Original Article

Comparison of the therapeutic effects of diclofenac sodium, prednisolone and an alpha blocker for the treatment of renal colic

Akut renal kolik tedavisinde diklofenak sodyum, metilprednizolon ve alfa blokör tedavilerinin karşılaştırılması

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ABSTRACT

Objective: In this study, we compare the efficacy of diclofenac sodium, methylprednisolone and alpha-blockers for the treatment of renal colic treatment.

Material and methods: A total of 30 patients between the ages of 18-70 were included in this study. Patients were referred to the Meram Medical Faculty Urology Department or Department of Emergency Medicine at Selcuk University between October 2008 and January 2009. This prospective study was approved by the Selcuk University Meram Medical Faculty Ethics Committee. Patients were randomly divided into 3 cohorts of 10 patients each. The first group consisted of patients receiving diclofenac sodium and an alpha blocker, the second group of patients received diclofenac sodium and prednisolone, and the third group of patients received diclofenac sodium alone. Each patient was diagnosed and evaluated by the same clinician. Evaluation was based on the Numerical Classification Score (NCS) and the Renal Colic Symptom Score (RCSS). Pain intensity was evaluated prior to medication administration and 5, 10, 15, 20, and 30 hours thereafter. Statistical analysis was performed using chi-squared analysis and the Kruskal-Wallis test. P-value of ≤0.05 were considered statistically significant.

Results: Symptoms immediatiely prior to medication administration and after 5, 10, 15, 20 and 30 hours are evaluated. There are no significant differences between the groups (p>0.05). In group 1, stone expulsion occured in 4 patients (40%), a finding that is statistically significant (p=0.01). No adverse events occurred in any group during this study.

Conclusion: Comparison of the therapeutic response among the 3 groups revealed no statistically significant difference. The most important aspects to consider in regard to a treatment modality include diminishing pain, dissolving blockage, a preservation of renal function and minimizing the side effects.

Key words: Alpha blocker; diclofenac; prednisolone; renal colic.

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ÖZET

Amaç: Renal kolik tedavisinde diklofenak sodyum, metilprednizolon ve alfa blokör tedavilerinin karşılaştırılmasını sunuyoruz.

Gereç ve yöntem: Ekim 2008-Ocak 2009 tarihleri arasında kliniğimize başvuran ve renal kolik tanısı alan 30 hasta çalışmaya alındı. Hastalar başvuru sırasına göre; diklofenak sodyum ve alfa blokör verilen 10 hasta, diklofenak sodyum ve prednizolon verilen 10 hasta ve sadece diklofenak sodyum verilen 10 hasta olmak üzere üç gruba ayrıldı. Tüm hastaların tedavi etkinliğinin değerlendirilmesi aynı klinisyen tarafından Sayısal Derecelendirme Skoru (SDS) ve Renal Kolik Semptom Skoru (RKSS) ile yapıldı.

Bulgular: Tek başına diklofenak sodyum alan grupta ve diklofenak sodyum ile prednizolon alan grupta tedavi sırasında taş düşüren hasta olmazken, diklofenak sodyum ve alfa blokör tedavisi alan grupta 4 hasta (%40) taş düşürdü. Taş düşürme yönünden diğer gruplar ile kıyaslandığında diklofenak sodyum ve alfa blokör kullanan grup istatistiksel olarak anlamlı bulundu (p=0.01). Her üç grupta da 5. 10. 15. 20 ve 30. saatte SDS'de ayrıca maximum ve minumum RKSS'de istatistiksel olarak fark tespit edilmedi (p<0.05).

Sonuç: Renal kolik tedavisi sırasında ağrı kontrolü için farklı tedavi ajanları kullanılabilir. Alfa blokör kullanımı taş düşürme açısından pozitif bir katkı sağlamaktadır.

Anahtar sözcükler: Alfa blokör; diklofenak sodyum; metilprednizolon; renal kolik.

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Introduction

Renal colic, which is usually associated with kidney stones, is an urgent urologic condition that presents with severe, acute pain and is usually diagnosed and treated in the emergency department.[1] Lifelong risk of renal colic is between 1-10%.[2]

Most patients diagnosed with renal colic have a kidney stone or a history of renal colic. The typical flank pain is described as blunt, permanent and torturing in character. This pain usually spreads to the umblicus or lower abdomen. Nausea, vomiting, psychomotor agitation and costovertebral tenderness may accompany the pain.[3] A combination of medical history, imaging methods and laboratory examination are used for diagnosis.[1]

Treatment is primarily aimed at pain control and removing the obstruction as soon as possible, before loss of kidney function occurs.[2] Medical treatment options include Non-Steroidal Anti-Inflamatuar Drugs (NSAIDs), alpha blockers, steroids and calcium channel blockers.[4]

In this study, we compare the efficacy of diclofenac sodium, methylprednisolone and alpha-blockers for the treatment of renal colic.

