
**Effect of Diclofenac
Sodium In Renal Colic**

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Introduction

Pakistan being located in the geographic belt of high incidence of stone disease, and having hot climatic conditions during summer months, faces the problem of insufficient number of hospitals with limited number of in-patient facilities. On the other hand calculus renal disease is a common urological problem^{5,6} with its common presenting symptom as renal colic, often necessitating hospital admission. Moreover, the high incidence of stone disease is in a stage of transition from the lower urinary tract to the upper tract with its close relation to industrialisation and socio-economic development⁷.

The most common cause of renal colic is a calculus impacted in the ureter or less frequently passage of blood clot, sloughed papilla and crystalluria.⁸ The incidence of crystalluria and colic dramatically rise during the summer months.^{9,10,11}

For many years it was assumed that ureteric spasm is responsible for the pathogenesis of pain. Thus the conventional treatment with spasmolytics and antimuscarinic drugs used to be instituted in the treatment of renal colic. The response of human ureteral tissue to acetylcholine is variable and no conclusions can be drawn concerning the presence or absence of muscarinic receptors,¹ hence one cannot expect antimuscarinic drugs like atropine, hyoscine butylbromide and propantheline bromide to be effective in renal colic, and pain relief afforded by these drugs is poor.^{2,8}

The common practice of hydrotherapy in renal colic on the premise that the diuresis will push the stone down has been re-evaluated recently by many observers. It has been suggested that the amount of fluid has no practical influence on the degree of pain nor the fluid intake influences the

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likelihood of spontaneous expulsion of stone.^{3,4} If we accept the recently evolved hypothesis that ureteric obstruction raises the intraluminal pressure and at the same time stimulates the synthesis of prostaglandins which further increases the renal pressure, it would be logical to institute measures to counteract the effects of prostaglandin with non-steroidal anti-inflammatory drugs.

The present study was conducted to compare anti-prostaglandin therapy with conventional medication in renal colic.

Method and Material

Seventy three patients of either sex in the age group 16-60 years suffering from acute renal colic were included in the trial.

They were randomly allocated in two groups for comparative study. Patients with severe renal colic and/or who had documented evidence of previous episodes of colic owing to calculi were considered. Pregnant females and patients with positive history of drug allergies were excluded from the study. Those with the positive history of narcotic abuse were also excluded. Patients with severe malfunction of the kidney resulting in metabolic disturbances, those with chronic cardiac, pulmonary, hepatic or peptic ulcerative disease, and those with known malignancy were also not considered.

After taking the history and physical examination performed, the random allocation of two groups of patients was made as under:-

Group I (n = 40): Patients of this group were treated with a single injection of 75 mg diclofenac sodium given intramuscularly.

Group II (n = 33): These patients were given 20 mg hyoscine butylbromide intravenously or some other spasmolytic drug with or without hydration therapy.

The response to treatment as relief of pain was assessed at 10 and 30 minutes after commencing therapy. Efficacy was evaluated on the basis

of verbal intensity scale. Patient's evaluation of pain was made as none(0), dull (+1), moderate (+2) or severe (+3).

Pain intensity differences based on verbal intensity scale were calculated for each patient by subtracting the pain level from the intensity at the time of drug administration. Efficacy was also evaluated by comparing proportions of patients who achieved effective pain relief in the two groups. Patients who required a second dose of test medicine or a standard analgesic were assigned having no relief.

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CLINICAL DATA:

Age and Sex:

Sixty eight males and 5 females ranging in age from 16 to 60 years were in both diclofenac (first) and hyoscine treated (second) groups. The age range in the first group (n = 40) was 17 to 60 years (35.50 + 2.01) while in the second group (n = 33) it was 16 to 50 years (32.82 + 1.36). In the first group there were 38 males and 2 females and in the second group 30 males and 3 females.

History of previous attacks:

Eleven of all cases had previous episodes of pain. Sixty two patients reported having no previous attack of renal colic (84.9%). An episode within previous 15 days was regarded as part of the present attack.

