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Effect of Early-Intervention Acupuncture on Pain Relief Among Emergency Department Patients with Suspected Acute Renal Colic Due to Urinary Calculi: Study Protocol for a Randomized Clinical Trial

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Introduction: Analgesia is often delayed for suspected acute renal colic due to urinary calculi (ARCUC) even in emergency department. Acupuncture has a rapid onset and is effective for analgesia, however, evidence about early-acupuncture for suspected ARCUC is limited. This trial aims to evaluate the efficacy of early-intervention acupuncture compared with sham acupuncture on pain relief among emergency department suspected ARCUC patients.

Methods and Analysis: A total of 84 eligible patients who are suspected diagnosed with ARCUC will be randomly allocated to the acupuncture group or the sham acupuncture group. Each patient will receive 1 session of acupuncture or sham acupuncture before diagnostic imaging. The primary outcome will be the response rate at 10 min after needle manipulation, defined as the proportion of patients whose Numeric Rating Scale (NRS) score decrease by at least 50% from baseline. Secondary outcomes will include pain intensity assessed by NRS, further analgesia requirement, revisit rate, surgical intervention rate, satisfaction evaluation, and adverse events. The final diagnosis rate determined by radiography will be recorded and reported. All patients who receive randomization will be included in the intention-to-treat analysis.

Conclusion: This study's findings are anticipated to evaluate the analgesic effect of early-intervention acupuncture for acute renal colic in emergency department, which could be useful for moving the timing of analgesia forward and aligning pain management for acute renal colic more with the guidelines.

Trial Registration Number: ChiCTR2100049069 (https://www.chictr.org.cn/showproj.html?proj=125338).

Keywords: acupuncture, complementary medicine, pain management, emergency medicine, renal colic

Introduction

Renal colic is described as one of the worst pains a patient can have, seriously affecting the quality of life.[1] It affects approximately 1.2 million people each year and accounts for 1% of all emergency department (ED) visits in America.[2] Notably, the recurrence rates are on the rise.[3] The classic presentation is the sudden onset of severe loin pain or abdominal pain, paroxysmal attack, accompanied by haematuria, nausea and vomiting.[4] The prompt administration of effective analgesia is

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imperative in ED to alleviate the excruciating pain experienced by patients with suspected renal colic due to urinary calculi (ARCUC).

Pain remains under-acknowledged, under-assessed and undertreated in ED.[5] ARCUC is one of the most frequently causes of acute abdominal pain. Although guidelines recommend prompt analgesic treatment for acute renal colic in adults before diagnostic imaging,[2,6] only a few physicians administered analgesia to patients with unexplained abdominal pain.[7,8] Moreover, nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids, as the mainstays of ARCUC treatment, neither is without drawbacks. NSAIDs have a relatively slow onset time and limited use in patients with complications such as upper gastrointestinal bleeding, and opioids are associated with adverse effects on gastrointestinal motility and abuse.[1,9] Many physicians believe that administration of analgesics without definitive diagnosis carries risks.[7] Due to the limited options of medication and patients' urgent needs for pain relief, additional therapeutic methods for suspected ARCUC in ED are necessary.

Studies have suggested that the effect of acupuncture for renal colic alone or in combination with analgesics,[10–12] but limited evidence of the treatment are available.[13] Previously, we found that acupuncture combined with diclofenac sodium could provide rapid pain relief for ARCUC patients compared to sham acupuncture with diclofenac sodium.[14] Acupuncture has been recommended as a safe and effective therapy that can be incorporated in ED to treat acute pain.[15] Early-intervention acupuncture may provide timely effective analgesia for patients, and allow physicians to apply without the worry of risks. To date, there are no existing study about early-intervention acupuncture for analgesia on patients with suspected ARCUC. This trial is designed to evaluate the effect of early-intervention acupuncture on pain relief among ED patients with suspected ARCUC.