Materials and methods

A total of 30 patients between the ages of 18-70 were included in this prospective study. Patients were referred to the Meram Medical Faculty Urology Department or Department of Emergency Medicine at Selcuk University between October 2008 and January 2009 This study was approved by the Meram Medical Faculty Ethics Committee of Selcuk University.

A detailed history and physical examination were conducted for all patients. In addition to routine urine analysis, ultrasonography was performed and X-rays were taken. Patients were excluded from the study if they had taken any analgesic within the last 24 hours, were allergic to NSAIDs, had active oral mucosal lesions or gastrointestinal bleeding, had a history of peptic ulcer, had received anticoagulant therapy, had a solitary kidney, or had a serum creatinin level over 2 mg/dL. In addition, women who were pregnant or lactating were also excluded.

Patients were randomly divided into 3 cohorts of 10 patients each. The first group consisted of patients receiving diclofenac sodium and an alpha-blocker, the second group of patients received diclofenac sodium and prednisolone, and the third group of patients received diclofenac sodium alone. The medication doses were either 75 mg of intramuscular [IM] diclofenac sodium, 10 mg of oral alfuzosin or 16 mg of oral prednisolone. Throughout the evaluation period, no changes were made to the dosages. No control group was designed because of the severe pain related to this clinical entity. Due to ethical concerns, it would be unreasonable to leave any patient suffering from renal colic pain untreated.

Each patient was diagnosed and evaluated by the same clinician. Evaluation was based on the Numerical Classification Score [NCS] and the Renal Colic Symptom Score (RCSS). Pain intensity was determined prior to medication administration and 5, 10, 15, 20, and 30 hours thereafter.

The NCS is utilized by showing patients a 10-cm scale that is divided into 10 equal parts in which "no pain" is defined as 0 points, and "severe pain" is defined as 10 points. Each patient rates his or her own pain (Fig. 1).

With regard to the Renal Colic Symptom Score, flank pain severity, costovertebral tenderness, psychomotor agitation and nausea are evaluated and rated by the physician as either "No=0, Slight=1, Mild=2, or Severe=3" (Fig. 2).

Vital signs including blood pressure, heart rate, and respiration were recorded for every patient prior to medication administration and 5, 10, 15, 20, and 30 hours thereafter. A 50% or more decrease in the NCS and the RCSS after 30 hours was considered successful. If pain persisted after a single dose of therapy, 50 mg of IM pethidine was provided to the patient and ureterorenoscopy was performed.

Statistical analysis was performed using chi-squared analysis and the Kruskal-Wallis test. The results were considered significant when $p \leq 0.05$.

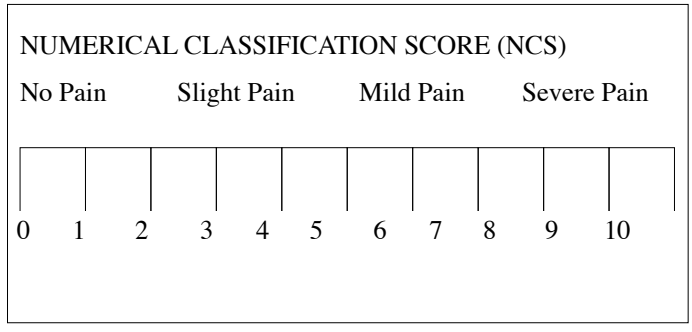

Figure 1. Numerical Classification Score (NCS)

	NO	SLIGHT	MILD	SEVERE
Flank Pain	0	1	2	3
CVAT	0	1	2	3
Psychomotor Agitation	0	1	2	3
Nausea	0	1	2	3

Figure 2. Renal Colic Symptom Score (RCSS)

Results

A total of 30 patients, 20 men and 10 women, were evaluated in this study. Patients were between the ages of 20-57 years in group 1 (alpha-blocker & diclofenac sodium), 21-68 years in group 2 (diclofenac sodium & prednisolone), and 19-51 years in group 3 (diclofenac sodium alone) (Table 1).

In Table 2, symptoms are presented for each group. In contrast to the other 2 groups, stone expulsion occured in 4 patients in group 1 (40%), which was a statistically significant finding (p=0.01).

Table 3 documents patient symptoms immediately prior to medication administration and 5, 10, 15, 20 and 30 hours thereafter. There are no significant differences between the groups (p>0.05). No adverse events occurred in any group during this study.

