Comparison of the efficacy of diclofenac, acupuncture, and acetaminophen in the treatment of renal colic

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Objective: The objective is to compare the analgesic effects of diclofenac, acetaminophen, and acupuncture in urolithiasis-driven renal colic pain relief.

Methods: Renal colic patients were divided randomly into 3 groups. Patients in group I (n = 40) were treated with intravenous acetaminophen, those in group II (n = 41) with acupuncture, and those in group III (n = 40) with a 75-mg intramuscular injection diclofenac sodium. Visual analogue scale (VAS) and verbal rating scale (VRS) were used to assess pain intensity after 10, 30, 60, and 120 minutes.

Results: No significant differences in baseline VAS or VRS were found with regard to age or sex. After 10 minutes, all 3 groups experienced a significant decrease in VAS and VRS scores, with the most drastic decrease occurring in group II. After 30 minutes, there was a significantly higher decrease in group III than in group I (P = .001). After 60 minutes, mean VAS scores of groups I and III (P = .753) were similar. The mean VAS score of group III was lower than that of group II (P = .013). After 120 minutes, the difference in the VAS scores was (P = .000) between groups I and II, and between groups II and III. Yet, the VAS evaluation made after 120 minutes revealed statistically similar outcomes for groups I and III (P = .488). The statistical findings for VAS evaluations made after 10, 30, 60, and 120 were similar to those for VAS.

Conclusions: In renal colic patients with a possible nonsteroidal anti-inflammatory drug and acetaminophen side effect risk, acupuncture emerges as an alternative treatment modality.

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1. Introduction

Acute renal colic, with sudden intense agonizing flank pain, is among the most distressing forms of pain, requiring immediate diagnosis and treatment. Excepting trauma cases, up to 7% to 9% of calls for an ambulance are due to renal colic. The lifetime risk of developing an acute attack of renal colic is estimated to be 1% to 10% [1]. Most urinary stones lead to urinary tract obstruction and distension, which in turn lead to an acute attack of pain. Renal colic pain results from urinary flow obstruction, with a subsequent urinary tract wall tension increase and stimulation of submucosal nerve ends. The increasing pressure in the renal pelvis stimulates local synthesis of prostaglandin (PG). The release of this hormone and subsequent vasodilatation cause diuresis, increasing intrarenal pressure [2].

The first therapeutic step for acute renal colic is to provide relief from the sudden, agonizing pain [3]. In relieving acute stone colic patients from traumatizing pain, nonsteroidal anti-inflammatory drugs (NSAIDs) are the preferred first treatment option. However, opioids are considered if NSAIDs are insufficient [4]. In recent years, a third alternative has emerged: intravenous (IV) acetaminophen [5,6]. Acupuncture, used for centuries in traditional Chinese medicine, is known for its analgesic effects due to underlying neurohumoral and neurophysiologic mechanisms [7]. Increasingly accepted by Western medical practitioners, acupuncture has been used as alternative treatment modality in the field of urology, particularly in shock wave lithotripsy (SWL) and renal colic treatment [8,9].

In the present randomized, controlled, prospective study, the clinical efficacy of diclofenac (the most widely used NSAID), IV acetaminophen, and acupuncture was compared as interventions in urolithiasis-driven renal colic pain.

2. Methods
2.1. Participants

Of the 182 patients applying to 3 clinics between May 2011 and December 2013 for urolithiasis-driven renal colic, 121 were considered...
eligible to participate in the present randomized study. All participants read and signed the informed consent form, which was approved by the local institutional ethics committee. The study protocol and procedures complied with the principles of the Helsinki Declaration. Our institution's review board for the protection of human subjects approved the study protocol and the patients’ informed consent procedures. All the patients were divided at random into 1 of 3 groups. For patients in the acupuncture group, an explanation of the technique was provided. We enrolled all consecutive consenting patients (≥ 18 years) who were experiencing renal colic clinical symptoms. Standardized screening forms were used to help identify eligible patients. Urinalysis, x-ray, ultrasonography, and computed tomography images were used to confirm the presence of urolithiasis clinical symptoms leading to renal colic. Exclusion criteria were the presence of coronary artery disease, coagulopathy, anticoagulant therapy, peptic ulcer, renal failure, hepatic failure, pregnancy, the need for immediate surgical or other intervention, NSAID or acetaminophen hypersensitivity, fever, renal colic due to reasons other than urolithiasis, and the use of other analgesics within 6 hours of the treatment at our facility.