Methods and Design

Study Design

This single-centre, randomized, sham-controlled, superiority trial will be conducted in an emergency department in China. Eighty-four eligible patients will be randomly assigned to the acupuncture group or sham acupuncture group in a 1:1 ratio. Each participant will receive one session of acupuncture or sham acupuncture and be followed up for 3 days after treatment. Figure 1 shows the trial flowchart. The study is guided by the Declaration of Helsinki,[16] the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) (SPIRIT Checklist),[17] and standards for reporting interventions in controlled trials of acupuncture (STRICTA).[18]

Participant Recruitment

Patients will be recruited at Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University. The recruitment strategy will primarily contain advertisements in outpatient clinics, emergency department visits, and referrals from urology and nephrology departments. Written informed consent will be obtained by patients through a research assistant before randomization.

Eligibility Criteria

Inclusion Criteria

The inclusion criteria for patients are as follows:

1. Suspected ARCUC according to the guidelines of the European Association of Urology (EAU) (2017) (eMethod).[2]
2. Men or women aged 18–80 years.
3. Presented with moderate to severe pain intensity on a Numerical Rating Scale (NRS) score of 4 or higher (range, 0–10, with higher scores indicating greater pain).[19]
4. Signed the written informed consent.

Exclusion Criteria

1. Used any analgesic in the last 6 hours.
2. Pain due to tumors, rheumatoid arthritis, osteoarthritis and other causes.
3. Use of anticoagulants, or blood system diseases such as hemophilia, thrombocytopenia ($< 50\times10^9$/L).
4. History of serious adverse events (AEs) to acupuncture.

