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Does salbutamol reduce the pain of kidney stones when used alongside normal pain relief?

Submission date
01/07/2019

Recruitment status
No longer recruiting

Registration date
22/07/2019

Overall study status
Completed

Last Edited
14/04/2025

Condition category
Urological and Genital Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Kidney stones can become stuck in the ureter (the tube between the kidney and the bladder) in a condition known as renal colic. Patients with renal colic often attend the Emergency Department due to high levels of pain. Traditional painkillers are only partly effective in reducing this pain and can have side effects such as sleepiness and being sick. There is evidence that salbutamol (a drug used to treat asthma) relaxes the human ureter and this may reduce the pain associated with kidney stones, but there have been no studies in humans to demonstrate this effect. This is the first trial investigating this treatment for renal colic so the researchers are conducting a small study of about 100 patients with the condition. The main aim is to see if salbutamol has any possible effect on the pain caused by kidney stones and the results of this study will help with the design of a further, much larger research project to further explore this.

Who can participate?
Patients aged 18 and over with suspected kidney stones

What does the study involve?
Participants are randomly allocated to receive an intravenous injection of either salbutamol (the active drug) or placebo (saline). The study is double-blind, so neither the patient nor the research team know which drug was given. Information is collected about patients' pain levels over the following 24 hours, along with information on their vital signs, such as their heart rate to monitor the drug's effectiveness. Patients are still given all normal pain relief, both on their arrival and during their time in hospital.

What are the possible benefits and risks of participating?
There are no guaranteed benefits to taking part in the study as it is not yet known if using salbutamol will be effective at relieving renal colic pain. Salbutamol is a commonly used drug with few significant side effects. Side effects include tremor, muscle cramps, headache and raised heartbeat. Participation will not affect the duration of hospital stay or require participants to return for further follow-up.

Where is the study run from?
University Hospitals of Derby and Burton NHS Foundation Trust (UK) https://www.uhdb.nhs.uk/derby-ctu

When is the study starting and how long is it expected to run for?
April 2019 to September 2022

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2018-004305-11

Integrated Research Application System (IRAS)
252075

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
42298, IRAS 252075

Study information

Scientific Title
Salbutamol for Analgesia in Renal Colic (SARC) v1.0: a prospective, randomised, placebo-controlled Phase II trial

Acronym
SARC

Study objectives
There is evidence that salbutamol (a drug used to treat asthma) relaxes the human ureter and we believe this may reduce the pain associated with kidney stones, however, there have been no studies in humans to demonstrate this effect. This is the first trial investigating this treatment for renal colic so we are conducting a small study of approximately 100 patients with the condition. The main aim is to see if salbutamol has any possible effect on the pain caused by kidney stones and the results of this study will help with the design of a further, much larger research project to further explore this.

Null Hypothesis: Salbutamol is no better than placebo when added to the standard analgesic regime for managing the pain associated with renal colic.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 10/06/2019, West of Scotland REC 1 (Research Ethics, Clinical Research and Development, Ward 11, Dykebar Hospital, Grahamston Road, Paisley PA2 7DE, UK; Tel: +44 (0) 141 314 0212; Email: WoSREC1@ggc.scot.nhs.uk), ref: 19/WS/0087

Study design
Randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Renal colic

Interventions
The study is a placebo-controlled randomised trial, therefore the participants will receive either salbutamol or placebo in addition to their standard pain relief and this allocation will be 1:1.

A patient will present to the emergency department at the Royal Derby Hospital complaining of pain. They will be assessed on arrival and receive treatment for their pain, as per standard care. When it is felt by the assessing clinician that renal colic is the likely diagnosis, they will be assessed against screening criteria and approached about the trial.

They will be provided with written information about the trial by a GCP trained member of staff. They will be given time to consider this and given the opportunity to ask questions and if they are happy to take part in the trial, asked to complete the consent form.

Given the nature of the condition being studied, consent will need to be given within a short time-scale. Previous emergency department pain studies have achieved this. In addition, the Patient and Public Involvement group (which has representation from patients with previous renal colic) have felt that this is appropriate and achievable.

The treating clinician will then prescribe trial medication on the department prescription chart. This will be taken to another part of the department with staff not involved in the care of the patient. They will draw a pre-made scratch card from a sealed box, which will reveal the treatment allocation for the participant. They will prepare either the active drug or placebo and take this to the treating team.

Scratch cards have been used for randomisation processes in other studies, chiefly in the ambulance services. They are ideal for time-pressured environments and when access to computer randomisation may be limited. Patients with renal colic can present to the emergency department at any time, therefore we will be recruiting 24 hours a day. Having dedicated research staff available is not feasible for that, therefore trained emergency department staff will be recruiting. It was felt that requiring them to have another set of computer logins to remember and the added logistics it would require would prove a significant barrier to recruitment.

