Acupuncture versus titrated morphine in acute renal colic: a randomized controlled trial

Objective: The objective of this study was to compare the analgesic effect and tolerance profile of acupuncture versus intravenous (IV) titrated morphine in patients presenting to the emergency department (ED) with renal colic.

Materials and methods: A total of 115 patients were randomized into two groups. Patients in the IV titrated-morphine group (n=61) received 0.1 mg/kg morphine every 5 minutes until pain score dropped by at least 50% of its baseline value. Patients in the acupuncture group (n=54) received an acupuncture session of 30 minutes following a prespecified protocol. The visual analog scale (VAS) was used to assess pain intensity at baseline and at 10, 20, 30, 45, and 60 minutes following the start of the treatment protocol. Possible treatment side effects were also recorded.

Results: No significant differences were found between the two groups concerning age, sex, or baseline VAS score. From the 10th minute until the end of the intervention, acupuncture was associated with a deeper analgesic effect than titrated morphine (P<0.05 from the 10th minute and over). Analgesia was also faster in the acupuncture group, with time to obtain 50% reduction of baseline VAS of 14 minutes in the acupuncture group versus 28 minutes in the IV titrated-morphine group (P<0.001). Only three patients in the acupuncture group experienced minor side effects versus 42 in the morphine group (P<0.001). No major side effects were observed in this study.

Conclusion: In ED patients with renal colic, acupuncture was associated with a much faster and deeper analgesic effect and a better tolerance profile in comparison with titrated IV morphine.

Keywords: acupuncture, morphine, renal colic

Introduction

Renal colic (RC) is one of the commonest complaints in the emergency department (ED).1,2 It accounts for ~1% of all ED visits and hospitalizations,3 and is more frequent in men.3–5 The prevalence of urinary stones in RC is 10%–15%.6 Pain experienced in the acute phase of RC is often described as “the worst pain ever”,7 making effective pain control a priority in RC management. Currently, analgesics represent the mainstay treatment for this condition, and for many years, opioids have been used as first-line treatment.6,8 However, concerns have been raised about the correlation between opioid dose and side effects, including respiratory depression, gastrointestinal disorders, and hypotension.10 Acupuncture, a branch of traditional Chinese medicine, has been proven to be effective in the management of pain and other acute/chronic conditions, including RC.11,12 However, its application in the ED setting is insufficient and needs further exploration.13 The aim of this study was to compare the analgesic effects and tolerance
of acupuncture compared to intravenous (IV) morphine in patients presenting to the ED with RC.

Materials and methods

Study design

This randomized controlled trial was carried out in the ED of Fattouma Bourguiba University Hospital from July 2014 to June 2015. It was registered at ClinicalTrials.gov (NCT02781415). The protocol was approved by the ethics committee of Fattouma Bourguiba University Hospital.

Inclusion criteria

We included all consecutive patients aged >18 years and presenting to the ED with the clinical suspicion of uncomplicated RC and a pain score >70 (ranging from 0 for no pain to 100 for maximum imaginable pain) using the visual analog scale (VAS). RC was considered if the patient description of pain included sudden onset of symptoms; unilateral flank or lower abdomen pain; irradiation to the back, side, or groin region; urination problems, including urinating difficulty and/or an abnormally dark or red urine; and the absence of other obvious conditions explaining patient symptoms.

Exclusion criteria

We excluded patients with complicated RC, defined by the presence of bilateral pain, fever, and/or decreased urine output (<500 mL per day). Patients presenting with post-traumatic pain, those taking anticoagulant medications or with coagulation problems, those with skin afflictions (infections, hematoma, dermatosis) that would impair the use of certain acupuncture points, those unable to assess the degree of pain using the VAS, those who had received analgesics in the 6 hours prior to enrollment, those refusing or unable to give written consent, and pregnant women were also excluded from this study. All participants read and signed the informed consent form of the study, which was approved by the ethics committee of Fattouma Bourguiba University Hospital.

Interventions

Patients were randomly assigned to one of the two study groups using a randomly generated number protocol and sealed envelopes. Patients allocated to the titrated-morphine group received a bolus of 0.1 mg/kg body weight was repeated every 5 minutes until reaching the therapeutic goal.

In the acupuncture group, patients underwent a 30-minute acupuncture session with a licensed physician. Skin was disinfected with chlorhexidine at the needle insertion site. Sterile acupuncture needles were used (0.25×0.5 mm). Patients were installed in a seated position and needles inserted perpendicularly through the skin to a depth of 1–2 cm until deqi, a feeling of numbness and tingling within the range of the acupuncture point, was achieved. Insertion sites correspond to the urinary bladder meridian points to the side of the pain (UB1–24, UB26, UB45–49). All details regarding our protocol intervention, assessed by the standards for reporting interventions in controlled trials of acupuncture, are reported in Table S1.

