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Research Article

Lornoxicam versus diclofenac sodium in acute renal colic: a prospective randomized trial

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ABSTRACT

Background: Acute renal colic is excruciatingly painful event, opioid analgesics and nonsteroidal anti-inflammatory drugs remain the mainstay of treatment for acute renal colic. This study compares diclofenac and lornoxicam in their efficacy to relieve pain of renal origin.
Methods: Prospective, randomized, double blind clinical study including eighty patients with renal pain admitted in emergency department of a tertiary care teaching hospital. Parameters were observed at baseline and after 15, 30, 60, 180 minutes and 5hrs of drug treatment. The efficacy of the drug was measured by observing: Pain score, onset & duration of action, rescue drug use, global patient and physician impression.
Results: Both drugs are effective in relieving pain of renal origin (p<0.05) and maintaining it over time as well. When decrease in value of pain score compared between two groups at various interval there was statistically significant (p<0.05) decrease in pain score only at 15 minutes in lornoxicam group showing this slightly more effective in early phase compared to diclofenac. In either group there is no statistically significant difference regarding onset of action, duration of action and side effect profile.
Conclusions: Both the drugs are equally effective and safe in renal colicky pain with added advantage of lornoxicam being more effective in early period.

Keywords: Renal colic, Lornoxicam, Diclofenac

INTRODUCTION

Acute renal colic is probably the most excruciatingly painful event a person can endure. The pain is often described as being worse than childbirth, broken bones, gunshot wounds, burns, or surgery. Renal colic affects approximately 1.2 million people each year and accounts for approximately 1% of all hospital admissions in emergency and casualty ward. The pain generated by renal colic is primarily caused by the dilation, stretching, spasm, ureteral peristalsis, stone migration, and tilting or twisting of the stone with subsequent intermittent obstructions leading to exacerbation or renewal of renal colic pain. The most effective pain relief is achieved after relieving the obstruction by spontaneous passage or surgical removal of renal calculus.[1] Opioid and nonsteroidal anti-inflammatory drugs (NSAIDS) remain the mainstay of treatment for acute renal colic. However; prolonged opioid use may cause dependence, tolerance and side-effects like nausea, vomiting, constipation and drowsiness. Larger doses even cause respiratory depression and hypotension. Diclofenac is amongst the most extensively used NSAIDs still preferred first line drug in renal colic pain. Another class of drug which has shown the efficacy in renal colicky pain is oxicam derivatives. Both piroxicam and tenoxicam have been extensively used, recently lornoxicam has been introduced in Indian market in oral, intravenous and intramuscular formulations. There is plenty of literature available on the effect of lornoxicam on chronic and acute pain management.[2]

Data from preliminary clinical trials suggest that lornoxicam is as effective as the opioid analgesics in relieving postoperative pain. Lornoxicam has a favourable tolerability profile and acceptable

gastrointestinal and renal side effects.[3] There are several articles, reporting efficaciousness of members of oxicam group in acute renal colic treatment. It is important to establish the efficacy and safety profiles of lornoxicam in acute renal colic as only few studies are available in literature.[2] Lornoxicam has been recently introduced in our setup and careful search of recent literature did not show its use for renal pain relief in India. Hence, the present study was conducted to compare the analgesic efficacy of lornoxicam and diclofenac in renal pain relief in Indian population.

Aims and Objectives

To evaluate efficacy and tolerability profiles of lornoxicam in acute renal colic and to compare with diclofenac sodium in the management of acute renal colic.

METHODS

The study was conducted in tertiary care teaching hospital on 80 patients having pain of renal origin based on typical clinical history and relevant radiological investigations. The study protocol was approved by institution's ethical committee. Patients aged 18-65 yrs of either sex willing to give informed consent who should not have taken any analgesics at least within last two hours were included, patients with previous renal surgery, liver and renal failure, hypersensitivity to lornoxicam or diclofenac, pregnant/lactating women, bronchospastic disease, urine examination showing more than 5 leukocytes suggestive of pyuria were excluded from study.

Study design

Prospective, randomized, double blind manner, drug solution was administered intramuscularly to all patients by a nurse who was not having any knowledge of the study protocol and observation of various parameters were done by the doctor who was also have no knowledge of administered drugs. The patients were randomly allocated into two groups consisting of 40 patients each and they received drugs as follows:
Group-I: lornoxicam 8mg,
Group-II: diclofenac sodium 75 mg.

Clinical assessment

Parameters were observed at baseline and after 15, 30, 60, 180 minutes and 5hrs of drug treatment. The efficacy of the drug was measured by observing: pain score, onset & duration of action, rescue drug use, global patient and physician impression.