The participant will be provided with a booklet which contains a Visual Analogue Scale and McGill pain questionnaire. Prior to administration of the trial medication, baseline assessments will be taken (VAS Pain score, a McGill Pain questionnaire and physiological parameters). The trial medication will then be administered intravenously over 3-5 minutes.

The participant will then complete VAS and McGill pain questions at 15 minutes, 30 minutes, 60 minutes and 120 minutes from the time the trial medication was given. They will also be asked to complete information about any side effects they are suffering.

If a patient's pain completely resolves and there are no other reasons for admission to hospital, then they will be discharged from the emergency department and their involvement in the study will cease. If they require ongoing pain management or there is another reason for admission to hospital, they will be admitted to either the surgical assessment unit or the urology assessment unit (depending on the time of day) and looked after by the urology team. If they are admitted, they will be provided with another booklet, to record their pain scores at 4 hours, 8 hours, 12 hours, 16 hours, 20 hours and 24 hours from the time of trial medication administration, to be completed up until the time of discharge or 24 hours, whichever comes first.

A placebo-controlled study has been demonstrated to be the most effective at showing the effect of a studied drug. It was not felt that it was reasonable to withhold standard treatment for pain, given that this is an exploratory study, so all patients will still receive what is the current accepted standard approach for pain relief in this condition.

The dose and route of administration chosen for this phase II trial have been carefully considered and chosen in order to maximise any potential effect of the medication. Advice has been sought from a Professor with expertise in drug discovery and early-stage clinical trials.

This study represents a re-purposing of an established treatment. We have therefore employed the established maximum safe and effective intravenous dose used for acute exacerbations of asthma; this dose is safe for patients who meet the inclusion criteria, has proven systemic availability and action and an acceptable side effect profile.

Oral salbutamol is poorly absorbed in patients with acute severe pain due to gastroparesis and vomiting and does not reach as high levels in the bloodstream as other routes. Inhaled salbutamol, whilst potentially more rapidly administered, may not reach peak blood levels as rapidly as intravenous salbutamol, and peak levels
may be lower. Whether or not this difference is of clinical significance will be explored in the subsequently planned phase III trial.

Procedures in place to detect and compensate for any possible "researcher effects" and "researcher bias":
All emergency staff will be blinded to treatment allocation, through the aforementioned scratch-card system. The preparation of the trial medication will be carried out in a separate area of the department, where staff will not be involved in the care of patients with renal colic.

Salbutamol is a clear and colourless solution, appearing identical to the placebo and will be prepared in the same sized syringe.

The sampling and sample sizes for the project, including how participants will be identified, approached and sampled, and whether they are sufficient for the intended analysis:
Previous studies have defined the minimum clinically significant difference between consecutive ratings of pain to be 13 mm in emergency department patients. Assuming that a difference of 13 mm between groups in the change in pain score from baseline is clinically important then at 5% significance level with 90% power, 53 patients with confirmed renal colic should be recruited per group.

Planned Recruitment Rate
Four hundred and forty-seven patients were discharged from the Royal Derby Hospital Emergency Department between 17/11/2016 and 16/11/2017 with a final diagnosis of “Renal Colic” (approximately 37 patients per month). Approximately 10% of these participants will subsequently be found not to have a renal calculus (local audit data and previous research). Therefore approximately 34 patients per month will have a confirmed diagnosis of renal colic. The researchers estimate a recruitment rate of between 18% and 30% of eligible patients. This figure is derived from department recruitment to a comparable CTIMP (ISRCTN34153772), another trial in an ED setting and discussion with the PPI group.

Assuming a minimum recruitment rate of 18%, we estimate that 106 patients with confirmed renal colic could be recruited in 22 months. This allows for a slow start in recruitment (3 months to reach 20% recruitment rate) and recruitment plateau during the last five months (10% recruitment rate). This requires recruitment of approximately 118 patients with suspected renal colic.

(added 04/07/2024): Study data will be entered into Dacima (Electronic data capture system) by site staff

Prior to grant submission, the researchers brought together renal colic patients in a Research Design Service funded study-specific Patient and Public Involvement group. They discussed the trial details, particularly the consent process and frequency of observations. No concerns were raised at that time, indeed the group felt that regular reviews of pain would be a benefit.