Onset of pain:

Fifty seven out of 73 patients reported sudden onset of pain and in 16 cases (21.9%) the onset was insidious. No clear-cut relation was noted in intensity of pain with its onset. An insidious onset of pain rising to its peak with increasing rapidity was probably not appreciated by the patient in daytime till its stage of high intensity. Patients considered gradual onset

only when its intensity had reached to the maximum in hours and not in minutes.

Intensity of pain:

The description of pain was different from patient to patient but the degree of pain was assessed as:

Severe (+3) when insupportable walking was impossible and with extreme restlessness;

Moderate (+2) with a lesser degree of pain making the patient unable to carry out his normal activity, and.

Dull (+) with the patient being able to carry out only partial activity.

Most patients emphasised the constant nature of pain and alterations in intensity were never appreciable.

Sixty patients presented with acute, severe, incapacitating unilateral pain. Thirteen patients (17.8%) had moderate pain with radiographically confirmed ureteric calculus.

Location of pain:

Location of pain at its onset was accurately recorded. In 29 cases it was located in the back usually indicated in the renal angle, 28 in the loin, 4 in the hypochondrium or upper abdomen, and 5 in the testis. The pain was fixed in 14 cases having no shift or radiation. In 5 cases pain radiation was from iliac fossa or suprapubic region to the loin, whereas seven patients presented with radiation of pain from testis to loin. In one case the pain shifted from hypochondrium to epigastrium. Twenty four patients accounted for radiation of pain from loin to the groin and 21 patients from loin to the umbilical region.

X-Ray Finding:

In cases where stone was not detected on plain x-ray, diagnosis was made on positive previous history of urolithiasis, dilated pelvicalyceal system on ultrasonography and microscopic haematuria. Subsequent x-rays at weekly interval were done in cases when stone passage was not noted by the patient. Downward descent of the stone on x-ray associated with onset of further attack of pain was not observed in 26 cases except two patients who were having superimposed infection. Three patients underwent surgery and the rest reported spontaneous passage of stone.

Stone was detected on plain x-ray of the abdomen in 60 (82.2%) cases: 39 (53.5%) in the pelvic ureter commonly at the level of ischial spine, and 21 (28.8%) in the lumbar ureter usually at the level of 4th or 5th lumbar transverse process.

Symptoms associated with " Renal Colic" :

Fifty eight patients (79.4%) had nausea and vomiting and 50 cases (68.5%) reported with loss of appetite. Thirty one cases had abdominal distension (42.4%), 2 (2.7%) had dry mouth and 2(2.7%) had constipation. Burning and difficulty in micturition was present in 50 cases (68.5%). Two patients (2.7%) had complete urinary retention for which they were already catheterized. Naked eye haematuria was present in five cases (6.8%) and microscopic haematuria in 65 cases (89%). One patient was more disturbed by hiccups than pain which he suffered for 4 days. Hiccups were severe and regular and did not respond to antacids and antihistamines. Fever was associated in 8 cases (11%), of whom only two were having associated bacteriuria.

Analysis of pain relief:

Forty patients (54.8%), 38 males and 2 females, were treated with 75 mg of diclofenac sodium given as an intramuscular injection. Thirty three patients (42.5%) (30 males and 3 females) were given 20 mg of intravenous hyoscine butylbromide.

In diclofenac treated patients (group I) complete pain relief was achieved in 38 patients (95%) within 30 minutes. Within 10 minutes complete pain relief was afforded in 25 (62.5%) out of 40 patients. No side effects were noted. One patient, who was having severe hiccups for 4 days and did not respond to various medicines already used, had complete relief within 30 minutes. He did not respond to diclofenac sodium given alongwith intravenous fluids two days earlier. None of the diclofenac teated patients needed a second does of test medicine or any other standard analgesic within 24 hours of pain relief.