Pain score

Pain was assessed in detail, as patients of renal colic coming to emergency room are in severe agony, pain assessing scale that is simple and sensitive was used. Pain was assessed by visual analog scale (VAS) measuring 0-10cm line. Where 0 stands for no pain and 10 for worst possible pain, measurements taken at 0, 15, 30, 60, 180 minutes & 5 hrs. Patients were asked to make a mark on this line that was measured and recorded in millimeters.

Hemodynamic Parameters

Just before starting treatment heart rate and blood pressure were recorded in each patient so that any fluctuations in the clinical parameters after giving the drug could be analyzed. These parameters were recorded subsequently at 15, 30, 60, 180 minutes and 5 hrs.

Rescue drug use

Patients who were having no relief of pain with the drug in question after 30 minutes or VAS more than 40 mm were given intramuscular pethidine 50mg. Number of patients requiring rescue drug and time when required was noted in each group. More the number of patients requiring rescue drug, denote poor efficacy of drug used.

Onset and duration of action

Onset of action of drug was recorded as within 0-15 minutes and 15-30 minutes. The duration of action was taken as the time interval between the onset of action and first recurrence of pain or demand for analgesic.

Global impression of efficacy

At conclusion of study period all patients were asked to rate the overall efficacy of drug used as good, very good or excellent. Similarly attending physician gave his/her impression about the used drug efficacy.

Tolerability assessment

The tolerability of the drug was assessed on the basis of acceptance of the drug. The parameters assessed were-nausea & vomiting, epigastric pain, headache, dizziness/faintness, vertigo, allergic manifestations and injection site pain. These parameters were observed after 15, 30, 60, 180 minutes and 5 hrs of drug administration.

Statistical analysis

At the end of study, the data were compiled and pain score was evaluated by non parametric test (Mann Whitney test). Quantitative data was analyzed by using parametric test student's t-test and the value of $p<0.05$ regarded as statistically significant.

RESULTS

The mean age±SD (standard deviation) of the participants was 38.57±14.02 years (range 21–64 years in group I) and 37.82±13.43years (range 19–64 years in group II)

with male-to-female ratio 3:1. Mean age was comparable (p>0.05). The mean weight of the participants was 64.72±12.90 kg (range 38-87 kg in group I) and 65±13.10 kg (range 43–88 kg in group II). Mean weight of patients were also comparable (p>0.05).

X-ray KUB revealed renal calculus in four (10%) cases and ureteric stone in seven (17.5%) cases while USG has shown hydronephrosis in 33(82.5%) cases and calculus in 25(62.5%) cases in group I. In group II, X-ray revealed renal calculus in three (7.5%) cases and ureteric stone in four (10%) cases while USG has shown hydronephrosis in 32(80%) cases and calculus in 17(42.5%) cases. Thus ultrasonography was more sensitive in detecting renal calculus compared to plain x-ray.

The mean base line pain score was 84.21± 12.70 mm (66-100mm) in group I and 87.34± 10.91 mm (70-100mm) in group II and was not statistically significant (p>0.05). Hence both groups were comparable regarding base line pain severity score. The mean pain score at fifteen minutes after lornoxicam VAS15 was 54.18±16.12. When this reduction in pain score was compared with base line pain score VAS0 it was quiet significant (p<0.001) which suggest the effectiveness of lornoxicam in providing pain relief after fifteen minutes. The pain score at 30, 60, 180 minutes and 5 hrs were 26.14±7.21, 13.6±6.91, 6.96±6.31, 1.5±3.61 respectively. These scores at different time interval were statistically highly significant compared to base line pain score (p<0.005) (Table 1). This suggests that lornoxicam is effective analgesic in renal colic.

Table 1: Pain score at different interval in two groups.

Group		Time interval					
		0 min	15 min	30 min	60 min	180 min	5 hrs
VAS	I	84.21±12.70	54.18±16.12	26.14±7.21	13.64±6.91	6.96±6.31	1.52±3.61
	II	87.34±10.91	66.94±20.13	27.21±7.13	16.52±7.21	8.34±7.63	2.75±4.51
***p*-value**		>0.05	<0.05	>0.05	>0.05	>0.05	>0.05