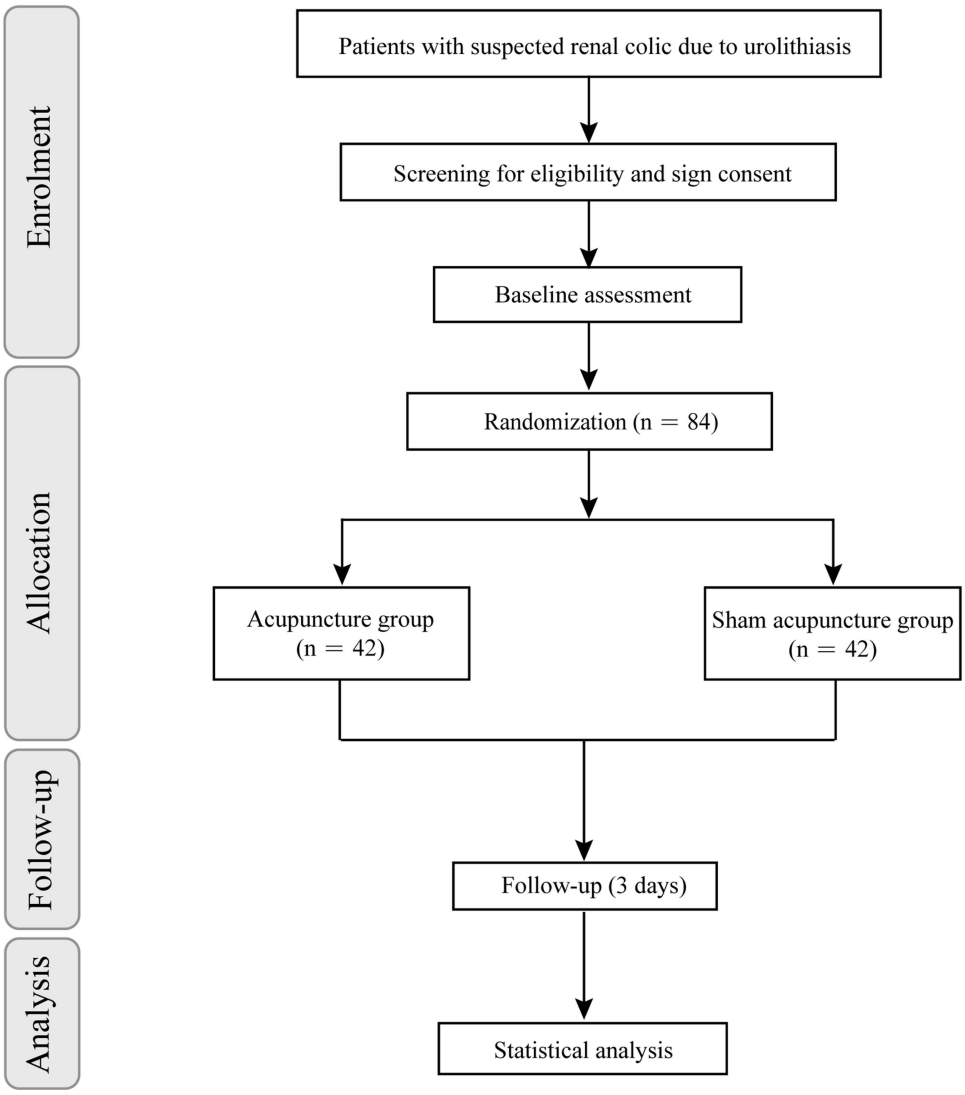

Figure 1 Trial flowchart.

5. Skin infections at acupuncture sites.
6. History of mental illness or previous diagnosis of severe cognitive impairment (dementia).
7. Pregnant or lactating.
8. Alcohol, substance use disorders, communication disorders, or inability to complete a scale.

Randomization and Blinding

Eighty-four eligible patients will be randomly assigned to the acupuncture group or sham acupuncture group in a 1:1 ratio. The randomization sequence will be generated by an independent statistician (Bo Li, Evidence Based Medicine Center, Beijing Institute of Chinese Medicine), who is not involved in the implementation and statistical analysis of the trial, using SAS statistical software version 9.4 (SAS Institute). Each allocated number will be put into a concealed opaque envelope, which is saved by a research assistant who does not take part in enrolling, treatment, or assessment. When eligible patients are enrolled into the trial, envelopes will be opened by acupuncturists in sequential order. Except acupuncturists, patients, outcome assessors, and the statistician will be masked to group allocation. Each patient will be treated in a private treatment room. All patients will be asked to guess whether they receive acupuncture or sham acupuncture after acupuncture treatment for the blinding assessment. The group assignments will be revealed only after statistical analysis is completed. Study procedures are shown in Figure 2.

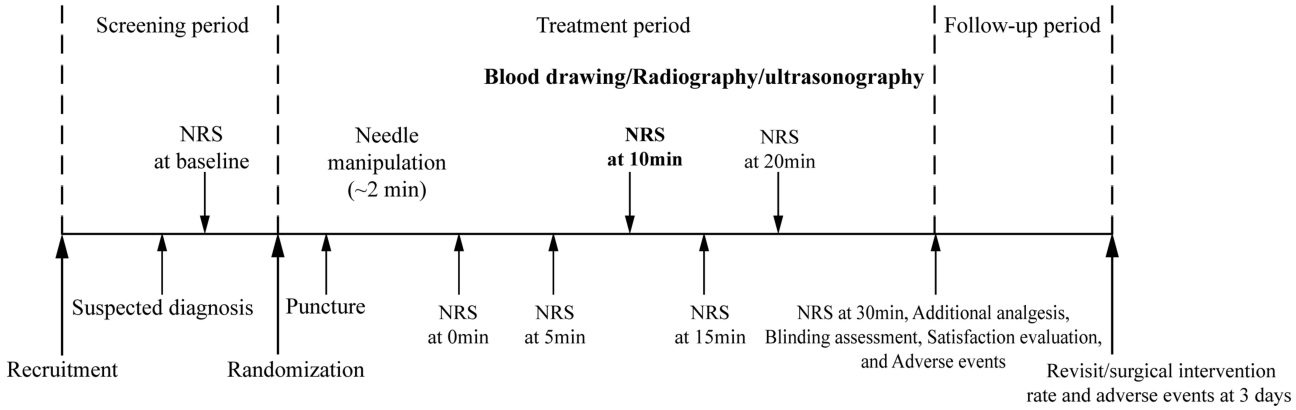

Figure 2 Study procedures.
Abbreviations: NRS, Numerical Rating Scale.