In hyoscine treated patients (group II) pain relief was achieved with 20 mg I.V. hyoscine butylbromide in 10 minutes in 7 patients (21.2%) out of 33; and in 30 minutes in 17 patients (51.5%). Out of 17 patients having complete pain relief with hyoscine compound, recurrence of pain necessitating a second dose within 24 hours was in 9 patients (53%). Blurring of vision, dryness of months, giddiness and vomiting were common in hyoscine treated patients even after relief of pain.

Table-I

**SEX AND AGE DISTRIBUTION AND ASSESSMENT
OF PAIN BEFORE TREATMENT**

Patients	Group-I Diclofenac Treated Patients	Group-II Hyoscine Treated Patients
Total	40	33
Male	38	30
Female	2	3
Pain intensity:		
Severe (+3)	32	28
Moderate (+2)	8	5
Age (years)	17 - 60 (years)	16 - 50 (years)

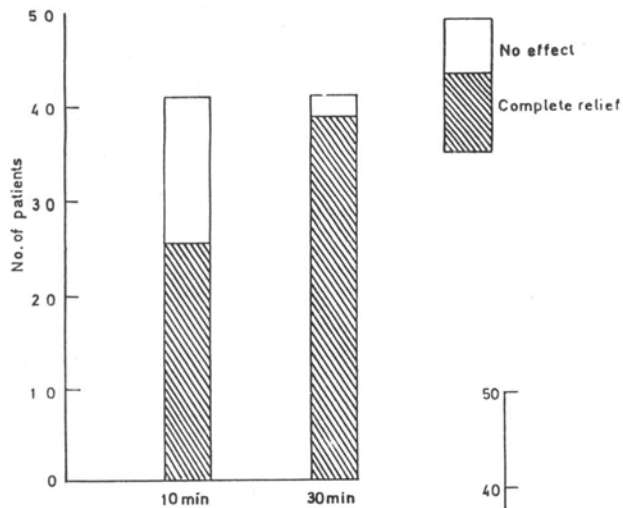


Fig. 1 Pain relief in 10 & 30 min after diclofenac therapy.

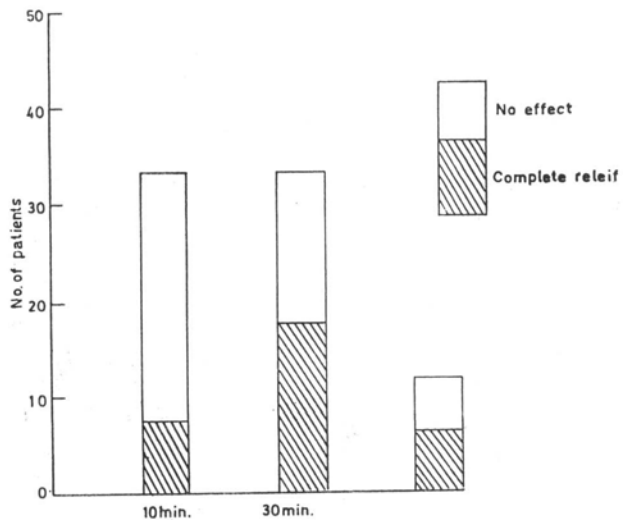


Fig. 2 Pain relief in 10 & 30 min after intravenous Hyoscinebutylbromide.