Discussion

Acute renal colic is one of the most painful urologic emergencies that is frequently encountered in emergency departments. The lifetime risk of having an episode of renal colic for all persons is between 1-10%.[1,2] Annually in the United States, more than 1 million patients are present to emergency departments for renal colic.[5] In Europe, approximately 7-9% of emergency ambulance service calls are due to acute renal colic pain.[6] No adequate records and information were available in the country of study regarding the frequency of emergency service requests for acute renal colic pain.[1]

A pain scoring system is used to determine the severity of pain in acute renal colic. Brown used a scoring system to show that pain was commonly at moderate-to-severe levels.[5] Altay et al. conducted a study of 80 patients divided into two groups with acute renal colic who were then treated with sublingual or IM forms of piroxicam. Patient pain levels were then compared using a pain scoring system.[7,8] Their study did not reveal any statistically significant differences. In our study, 3 groups of patients undergoing different treatments were evaluated with a scoring system prior to treatment. Similar to Altay et al., there were no statistically significant differences found among the groups.[9]

The Renal Colic Symptom Score [RCSS] was another scoring system utilized for the diagnosis of acute renal colic. Using this system, patients' flank pain, CVAT, psychomotor agitation, and severity of nausea were evaluated. The intensity of each parameter was documented as either "0=not present, 1=mild, 2=moderate, or 3=severe. The total number of points constituted a patient's symptom score.[10]

Results of the physical examination, laboratory studies, and imaging were collectively used for the diagnosis of acute renal colic.[1] In the present study, symptoms and laboratory findings were compared for all 3 groups. No statistically significant differences between the groups were found with regard to stone history, dysuria, flank pain, stone presence in X-ray and USG, presence of erythrocytes and leukocytes in urine screening, age, hemoglobin level, urea and creatinine. Flank pain was the primary complaint of acute renal colic patients. In addition, CVAT and nausea often accompanies the pain.[1] The pain is usually localized to the pathologic side.[2] Furthermore, psychomotor agitation may also accompany the pain in renal colic.[1] Altay et al.[9] evaluated the complaints of 2 groups of patients and reported no statistically significant differences between them. Similarly, we did not identify any statistically significant differences among the groups in the present study.

Routine blood tests, particularly the white blood cell count, might be regarded as nonspecific indicators of tissue damage and inflammation.[7] However, Eskelinen et al.[7] evaluated 57 acute renal colic patients who had an increased number of white blood cells and found no statistically significant differences. Brown evaluated over 1 million renal colic patients and determined that, only 46.8% of them had shown raised white blood cell measurement in complete blood count examination.[5] In the present study, the white blood cell count ranged between 5.500-15.000/mm^3 for the acute renal colic patients among the 3 cohorts. There were no statistically significant differences among the groups.

The aims of acute renal colic treatment include resolving pain effectively and eliminating the obstruction without causing a loss of renal function.[1,2] Although, in the past, the primary treatment options for renal colic were morphine and pethidine, beginning in the 1970s, NSAIDs have been used with proven efficacy.[1,9,11] NSAIDs were preferred, as they lacked the side effects of former treatment agents, including constipation, respiratory depression, mental changes and addiction.[1,9,12] The result

Table 1. Sex, age interval and mean age of patients in each group

	GROUP 1 Diclofenac Sodium + Alpha Blocker			GROUP 2 Diclofenac Sodium + Prednisolone			GROUP 3 Diclofenac Sodium Only		
		Age	Mean		Age	Mean		Age	Mean
Men	6	22-47	33.1	8	21-68	39.6	6	30-48	37.3
Women	4	20-57	39.2	2	38-49	43.5	4	19-51	35
Total	10			10			10		

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Table 2. Symptoms and history details for patients in each group

		GROUP 1 Diclofenac Sodium + Alpha Blocker		GROUP 2 Diclofenac Sodium + Prednisolone		GROUP 3 Diclofenac Sodium Only		
		Patient	%		%		%	p-value
Stone History	Yes	7	70%	9	90%	3	30%	
	No	3	30%	1	10%	7	70%	p>0.05
Total		10	100%	10	100%	10	100%	
Dysuria	Yes	6	60%	6	60%	2	20%	
	No	4	40%	4	40%	8	80%	p>0.05
Total		10	100%	10	100%	10	100%	
Stone Expulsion	Yes	4	40%	0	0%	0	0%	
	No	6	60%	10	100%	10	100%	p=0.01
Total		10	100%	10	100%	10	100%	
Flank Pain	Right	6	60%	7	70%	2	20%	
	Left	4	40%	3	30%	8	80%	p>0.05
Total		10	100%	10	100%	10	100%	
Stone detected by X-ray	Yes	4	40%	4	40%	2	20%	
	No	6	60%	6	60%	8	80%	p>0.05
Total		10	100%	10	100%	10	100%	
Stone detected by USG	Yes	3	30%	7	70%	4	40%	
	No	7	70%	3	30%	6	60%	p>0.05
Total		10	100%	10	100%	10		
Erythrocytes in GUE	Yes	7	70%	8	80%	6	60%	
	No	3	30%	2	20%	4	40%	p>0.05
Total		10	100%	10	100%	10	100%	
Leucocytes in GUE	Yes	5	50%	4	40%	0	0%	
	No	5	50%	6	60%	10	100%	p>0.05
Total		10	100%	10	100%	10	100%	