Interventions

Acupuncture or sham acupuncture will be provided in the shortest possible time after randomization. Both acupuncture and sham acupuncture will be performed by licensed acupuncturists with at least 5 years of experience. All acupuncturists will be trained on the location of acupoints and nonacupoints and the manipulation of needling before the trial began. Both acupuncture and sham acupuncture treatment will only consist of 1 session treatment with 30 min. Needles will be removed if the patients suffer from any adverse events. The patients will undergo blood drawing, diagnostic imaging and other related tests while taking acupuncture treatment, and will not receive any other treatment except acupuncture within 30 min. Diagnosis determined by radiography of all enrolled patients will be recorded.

Acupuncture

Sterile disposable acupuncture needles (length, 25 mm; diameter, 0.30 mm; Hwato, Suzhou, China) will be used in the acupuncture group. According to the National standard of the People's Republic of China, *EX-UE* 7 contains 2 acupoints on each side of the hand (4 needles totally), will be used in the acupuncture group according to traditional Chinese medicine and experience with clinical experts.[14] The one is between the second and the third metacarpal bones, and the other is between the fourth and the fifth metacarpal bones. These two points are of the same distance to the metacarpophalangeal joints and the transverse crease of the wrist. The localization of *EX-UE* 7 is exhibited in Figure 3. The angle of needle insertion will be 90° and the depth will be 0.5 cun (about 8–10 mm). Needle manipulation (twirling, lifting, and thrusting) will be performed for at least 30 seconds per acupoint to reach De qi sensation (soreness, numbness, distention, and heaviness), which is believed to be an essential component for acupuncture efficacy.[20]

Sham Acupuncture

Superficial skin penetration (0.6 mm in depth) at nonacupoints without manipulations will be performed in the sham acupuncture group. The first nonacupoint is on the ulnar side, halfway between the epicondylus medialis of the humerus and ulnar side of the wrist, and the second one is located in halfway between the tip of the elbow and the axillae. This method to define nonacupoints in sham acupuncture has been used in previous acupuncture trials.[21,22] Locations of nonacupoints are shown in Figure 3. The same number of sterile disposable intradermal needles (length, 0.6 mm; diameter, 0.20 mm; Seirin pyonex, Japan) will be used as in the acupuncture group. The angle of needle insertion will be 90°. The similarities and differences between acupuncture and sham acupuncture groups are summarized in eTable 1 in Supplement.

Outcomes

Primary Outcome

The primary outcome is the response rate at 10 min after needle manipulation. The response rate is defined as the proportion of patients whose pain score on NRS reduced by at least 50% compared with baseline.[1]

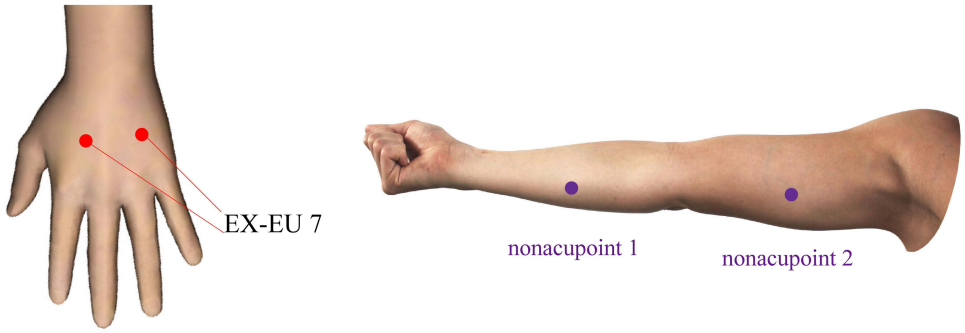

Figure 3 Locations of acupoints and nonacupoints. Red points are the acupoints used in the acupuncture group; purple points are the nonacupoints used in the sham acupuncture group.