2.2. Intervention

Patients treated for acute renal colic pain were divided randomly into 3 groups and received diclofenac, acetaminophen, or acupuncture. The 40 patients allocated to the diclofenac group were treated with 75 mg of diclofenac sodium in the form of a single intramuscular injection. The 40 patients in the acetaminophen group were treated with 1 g/100 mL of serum saline of IV acetaminophen (Perfalgan; Bristol Myers Squibb, Itxassou, France) for 15 minutes. The 41 patients in the acupuncture group underwent acupuncture by a licensed physician. After dermal disinfection with an appropriate antiseptic solution, acupuncture was applied to a seated patient using the urinary bladder meridian points to the side with acute renal colic pain (UB-21, UB-22, UB-23, UB-24, UB-45, UB-46, UB-47, and UB-48) (Fig. 2). Sterile acupuncture needles (0.25 × 25 mm) were inserted perpendicularly through the skin until reaching the trigger points. The needles were then manually stimulated, until the patient felt the “de-qi” or “de-chi,” a sensation of heaviness, soreness, or numbness in that region [8,9].

2.3. Method and measurement

One-dimensional pain scales such as visual analogue scale (VAS) and verbal rating scale (VRS) were used to assess pain intensity (PI) due to their applicability and ease of use [10]. Patients in the present study...
reported pain on both a 10-cm linear VAS (ranging from "no pain" to "unbearable pain") and a 4-point VRS (no pain, mild, moderate, or severe pain). Patients rated their levels of pain just before the intervention and at 10, 30, 60, and 120 minutes after, with all values being recorded (Table). The patients' demographic features, stone size, and stone localization adverse effects were also recorded.

2.4. Data analysis

Statistical analysis was performed using Statistical Package for the Social Sciences 20.0 (SPSS, Inc, Chicago, IL). Intergroup statistical significance was calculated using independent sample one-way analysis of variance. A P value < .05 was taken as the statistical significance threshold.

3. Results

Initially, 182 potential study candidates were enrolled in the study, and 121 of them met the inclusion criteria. These subjects were allocated randomly into 3 cohorts: the diclofenac, IV acetaminophen, and acupuncture groups. Data obtained from participants in these 3 groups were analyzed (Fig. 1). The 40 patients (22 male [M]/18 female [F]) in the acetaminophen group (group I) had a mean age of 46.3 (19-81) years. The 41 patients (28 M/13 F) in the acupuncture group (group II) had a mean age of 42.39 (18-71) years. The 40 patients (26 M/14 F) in the diclofenac group (group III) had a mean age of 37.98 (18-72) years. The mean stone sizes were 7.73 (4-18) mm for group I, 6.73 (3-18) mm for group II, and 7.25 (3-16) mm for group III. Group I had 11 kidney stones and 29 ureter stones. Group II had 15 kidney and 26 ureter stones, and group III had 12 kidney and 28 ureter stones.

There were no significant differences among the 3 cohorts with regard to age, sex, and baseline VAS and VRS. Renal colic patients' initial VAS and VRS were statistically similar to each other (VAS, \(P = .506\); VRS, \(P = .778\)). There was a significant decrease in the VAS and VRS scores among the 3 groups in the first 10 minutes after treatment application (\(P = .000\)). The most drastic decrease in VAS scores after 10 minutes was seen in group II, followed by group III, and finally group I. After 30 minutes, the VAS mean scores between groups I and II (\(P = .112\)) and of groups II and III (\(P = .223\)) were statistically similar. Yet, the decrease in scores for group III was significantly higher than in group I (\(P = .001\)). Sixty minutes after administering analgesia, the mean VAS scores of groups I and III (\(P = .753\)) were similar. The mean VAS score of group III was significantly lower than in group II (\(P = .013\)). Two hours after applying analgesia, significant statistical differences were seen between all 3 groups. After 120 minutes, there were significant differences in the VAS scores between groups I and II (\(P = .000\)) and groups II and III (\(P = .000\)). At the same time point, however, there were statistically similar outcomes for groups I and III (\(P = .488\)).