More recently, the research group of the Royal Derby Hospital Emergency Department (REMEDY) have formed a regular Patient and Public Involvement group, meeting every 3 months, to discuss and review departmental studies. This group has representation from patients with renal colic on it. They have reviewed the study processes and all the patient-facing documentation. This has resulted in changes in formatting and phrasing of these documents.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Salbutamol

Primary outcome(s)
Change in pain score measured using a 100 mm Visual Analogue Scale (VAS) at baseline and 30 minutes post drug administration in patients with confirmed renal colic

Key secondary outcome(s))
1. Change in pain score measured using a 100mm VAS at baseline and 30 minutes post drug administration in patients with suspected renal colic
2. Change in pain score measured using a 100mm VAS at baseline, 15, 60, 120, 240, minutes, and 4 hourly thereafter until 24 hours (or until hospital discharge)
3. Qualitative pain description measured using the McGill pain questionnaire at baseline, 15, 30, 60 and 120 minutes
4. Frequency and total dose of morphine measured in milligrams administered during the 24 hours after enrolment (or length of hospital stay if shorter)
5. All analgesics administered during trial period including time/type and dose
6. Length of hospital stay measured in days
7. Presence/absence, location and size (mm) of renal stone identified on routine imaging during hospital stay
8. Degree of hydronephrosis (if present) as identified on routine imaging radiology report performed during hospital stay
9. Frequency and type of serious adverse reactions reported during the hospital stay
10. The mean and standard deviation of the primary outcome
11. Screening rate/randomisation rate (reviewed retrospectively)

Completion date
22/09/2022

Eligibility

Key inclusion criteria
1. Subjects capable of giving informed consent
2. Age > = 18
3. Working diagnosis of renal colic, as suggested by severe flank/unilateral abdominal pain, +/- radiating to suprapubic/groin area
4. Experiencing severe pain with a requirement for intravenous analgesia

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
148

Key exclusion criteria
Current participant exclusion criteria as of 19/02/2020:
1. Abdominal aortic aneurysm not yet excluded and participant aged > = 50
2. Ectopic pregnancy not yet excluded in a female of child-bearing potential
3. Currently actively taking part in another CTIMP
4. Previous participant in this trial
5. Unable to understand verbal and/or written information in English
6. Known allergy to salbutamol
7. Evidence of sepsis or clinical suspicion of urinary tract infection
8. Serum potassium < 3.7mmol/l
9. Concomitant use of: beta blockers (including eye drops); prolonged release opiates; long-acting β-agonists
10. Use of short-acting β2-agonists within the 6 hours preceding presentation to the emergency department
11. Current arrhythmia
12. History of any of:
12.1. Ischaemic heart disease
12.2. Arrhythmogenic heart disease
12.3. Valvular heart disease
12.4. Unilateral kidney
13. Any other contraindication to the use of salbutamol

Previous participant exclusion criteria:
1. Abdominal aortic aneurysm not yet excluded and participant aged > = 50
2. Ectopic pregnancy not yet excluded in a female of child-bearing potential
3. Currently actively taking part in another CTIMP
4. Previous participant in this trial
5. Unable to understand verbal and/or written information in English
6. Known allergy to salbutamol
7. Evidence of sepsis or clinical suspicion of urinary tract infection
8. Serum potassium < 3.7mmol/l as measured on “point-of-care” venous blood gas
9. Concomitant use of: beta blockers (including eye drops); prolonged release opiates; long-acting β-agonists

10. Use of short-acting β2-agonists within the 6 hours preceding presentation to the emergency department
11. Current arrhythmia
12. History of any of:
12.1. Ischaemic heart disease
12.2. Arrhythmogenic heart disease
12.3. Valvular heart disease
12.4. Unilateral kidney
13. Any other contraindication to the use of salbutamol

Date of first enrolment
16/09/2019

Date of final enrolment
22/09/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals of Derby and Burton NHS Foundation Trust
Royal Derby Hospital
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Sponsor information

Organisation
Derby Hospitals NHS Foundation Trust

Funder(s)

Funder type
Government

Funder Name

National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Current IPD sharing statement as of 14/12/2022:
The datasets generated during and/or analysed during the current study are/will be available upon request from the Sponsor, uhdb.sponsor@nhs.net. The type of data that will be shared and the level of anonymisation will depend on the specific request for data sharing, the purpose, the proposed analysis methods, and the duration they are required for. All requests will be accessed for authorisation by the Sponsor Operational Group. Participants consented to the information collected about them to be used to support other future research and may be shared anonymously with other researchers.

Previous IPD sharing statement as of 09/12/2022 to 14/12/2022:
The datasets generated during and/or analysed during the current study will be available upon request.

Previous IPD sharing statement:
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		11/04/2025	14/04/2025	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet version v2.1	11/11/2025	11/11/2025	No	Yes
Plain English results		18/09/2023	18/09/2023	No	Yes
Protocol file		15/07/2019	22/07/2019	No	No