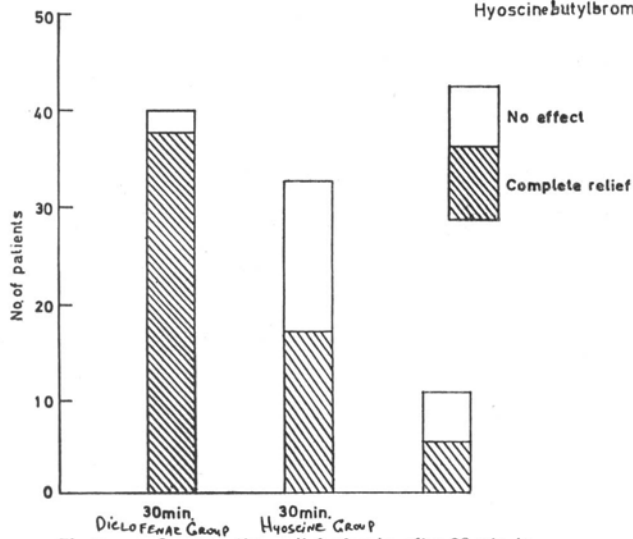


Fig. 3. Comparative relief of pain after 30 min. in diclofenac & hyoscine treated patients.

Conclusion

An hypothesis has been evolved which differs from the current understanding and practice in the management of 'Renal Colic'. Several points of interest have arisen which can provide material for further studies. Based on the previous teachings that the pain of renal colic is due to spasm and/or hyper-peristalsis of the ureter, it has been a general practice to administer spasmolytic drugs. These drugs were presumed to relax the ureteric smooth muscle and abolish not only the pain but also allow the passage of stone. It was interesting to know that spasmolytics, while giving the patient some relief, failed to reduce the raised intrapelvic pressure. The passage of stone is also not influenced by these drugs. The most interesting point to know is the 'Renal Colic' is not due to moving stone down the ureter but to its impaction. The stone stays somewhere in the ureter and due to inflammatory reaction there is oedematous swelling in the ureteric lumen distal to the stone. The frequent endoscopic finding of oedema in the region of the lower ureteric orifice with a stone impacted above it supports the hypothesis.

Impaction of stone closes the ureteric lumen and there is accumulation of urine proximally. The pressure in the renal pelvis rises due to imbalance thus created between the excretion and the drainage from the kidney substance. The pressure-rise thus results in renal pelvic distension and wall tension giving rise to pain. The intensity of pain is related to the rate of pressure-rise. The rapid the rise of pressure the severe the pain. The rise of pressure in the renal pelvis is dependent on the release of renal prostaglandin E₂. The increased synthesis of prostaglandin E₂ is associated early in ureteric obstruction and in turn increases renal blood flow and diuresis. Thus increased synthesis of PGE₂ gives rise to rapid increase in renal pelvic pressure and pain.

The pain increases in intensity until a constant level is reached when there is no more onward flow of fluid from the collecting tubules. Glomerular filtration continues as there is reabsorption of water and solutes via reflex pathways, creating room for continuing excretion.

The pain remains constant for varying period until spontaneous fall in renal pelvic pressure. This may take place either by resolution of the oedema in the ureteric lumen and the passage of urine at the sides of the stone or by increased reabsorption of fluid from the renal pelvis. Before spontaneous resolution to occur the pain is severe, intolerable and cannot be left unattended.

Diuresis induced at any stage of renal colic has counterproductive effect. Infusion of intravenous fluids and the use of diuretics in ureteric obstruction might aggravate or induce pain. This is explained on the basis of renal pelvic pressure-rise associated with these measures. This points to the importance of restricting fluids in acute renal colic. This, however, will not adversely affect the passage of stone.

Reduction of renal pelvic pressure is the cornerstone of management in ureteric obstruction and in alleviating pain. This can be promptly and effectively achieved by administering prostaglandin synthesis inhibitors. Our study on diclofenac sodium proved the importance of prostaglandin synthesis inhibition therapy in acute ureteric obstruction with a high rate of pain relief and minimum side effects. Pain relief thus achieved can be explained by the reduction in renal pelvic pressure and diuresis from the obstructed kidney.

A favourable effect on the passage of stone can also be expected by the use of prostaglandin synthesis inhibitor, diclofenac sodium. It has a potent analgesic, anti-inflammatory and anti-oedema activity, inhibiting the cyclooxygenase and lipoxygenase pathways of the arachidonic acid cascade. This activity might help in the passage of stone by reducing the distal oedematous bar formation responsible for the impaction of the stone.

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