of a meta-analysis conducted by Labrecque et al.[13] showed that intravenous NSAIDs are as effective as opiates in the treatment of acute renal colic. Currently, calcium channel blockers, steroids, NSAIDs and alpha-blockers are used as medical treatment agents for acute renal colic.[14]

Corticosteroids are used in the treatment of acute renal colic because of their anti-edema effect. Generally, these drugs increase the impact of combination therapy by reducing inflammation and enhancing stone passage.[15, 16]

The use of alpha-adrenergic blockers in the treatment of acute renal colic started in the 1970s after Malin et al.'s study identified alpha- and beta-adrenergic receptors in the human ureter and alpha-adrenergic receptors in the animal ureter.[17] Alpha-1-adrenergic receptors are present in the human, pig, dog and horse ureter. Alpha-1-adrenergic receptors, particularly the alpha-1D sub-group receptors, were found to be responsible for relaxation of the detrusor and spasm of the distal 1/3 of the ureter.[1,17,18] The objective of alpha-adrenergic blockade was to resolve this spasm and provide dilation, enabling pain relief and spontaneous passage of distal ureteral stones.[15,17] Yilmaz et al. treated patients with acute renal colic who had a lower ureteral stone with alpha-adrenergic blockers and proved that this treatment facilitated spontaneous stone passage.[17] In our study, spontaneous stone passage in the group treated with alpha blockers and diclofenac sodium was higher than the groups

Table 3. Response to therapy

	GROUP 1 Diclofenac Sodium + Alpha Blocker		GROUP 2 Diclofenac Sodium + Prednisolone		GROUP 3 Diclofenac Sodium Only		
Pain		**%**		**%**		**%**	**p-value**
Persisting	1	10%	0	0%	1	10%	p>0.05
Stopped after 5 h	2	20%	1	10%	1	10%	p>0.05
Stopped after 10 h	4	40%	5	50%	7	70%	p>0.05
Stopped after 15 h	3	30%	2	20%	0	0%	p>0.05
Stopped after 20 h	0	0%	2	20%	0	0%	p>0.05
Stopped after 30 h	0	0%	0	0%	1	10%	p>0.05
Total	10	100%	10	100%	10	100%	

treated with diclofenac sodium only or diclofenac sodium and prednisolone. This result was statistically significant (p=0.001).

According to the 2007 European Association of Urology Urolithiasis Guidelines, diclofenac sodium, indomethasine, ibuprofen, hydromorphine hydrochloride + atropine sulphate, metamizol, pentazocine, and tramadol are recommended for the treatment of renal colic, with diclofenac sodium listed as the first-line agent.[19] Many studies have investigated the effectiveness of these various treatment options. In a single-center, double-blind, randomized study conducted by Cohen et al.,[20] a total of 55 renal colic patients were divided into 2 groups. Diclofenac sodium was provided to the first group and ketorolac to the second group. The comparison of effectiveness and side effects showed no significant differences between the groups. Altay et al. conducted a study of 80 patients who were diagnosed with acute renal colic and divided them into 2 groups. The first group received sublingual piroxicam and the other received IM piroxicam.[9] In this double-blind, randomized study, no statistically significant differences were found between the groups in terms of effectiveness or side effects. Lasoye et al.[21] identified that the most common treatment agent for acute renal colic in the emergency departments and urology clinics in England is diclofenac sodium. Yilmaz et al. divided 114 patients with acute renal colic into 3 groups and treated them with 3 different alpha-blocker therapies. They found no statistically significant difference among the groups.[17]

In our study, we have evaluated the response to treatment 5, 10, 15, 20 and 30 hours after medical therapy. A comparison of the groups' therapeutic response revealed no statistically significant differences. In both the diclofenac sodium alone and the diclofenac sodium and alpha-blocker groups, one patient reported continuing pain. For patients with ongoing pain, a 50-mg single dose of IM pethidine was provided and ureterorenoscopy was performed.

Acute renal colic is an urgent and extremely painful urological condition with various treatment options that result in good patient response. Despite the many available treatment options, a gold standard has yet to be identified.

The most important aspects to consider when selecting a treatment modality include reducing pain and dissolving the blockage while preserving renal function.

Conflict of interest

No conflict of interest was declared by the authors.

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