	Group-I	Group-II	P-value
0 hour	88±6	89±5	>0.05	76±4	75±6	>0.05
1 hour	90±4	93±5	<0.05	83±3	85±3	<0.05
2 hours	89±3	90±3	>0.05	83±2	85±5	>0.05
3 hours	87±4	88±4	>0.05	74±6	75±5	>0.05
4 hours	88±2	89±3	>0.05	85±3	84±3	>0.05
6 hours	98±6	100±7	>0.05	84±3	88±4	<0.05
12 hours	103±3	104±4	>0.05	92±3	94±3	<0.05
24 hours	94±3	92±4	<0.05	84±4	81±6	<0.05
36 hours	99±4	101±3	<0.05	87±2	89±3	<0.05
48 hours	90±5	92±4	>0.05	80±5	81±6	>0.05
72 hours	89±4	94±4	<0.05	89±3	80±5	<0.05

P<0.05 significant difference between both the group.
P>0.05 in significant difference between both the groups.

Table-4: Comparison of oxygen saturation (SaO_2) and respiratory rate (R.R)

Time in hours	SaO_2			R.R		
	Group-I	Group-II	P-value	Group-I	Group-II	P-value
0 hour	97±0.3	97±0.2	<0.05	19±0.8	19±0.8	>0.05
1 hour	97±0.3	97±0.4	<0.05	19±0.5	10±0.4	<0.05
2 hours	97±0.2	97±0.2	<0.05	19±0.9	19±0.7	>0.05
3 hours	97±0.5	97±0.5	<0.05	19±0.6	19±0.5	>0.05
4 hours	94±0.7	95±0.6	>0.05	18±0.8	18±0.9	>0.05
6 hours	97±0.9	97±0.8	<0.05	20±0.9	20±0.7	>0.05
12 hours	96±0.5	96±0.2	>0.05	18±0.7	18±0.5	>0.05
24 hours	97±0.7	97±0.6	>0.05	20±0.8	20±0.6	>0.05
36 hours	94±0.9	95±0.8	<0.05	18±0.7	18±0.4	>0.05
48 hours	95±0.6	96±0.4	<0.05	18±0.6	18±0.4	>0.05
72 hours	950±.7	96±0.4	<0.05	18±0.6	18±0.5	>0.05

P<0.05 Significant difference between the group.
P>0.05 Insignificant difference between both the groups.

reduce the intensity and duration of postoperative pain. The provision of analgesia is important, as it determines the physiological and psychological outcome of the patient.

The objective of providing good pain control has led researchers to invent various methodologies and modalities. An analgesic drug having prompt and lasting action, with minimum adverse effects is still desired to be found. No single analgesia technique has so far been developed to provide sufficient pain relief without untoward effects [1].

Postoperative pain relief is commonly being provided with drugs of two main categories, Non-steroidal anti-inflammatory drugs (NSAIDs) and narcotic analgesics [1,2]. A similar research has led to the development of Ketorolac tromethamine. A standard dose of Ketorolac (15-30mg) provides analgesia equivalent to 6-12 mg of morphine administered by same route. Its time of onset is similar to morphine, but ketorolac has a longer duration of action (6-8 hours) [3,4].

Piroxicam also has intense analgesia activity, comparable or superior to other drugs (aspirin and many other NSAIDs) and a prolonged duration of action (distribution half life 50 minutes). The incidence of untoward effects remained negligible.

Both the drugs are free from side effects of respiratory depression and nausea and vomiting which the opioids have. The present study provided a comparison between these two drugs as far as their pain control and side effects are concerned.

The results are almost equivocal for both the drugs. Ketorolac proved to be superior agent as far as its pain control and quality of analgesia is concerned. The number of patients who required the dose of rescue analgesia was less with ketorolac than with piroxicam (Table-5) but this difference is not statistically significant (p-value >0.05).

There was no significant effect on heart rate, mean arterial pressure and respiratory rate in either group (Table-3,4). Also there was no significant postoperative nausea and vomiting in both the groups.

Several clinical studies have established the ability of Ketorolac and Piroxicam for relief of postoperative pain after different procedures. On the review of the literature we could find studies in which Ketorolac and Piroxicam were comparable as far as their analgesia potency is concerned [5]. These drugs have also been found to produce effective analgesia after orthopedic surgery, laparoscopy, day case procedures and cholecystectomy [6].

In one study intramuscular Ketorolac, Piroxicam and diclofenec sodium were compared for relief of postoperative pain after laparoscopy with similar results (P>0.05). A few of the patients, in all the three drugs in comparison in that study, also required further analgesia (rescue analgesia) but the difference between the individual groups was not of statistical significance.

In our study, there was no report of increased bleeding or haematoma formation at operation site, bronchoconstriction, bleeding from gastrointestinal tract, renal impairment or pain at the site of injection. This study showed that both these drugs are effective in providing postoperative analgesia. However, in the patients with upper gastrointestinal bleeding, renal impairment and patient having allergies to NSAIDs, one shall resort to other modalities for pain relief.

It is seen in our study that both these agents can be used effectively to control postoperative pain up to acceptable levels. However, still better results might be achieved with combining one of the agents of this study (i.e. Ketorolac or Piroxicam) and a narcotic analgesic (in the form of balanced analgesia) [7].

Out of the two drugs in our study, Piroxicam was found to be cost effective.

Limitations of the Study

Following pitfalls were observed in our study.

a. The rout of administration of both the drugs was not same

b. The drugs under study had different half-lives and therefore, the frequency of doses remained different.

c. Rescue analgesia with injection pethidine had to be administered to a few patients in both the groups.

d. The number of patients under study was limited to 50 only.

Despite the above-mentioned shortcomings the control of postoperative pain remained in acceptable limits.

CONCLUSION

We conclude that both Ketorolac and Piroxicam provide adequate pain relief. By using these drugs we can prevent untoward effects of traditional narcotic analgesics (nausea, vomiting, respiratory and cardiovascular depression etc.). Our patients can remain pain free and at the same time fully awake. These agents can make good choice for day care surgery as well. These drugs can effectively be used for short-term control of postoperative pain.

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