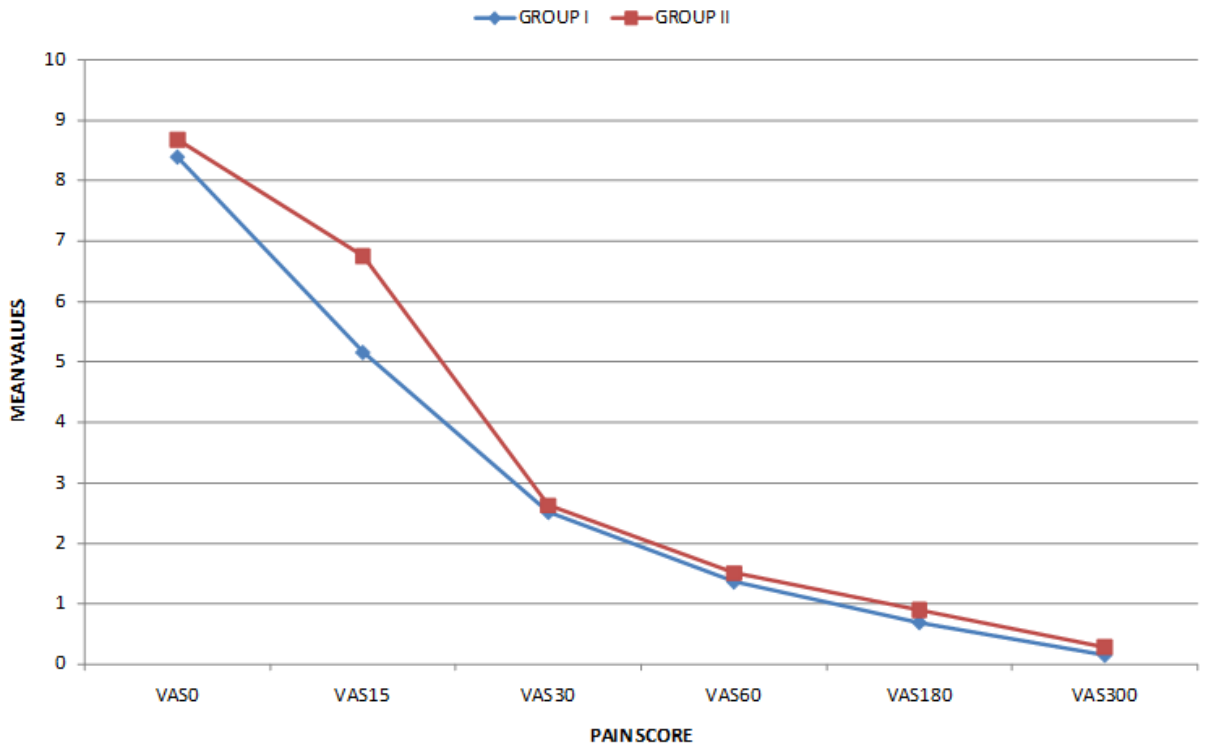

Figure 1: Showing pain scores at different intervals in two groups.