Method of measurement

A 100-mm linear VAS was used to measure pain intensity in all participants. Patients rated their pain just before the intervention and at 10, 20, 30, 45 and 60 minutes after it. Patients were followed during the whole protocol period and until discharge for the occurrence of side effects, including drowsiness, dizziness, nausea and vomiting, respiratory distress, and hypotension in the morphine group and local rash/bleeding, itching, needle blockage, and fainting in the acupuncture group. For all subjects, we collected demographic and clinical data, VAS scores, and potentially treatment-related side effects.

Efficacy outcome

The efficacy of each treatment strategy was judged based on two conditions: success rate in achieving durable analgesia, defined by a drop in VAS score of at least 50% from baseline (T0) at 30 minutes following the start of the protocol and lasting till the end of the intervention (T60), and rapidity in obtaining an analgesic effect, defined by the interval between the start of the protocol (T0) and the decrease in VAS score of at least 50% from baseline.

Safety outcome

Possible adverse events related to the care delivered were investigated via a checklist during the 1-hour protocol treatment and until the patient had been discharged from the ED.

Statistical analysis

Variables are expressed as means ± SD, medians with 25%–75% interquartile range (IQR), or values with 95% CIs as appropriate. The normality of the parameters was tested with
the Kolmogorov–Smirnov test. Comparison of data between the groups was performed using a two-sample Student’s t-test or Mann–Whitney U test, as appropriate. All tests were two-tailed, and $P<0.05$ was considered statistically significant. Calculations were performed with SPSS version 19.

**Results**

A total of 153 consecutive patients who presented to our ED with signs and symptoms suggestive of RC were screened during the study period. Of these, 19 did not meet the inclusion criteria, and 15 declined to participate in the study. The remaining 119 patients were randomly allocated to two groups: 57 patients in the acupuncture group and 62 in the morphine group. Of these, four patients were lost to follow-up during the study period. Overall, 115 patients completed the present study, and data from all these patients were analyzed (per-protocol analysis), as shown in Figure 1. Baseline characteristics were similar between the two study groups, and there were no differences in age, sex, medical history, or baseline VAS scores between the groups (Table 1). As shown in Table 2, there was a statistically significant decrease in VAS scores in both groups (difference between baseline and after 60 minutes 77 in the acupuncture group and 64 in the morphine group, $P<0.001$). Success rates were similar between the groups, with 87% of participants achieving the main goal in the acupuncture group and 83% in the morphine group ($P=0.6$). Mean pain scores were significantly lower in the acupuncture group than in the morphine group from the 10th minute of the protocol start until the 60th minute ($P<0.005$ at all-time points). Acupuncture was associated with a faster analgesic effect, with time to achieve 50% reduction in baseline pain score being almost half that obtained with morphine in reduction time. In fact, with acupuncture, a 50% reduction in baseline pain score was achieved in half the time taken by morphine (14 versus 28 minutes, $P<0.001$) (Figure 2). At the end of the 60-minute study period, 24 patients in the morphine group and 35 in the acupuncture group were pain-free (VAS score 0). In this trial, the mean dose of opioids used per participant in the morphine group was 16.7±6 mg of morphine chloral hydrate (10–27 mg). Side effects were observed more frequently in the morphine group than in the acupuncture group (42 versus three, $P<0.001$). There were no major side effects recorded in this study (Table 3).

**Discussion**

Although success rates were similar in both groups, the analgesic effect of acupuncture was significantly faster than that of morphine. Both titrated morphine and acupuncture

![Patient flowchart](Image)
succeeded in achieving a 50% reduction in baseline VAS scores in most patients with RC; nevertheless, acupuncture was much better tolerated. Through their everyday work, emergency physicians are confronted with a variety of painful conditions, including severe pain syndromes. Alleviating pain represents a health-care priority worldwide.15 RC is often described by patients as “the worst pain ever”. In patients with acute severe pain, opioids tend to be prescribed by ED physicians as first-line treatment.16 Nevertheless, systemic administration of opioids carries a high risk of side effects that correlates with dose given.17 Many other analgesic modalities have been investigated, including such nonpharmacologic pain relief techniques as acupuncture. Acupuncture is growing in popularity worldwide. The World Health Organization stated

Table 1 Baseline characteristics of patients

| Characteristics                      | Acupuncture, n=54 | Morphine, n=61 | P   |
|--------------------------------------|-------------------|---------------|-----|
| Age, years                           | 42±14.8           | 41.8±13.21    | 0.82|
| Sex, female/male                     | 28/26             | 26/35         | 0.32|
| Medical history, n (%)                |                   |               |     |
| Diabetes                             | 7 (12.9)          | 7 (11.4)      | 0.8 |
| Hypertension                         | 8 (14.8)          | 7 (11.4)      | 0.59|
| Gastrointestinal ulcer               | 2 (3.7)           | 4 (6.5)       | 0.49|
| Previous renal colic                 | 13 (24)           | 11 (18)       | 0.42|
| History of urolithiasis              | 5 (9.2)           | 8 (13.1)      | 0.51|