Secondary outcomes

Response Rate at Other Times

The response rate at 0, 5, 15, 20, and 30 min after needle manipulation.

Pain Intensity

Evaluated using the NRS at 0, 5, 10, 15, 20, and 30 min after needle manipulation. The NRS scale uses numbers from 0 to 10 to represent the intensity of pain, and higher scores indicate greater pain.[19]

Further Analgesia Requirement

The proportion of patients need further analgesia at 30 min after needle manipulation. Rescue analgesia (tramadol or morphine) will be given to patients with a score of NRS $\geq$ 4 at 30 min after needle manipulation.

Revisit Rate

The revisit rate during 3 days after acupuncture treatment. The numbers of patients who revisit for pain will be recorded during 3 days after acupuncture treatment.

Surgical Intervention Rate

Surgical intervention rate during 3 days after acupuncture treatment. The numbers of patients who need surgical intervention (including ureteroscopy, percutaneous nephrolithotomy, and shockwave lithotripsy) for renal colic during 3 days after acupuncture treatment will be evaluated.

Satisfaction Evaluation

Satisfaction evaluation after acupuncture treatment. Patient satisfaction will be evaluated using a 5-point Likert scale (5 = "Excellent", 4 = "Good", 3 = "Neutral", 2 = "Bad", and 1 = "Very bad", with a higher score representing greater satisfaction).

Adverse Events

Adverse events related to acupuncture or not. Adverse events will be assessed by the trained researchers contacting the patients after acupuncture treatment face-to-face or over the telephone during the followed 3 days. Adverse events of acupuncture may include fainting, sticking of the needle, bending of the needle, and haematoma. Serious adverse events (resulting in death, life-threatening, inpatient hospitalization or prolongation of existing hospitalization, resulting in persistent or significant disability/incapacity, or a congenital anomaly/birth defector) will be reported to the ethics committee, and patients can quit at any time during the trial to protect their rights.

The study procedures, including schedule of enrolment, intervention, and assessments is shown in Table 1.

Table 1 Study Timetable

	Enrolment	Allocation	Treatment Period*							Close-out
TIMEPOINT			0*	1 min	5 min	10 min	15 min	20 min	30 min	3 days
ENROLMENT:										
Eligibility screen	X									
Informed consent	X									
Randomization		X								
INTERVENTIONS:										
Acupuncture			X	X	X	X	X	X	X	
Sham acupuncture			X	X	X	X	X	X	X	
ASSESSMENTS:										
Response rate				X	X	X	X	X	X	
Pain degree		X	X	X	X	X	X	X	X	
Further analgesia requirement									X	
Blinding assessment									X	
Satisfaction evaluation									X	
Revisit rate										X
Surgical intervention rate										X
Adverse events			X	X	X	X	X	X	X	X

Notes: *Timing starts after the end of needle manipulation.

Data Management

Both the paper files and electronic documents will be preserved for at least 5 years after publication. Original data can be accessed by contacting the corresponding author. Patient information will remain anonymous, including name, ID number, and mobile phone number. Metadata will be recorded through a CRF form, and then be cross-checked and transcribed to an electronic database file based on Epidata software. All the data management will be handled by a dedicated person. On-site monitoring will be adopted in this trial per 3 months. The ethics committee of Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University will audit trial conduct per 12 months. Modifications or termination of the trial could be performed by the committee. The data monitoring committee is independent of the sponsors and has no conflicts of interest. The data presented in this study are available upon reasonable request until 6 months after publication, via the corresponding author.

Sample Size Estimation

The sample size was precalculated based on our previous trial,[14] in which the response rates at 10 minutes of the acupuncture and sham acupuncture groups were 77.5% and 10.0%, respectively. In this trial, the response rates in the acupuncture group and sham acupuncture group are conservatively expected to be 70% and 30%, respectively. We calculated that 42 patients would need to be included in each trial group to provide 80% power to detect a minimally important absolute difference of 10 percentage points between the acupuncture group and the sham acupuncture group in the response rate at 10 minutes, at a one-sided alpha level of 0.025 and a 10% dropout rate, using PASS11.0 software.