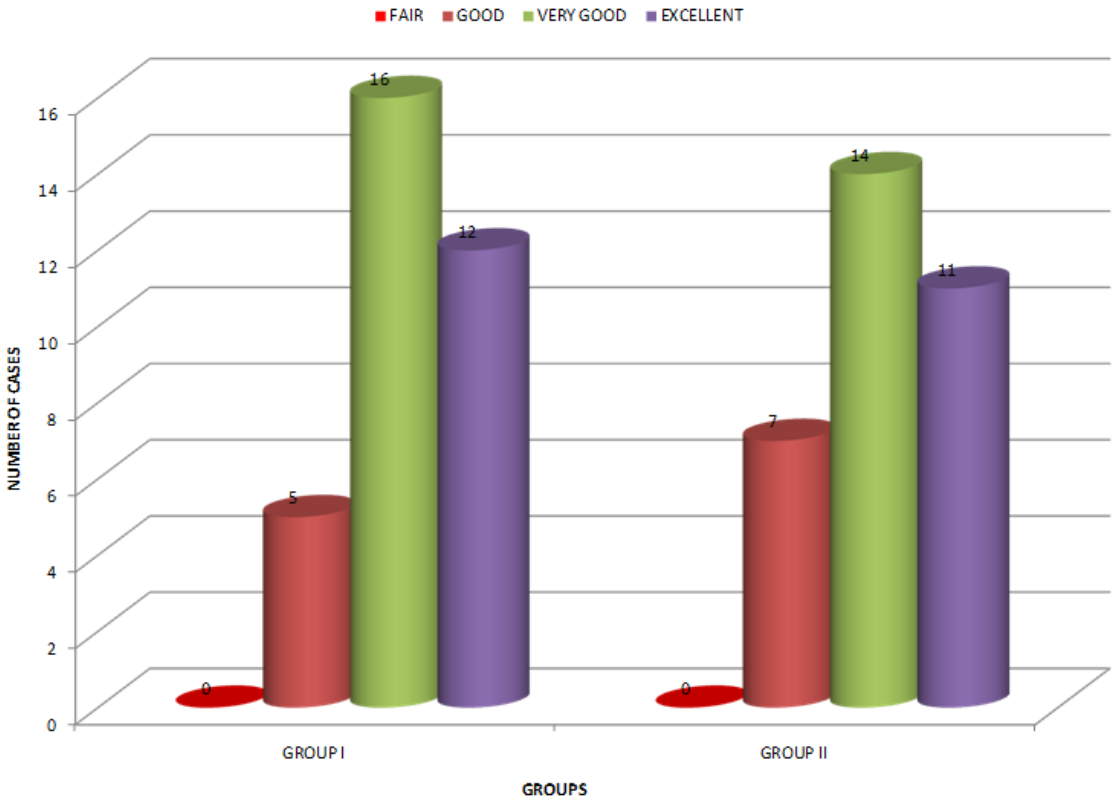

Figure 2: Showing patient global impression in two groups.

Similarly in group II after diclofenac pain score at fifteen minutes was 66.94±20.13, compared with base line pain score was quiet significant (p<0.05). The pain score at 30, 60, 180 minutes and 5hrs were 27.21±7.13, 16.52±721, 8.34±7.63 and 2.75±4.51. These scores compared to base line pain score are significantly decreased (p<.005).

Pain intensity decreased significantly over time in both groups, but the lornoxicam group had significantly lower pain scores than the diclofenac group at 15 minutes (p<0.05).Thus lornoxicam was slightly more effective in pain relief, after this interval both drugs were equally potent in relieving pain and maintaining its efficacy over observation period (Figure 1).

The mean onset of action was 27.27±12.69 min (range 15-60 minutes in group I) and 22.80±7.64 min (range 15-30 minutes) in group II. Mean onset of action in either group was comparable (p>0.05) and did not show any significant difference statistically. Hence both drugs are equally effective regarding onset of action. None of the patient in either group required repeat dose of same or different drug, provided the drug was effective in initial period, during observation period. Hence both drugs are equally effective regarding duration of action.

Seven patients (17.5%) in group I and eight (20%) patients in group II required rescue drug as the drug in question was not effective (VAS more than 4 at 30 minutes). Thus one more patient in group II required rescue drug which is not statistically significant (p>0.05). So both groups were similar as far as rescue drug requirement is concerned.

At conclusion of study period all patients were asked to rate the overall efficacy of drug used as good, very good or excellent. In group I, twelve patients rated the drug used as excellent, sixteen patients as very good while five patients were just satisfied about the drug. In seven patients (17.5%) drug was not effective and they required rescue drug. In group II, eleven patients rated the drug used as excellent, fourteen patients as very good while seven patients were just satisfied about the drug (Figure 2). In eight patients (20%) drug was not effective and they required rescue drug.

Physician assessed the overall efficacy of drug used as good, very good or excellent. In group I physician rated drug as excellent in ten, as very good in fifteen and just satisfied in eight cases. In seven patients (17.5%) drug was not effective and they required rescue drug. In group II, physician rated drug as excellent in nine, as very good in twelve and just satisfied in eleven cases. In eight patients (20%) drug was not effective and they required rescue drug.

Two patients in Group I and four in Group II had nausea and vomiting while in addition one patient in Group II complained of epigastric pain. None of the patients in any of the group reported other events like dizziness, headache, mental confusion, bleeding, allergy, pruritus, pain at injection site etc. Therefore both the drugs were fairly well tolerated.

Overall efficacy: Summing up the weightage points of pain score, onset of action and duration of action we assessed overall efficacy of drug. Regarding pain relief there is significant decrease in pain score over time in both groups and this effect is lasting till study period of 5 hrs. So both the drugs are effective in relieving pain of renal origin and maintaining it over time as well. When decrease in value of pain score compared between two groups at various intervals then there is statistically significant decrease in pain score only at 15 minutes in lornoxicam group showing that lornoxicam is slightly more effective in early phase as compared to diclofenac. In either of group there is no statistically significant difference regarding onset of action, duration of action and side effect profile. So both the drugs are equally effective and safe in renal colicky pain with added advantage of lornoxicam being more effective in early period.