**Physical examination findings**

| Heart rate, bpm                      | 83±12             | 81±14         | 0.51|
| Systolic blood pressure, mmHg        | 136±27            | 133±20        | 0.42|
| Diastolic blood pressure, mmHg       | 80±21             | 78±12         | 0.62|
| Oxygen saturation, %                 | 98±1              | 98±1          | 0.94|
| Temperature, °C                      | 36.9±0.3          | 36.9±0.3      | 0.24|

Table 2 Main outcomes in the two study groups

| Outcome criteria                      | Acupuncture, n=54 | Morphine, n=61 | P   |
|---------------------------------------|-------------------|---------------|-----|
| VAS at admission, median (IQR)        | 83 (77–92)        | 85 (75–96)    | 0.5 |
| VAS at 60 minutes, median (IQR)       | 10 (6–15)         | 22 (14–26)    | 0.002|
| Success rate* at 60 minutes, n (%)    | 47 (87)           | 51 (83)       | 0.6 |
| Resolution time** (minutes), mean ± SD| 14.5±7.8          | 28.2±12.4     | <0.001|

Notes: *Decrease in admission VAS of at least 50%; **time to obtain decrease in VAS of at least 50%.

Abbreviation: IQR, interquartile range; VAS, visual analog scale.

Figure 2 Visual analog scale (VAS) score over time in patients with renal colic.

Notes: Repeated VAS score analysis showed a significant and greater reduction of pain intensity in the acupuncture group compared to the morphine group from the 10-minute to the 60-minute time points.
more than 40 diseases could benefit from acupuncture treatment, and recently, many comprehensive review articles have been published regarding this matter, with a particular emphasis on the analgesic effect of acupuncture.
The effect of this technique on pain is related to the release of endogenous opioids, modulation of the adrenergic system, the 5-hydroxy tryptamine-signaling system, and the N-methyl-D-aspartate-signaling system. In addition, acupuncture seems to have an anti-inflammatory effect and to activate the diffuse nociceptive inhibitory control system. Although very few studies have been carried out on the use of acupuncture in the management of severe acute pain, some results are encouraging. In a randomized controlled trial of 607 healthy women in labor, Borup et al demonstrated that acupuncture was efficient in relieving pain during delivery and reduced the need for pain medication. In a study comprising 120 patients with acute dental pain with a mean baseline VAS score of 65±1.8, Grillo et al showed that acupuncture was a good method to control pain. Goertz et al included 100 patients with acute pain in a protocol comparing auricular acupuncture with standard ED care versus standard ED care. The authors demonstrated that acupuncture was significantly higher and quicker than titrated morphine in ED patients with RC. This represents an alternative to currently available analgesic drugs, especially in patients with high risk of adverse events.

Table 3 Adverse effects

| Outcome criteria                          | Acupuncture, N=54 | Morphine, N=61 | P     |
|------------------------------------------|-------------------|---------------|-------|
| Minor, n                                 |                   |               |       |
| Drowsiness                               | 0                 | 1             | 0.356 |
| Dizziness                                | 0                 | 26            | <0.001|
| Nausea and vomiting                      | 0                 | 13            | <0.001|
| Rash                                     | 0                 | 1             | 0.356 |
| Hypotension                              | 0                 | 1             | 0.356 |
| Needle blockage                          | 1                 | 0             | 0.376 |
| Itching/rash/bleeding at insertion point | 2                 | 0             | 0.179 |
| Major, n                                 |                   |               |       |
| Dizziness                                | 0                 | 26            |       |
| Nausea and vomiting                      | 0                 | 13            |       |
| Rash                                     | 0                 | 1             |       |
| Hypotension                              | 0                 | 1             |       |
| Needle blockage                          | 1                 | 0             |       |
| Itching/rash/bleeding at insertion point | 2                 | 0             |       |
| Total, n                                 | 3                 | 42            | <0.001|

Conclusion
In this study, we demonstrated that the analgesic effect of acupuncture was significantly higher and quicker than titrated morphine in ED patients with RC. This represents an alternative to currently available analgesic drugs, especially in patients with high risk of adverse events. Its place in the ED analgesic armamentarium deserves to be further investigated.

Disclosure
The authors report no conflicts of interest in this work.

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# Supplementary material

## Table S1 Quality report of acupuncture intervention

| Style of acupuncture | Local and distal points |
|-----------------------|-------------------------|
| Technique             | Bilateral and unilateral |
| Number of needles     | Left to the discretion of the physician, perhaps 2–16 |
| Needling depth        | As we felt the deqi, we stopped, as described in traditional texts |
| Deqi                  | Mentioned               |
| Type of stimulation   | Manual only             |
| Needle retention time | 20 minutes              |
| Needle gauge and length | 0.25×50 mm             |
| Rationale of acupuncture | TCM diagnosis-based    |
| Practitioner’s background | GP registered with Tunisian medical acupuncture society, with >3 years’ acupuncture treatment experience |
| Treatment regimen     | For kidney colic only, one session |
| Control intervention  | Conventional treatment (morphine) |
| Cointervention        | None                    |

**Note:** Assessed by the standards for reporting interventions in controlled trials of acupuncture.

**Abbreviations:** GP, general practitioner; TCM, traditional Chinese medicine.