Verbal rating scale evaluations made 10 minutes after inception of renal colic pain treatment revealed statistically significant differences between groups I and II (\(P = .000\)) and groups II and III (\(P = .000\)). The difference in VRS for groups I and III (\(P = .788\)) was not significant. There were no statistically significant differences in the VRS scores among the groups 30 minutes (\(P = .178\)) and 60 minutes (\(P = .093\)) after beginning renal colic pain management. The evaluation of the VRS scores from 120 minutes after analgesic intervention revealed statistically significant differences between groups I and II (\(P = .000\)) and groups II and III (\(P = .005\)). However, there was no statistically significant difference in the VRS scores obtained after 120 minutes for groups I and III (\(P = .459\)) (Fig. 3A and B).

To summarize, whereas the patients of all groups had similar initial scores, in group I, the analgesic efficacy of acetaminophen continued 120 minutes after infusion. In group III, the analgesic effect of diclofenac was the highest among the 3 groups after 30 minutes after renal colic pain intervention. The analgesic effect continued similar to acetaminophen at 120 minutes after treatment. In group II, acupuncture led to the most rapid decrease in both VAS and VRS at the 10-minute mark, but both scores had increased by 30 minutes posttreatment.

In the present study, diclofenac caused the following side effects: rash in 1 patient and abdominal burning/pain in 2 patients. The side effects of acetaminophen were an allergic reaction in 1 patient and mild dizziness with vomiting in 1 patient. Patients in the acupuncture group did not experience any adverse side effects.

4. Discussion

Urolithiasis-induced renal colic pain is severe, immediate, and strong, requiring immediate anodyne treatment. Renal colic pain, often
accompanied by symptoms such as urgency, dysuria, oliguria, hematuria, acute nausea, and vomiting, typically spreads radially from the costovertebral angle to the lower abdominal and groin areas. Most of the urolithiasis leading to renal colic passes spontaneously. Nevertheless, rapid pain relief, confirmation of the diagnosis, and recognition of complications requiring immediate intervention should be considered throughout. Renal colic has been described as ureteric obstruction inducing a direct increase in intraluminal pressure of the collecting system, physically stretching it, and stimulating nerve endings in the lamina propia [1]. During obstruction-driven renal colic, an increase in the pressure of the local mediator’s production accounts for the increased eicosanoids, mainly PG E2 and prostacyclin, angiotensin II, and thromboxane A2 release. This results in changes in renal blood flow [11]. In prolonged obstruction, the isotonic contraction and spasms in the smooth muscle lead to an increase in lactic acid production, which irritates both slow-type A and fast-type C fibers. Afferent impulses are generated and traveled to the spinal cord, adjoining it at the T11 to L1 levels, with subsequent projections to higher levels of the central nervous system (CNS). These are also perceived by any organ sharing the urinary tract innervation, such as the gastrointestinal organs and other components of the genitourinary system [12].

According to European Association of Urology guidelines, NSAIDs such as diclofenac, indomethacin, or ibuprofen are suggested as the first choice treatment when renal colic is initially diagnosed. Opioids such as hydromorphone, tramadol are suggested as the second choice [13]. Nonsteroidal anti-inflammatory drugs have a direct impact on PG release, the main cause of pain. They are proven to be effective, particularly if applied intravenously [2]. In the short run, compared with opioids, NSAIDs achieve greater reductions in pain scores and are less likely to require further analgesia. Opioids, especially pethidine, are associated with higher vomiting rates [2]. Without opioids having adverse effects such as vomiting, nausea, respiratory suppression, and drowsiness, the potential adverse effects of NSAIDs include platelet dysfunction, nephropathy, and peptic ulcer [14]. Rather than using the NSAID piroxicam or the narcotic analgesic morphine, IV acetaminophen could be promoted for use in renal colic patients due to its pharmacologic characteristics [6,15]. Intra- venous acetaminophen is already widely used in emergency medicine. Parenteral NSAID should be the first choice, as they do have a better analge sic efficacy compared with opioids according to European Association of Urology guideline in acute renal colic pain management. Nonsteroidal anti-inflammatory drug tablets or suppositories may help reduce inflammation and risk of recurrent pain, and daily & blockers reduce recurrent colic. As renal colic pain is often accompanied by symptoms such as acute nausea and vomiting [2]. Without opioids having adverse effects such as vomiting, nausea, respiratory suppression, and drowsiness, the potential adverse effects of NSAIDs include platelet dysfunction, nephropathy, and peptic ulcer [14]. 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