DISCUSSION

Renal colic is an important and frequent occurrence in clinical practice. It affects 1-5% of the population in industrialised countries, with a lifetime risk of 20% in white men and 5-10% in women.[4] In our study majority of the patients were male (M:F 3:1) in their 3rd to 4th decade with mean age of 38.57 years. Similar observation was made by Pincus et al, in their study majority of patients were male upto 85% with maximum incidence in 3rd to 4th decade of life.[5] Typically caused by obstruction of the ureter by a calculus, it is one of the most severe pain experienced by human. Patients with suspected renal and ureteric colic are a common referral made to acute urological services. The main goal of the emergency department is the relief of this pain until spontaneous passage of the calculus occurs, or until surgical management is started. The choice of analgesia used in the management of acute renal colic is changing, with increasing use of NSAIDs. Most studies have shown these drugs to be as effective as opioids.[6-9] There are many NSAIDs available; the main differences amongst them are the incidence and type of side-effects, predominantly gastric irritation and ulceration. Lornoxicam is a strong analgesic and anti-inflammatory NSAID with balanced COX-l/COX-2 inhibition and excellent tolerability. Lornoxicam has a better gastrointestinal tolerability profile than other oxicams.[8,10] This has been attributed to lornoxicam's shorter half-life (~4 hours) compared with more than 24 hours for the other oxicams.

In present study good pain relief was seen with lornoxicam and diclofenac sodium within 30 minutes. The analgesic effect of lornoxicam is similar to that of diclofenac at therapeutic doses in terms of onset, degree and duration of analgesia. In our study before treatment, mean pain scores in lornoxicam group were found to be 84.21 whereas before treatment mean pain score in diclofenac group was 87.34. While means of pain scores at 15, 30, and 60 minutes were found as 54.18, 26.14 and 13.6 respectively in lornoxicam group, in diclofenac group, these values were found as 66.94, 27.21 and 16.52 respectively and it was found that there was a statistically significant difference between the values (p<0.005). Similarly study conducted by Gokhan et al has compared lornoxicam with diclofenac in 129 patients with acute renal colic and there was statistically significant pain relief in both groups before and after treatment.[2] Our study results have also shown efficacy of lornoxicam in relieving pain of renal colic as good as diclofenac sodium. We have observed statistically significant pain reduction in lornoxicam as compared to diclofenac group at 15 minutes after injection (p<0.05), hence lornoxicam is slightly faster acting than diclofenac sodium.

In our study tolerability profile of lornoxicam was found to be excellent. Only two patients in lornoxicam group had nausea and vomiting while four patients in diclofenac group complained of nausea and vomiting. None of the patient in lornoxicam group had serious side effects i.e. mental confusion, dizziness, bleeding or allergy etc.

There are large numbers of controlled trial articles in literature showing safety and efficacy of lornoxicam in chronic painful conditions. There are few studies in literature showing efficacy of lornoxicam in acute postoperative and other painful conditions showing similar pain relief compared with commonly used opioids and NSAIDS with good tolerability profile.[11-13] A prospective, randomised, double-blind, placebo-controlled trial comparing the efficacy of lornoxicam versus parecoxib for the management of pain after laparoscopic cholecystectomy concluded that parecoxib 40 mg i.v. and lornoxicam 8 mg i.v. had equal analgesic potency and were both more efficacious than placebo for the management of pain after laparoscopic cholecystectomy.[14] The assessment of analgesic drugs is notoriously difficult. Generally, analgesics may be tested either against experimentally induced pain or pathological pain. In extensive reviews on the study of pain and analgesia, pathological pain has been discussed as a better basis than experimentally induced pain for the study of analgesics.[15,16]

Our study was based on the “intention to treat” and thus included all patients, except for the exclusion criteria in whom the initial diagnosis on presentation, by the attending physician, was renal colic. Thus, confirmation of the diagnosis was not required for inclusion in the study. This more accurately reflects the emergency clinical setting where analgesia is required before diagnostic tests are completed.

The present study had certain limitations, as no placebo control was used in the patients in view of the ethical problems, so a comparison was made using an active control only. The study measured the adverse effect of drugs for a short time only because the study duration was only 5 hrs. Also number of patients in each group was relatively small. It was beyond the scope of the present study to observe limitations as the number of patients included in the groups were small in numbers and restriction of the period of study which prevented the extrapolation of the results to the general population where the numbers of cases are large.

CONCLUSION

In acute renal colic treatment, lornoxicam can results in significant decrease in pain within a short time and is well tolerated by most patients. Though we acknowledge the pitfalls in the subjective assessment of analgesic activity, we feel our rigorous methodology provided a true comparison of the efficacy of lornoxicam and diclofenac in renal colic pain. However, multicentric trials with more number of patients are required to address these issues further.

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