Statistical Analysis

Continuous variables will be described using the mean (standard deviation), or the media (interquartile range) if the normality assumption is violated. Student's *t*-test or Mann–Whitney test (if normality is violated) will be used for comparison of continuous variables between two groups. Categorical variables will be described using the frequency (percentage) and compared using the chi-squared test. Patients' baseline characteristics will be summarized based on groups. All efficacy analyses will be performed using the intention-to-treat set, which includes all randomized patients. In addition, per-protocol analysis will be performed for the primary outcome only in patients with good compliance (have received 1 session treatment and completed the content specified in the CRF). Missing data will be dealt with the last

observation carried forward. All analyses will be performed using SPSS version 23.0 (IBM SPSS Statistics, NY, USA). P value < 0.05 will be considered statistically significant.

Ethics and Dissemination

The present study has been approved by the ethics committee of Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University. Written informed consent will be obtained from patients before randomization. The results will be published in peer-reviewed journals. Personal information is confidential.

Discussion

ARCUC is a common disease in ED that accounts for a large number of ED visits.[23] In the pain management of acute renal colic, one of the priorities is to provide quick and safe analgesia. However, prompt and effective analgesia can be practically challenging in an ED with a diverse population and a high volume of patients being managed concurrently. This study may improve suspected ARCUC patients' medical experience and provide an alternative approach to pain management in ED.

In clinical practice, we have found that patients were suffering from intolerable pain during the diagnostic process. However, whether pharmacological analgesia should be given before a definite diagnosis of ARCUC is still controversial. Our previous study shows that acupuncture combined with analgesics treatment could be effective in reducing the pain of patients diagnosed ARCUC, and has few side effects.[14] Early-intervention acupuncture can be performed immediately after visits to hospital without waiting for the diagnosis, which the timing of analgesia could be moved forward. This approach is more aligned with current guidelines and aims to improve patients' clinical experiences in the ED.[2,6] Furthermore, the acupuncture prescription involves just one acupoint, making it both feasible and safe for ED use, thus enhancing the practicality of early-intervention acupuncture. This trial meets the methodological demand for adequate randomization, allocation concealment, and blinding of patients, outcome assessors, and statisticians. Blinding patients to interventions is more important, especially when the primary outcome is subjective, such as alleviation of pain. We will perform a prespecified standard operating procedure, including screening patients, acupuncture, filling out the CRF, assessing outcomes, and data management.

This trial has limitations. First, the acupuncturists will not be masked due to the responsibility of providing the intervention. However, the patients and outcome assessors will be blinded to reduce the bias for the subjective symptom. Second, patients aged over 80 will not be recruited in this trial. The generalisability of findings may be limited, although the age criteria was expanded compared to our previous trial.[14] Last, as a single-centre, sham-controlled, randomized clinical trial will be conducted in a Chinese emergency department, the generalisability of the findings may be limited.

Conclusions

This study aims to evaluate the effect of early-intervention acupuncture for acute renal colic in emergency department, and moves the timing of analgesia forward. The results of this study are expected to align pain management for acute renal colic more with the guidelines, and may help to improve guidance for protocolised analgesia.

Trial Status

Protocol: version 1.0, 20 July 2021.
Date opened to recruitment: 25 July 2021.
Recruitment closure: 26 June 2024.

Data Sharing Statement

All the data will be shared 6 months after publication with the patients' relevant data de-identification. Other documents will be available as well, including the study protocol, statistical analysis plan and analytical code. Other researchers may request the data set by emailing to the corresponding author. The results of this study will be submitted for publication in peer-reviewed publications.

Ethics Statements

Ethics was approved by the ethics committee of Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University (2021BL02-053-02). Consent obtained directly from patient(s).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas: took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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