Paramedic-administered pain relief comparing ketamine and morphine in trauma

Submission date Recruitment status [X] Prospectively registered

11/09/2020 No longer recruiting [X] Protocol

Registration date Overall study status [X] Statistical analysis plan

22/10/2020 Completed [X] Results

Last Edited Condition category [Individual participant data

07/04/2025 Other

Plain English summary of protocol

Background and study aims

Pain after an injury is common. The strongest painkiller that UK paramedics routinely give for severe pain is morphine. Morphine can be slow to work and may cause side effects such as vomiting, drowsiness or low blood pressure. Because of this morphine might not be the best pain killer to use. Ketamine is another strong painkiller. It acts very quickly to reduce pain and may have fewer unwanted side effects. In some parts of the world (Australia, Canada and America) paramedics are allowed to give ketamine, rather than morphine, to patients who have severe pain following injury. Research from these countries tells us that ketamine might be better than morphine, but the research isn't good enough to be sure. The aim of this study is to investigate if ketamine is better than morphine for severe pain after injury and to decide if it suitable for use by UK paramedics.

Who can participate?

If an ambulance is called to a patient with severe pain after an injury, paramedics will check to see if the patient is suitable for this study. They will consider patients who are 16 years of age or over, have suffered an injury which is causing severe pain, and are able to have a strong pain killer administered by injection.

What does the study involve?

Eligible participants will be enrolled by the attending paramedic and randomly allocated to be treated with either ketamine or morphine. After 3 and 6 months participants will be asked to complete questionnaires about their recovery. Data will be collected from the ambulance services about the patients' injury and treatment, and about their stay from the hospital where the participant was taken.

What are the possible benefits and risks of participating?

The potential risk for the patient would be a reaction to ketamine or morphine. This will be minimised by paramedics following the guidelines in the trial protocol for administering ketamine and morphine. The study provides naloxone and midazolam for treating the side effects of morphine and ketamine. Paramedics already use morphine so are trained in administering this. Training will be provided on the use of ketamine. Training will also be provided on how to randomise the patient and administer ketamine or morphine. There may be

a slight burden to participants completing the follow up at 3 and 6 months. This follow-up is most likely to be completed via a telephone call with one of the researchers who can talk a participant through the questionnaires, explaining and answering any questions they have. There is a risk the patient may feel some distress when completing the questionnaires as it may remind them of their injury. The researchers will provide contact details for the participant to speak to the PI and research team to gain support. If they answer the questionnaires with a researcher via the telephone, the researcher will be able to support the participant at the time of discussion.

Where is the study run from? Warwick Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for? April 2018 to November 2023

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

Who is the main contact? Charlotte Scomparin packman@warwick.ac.uk

Contact information

Type(s)

Scientific

Contact name

Dr Charlotte Scomparin

Contact details

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Type(s)

Scientific

Contact name

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Additional identifiers

Clinical Trials Information System (CTIS)

2020-000154-10

Integrated Research Application System (IRAS)

1003404

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

CPMS 46938, IRAS 1003404

Study information

Scientific Title

Paramedic Analgesia Comparing Ketamine and MorphiNe in trauma (PACKMaN)

Acronym

PACKMaN

Study objectives

Ketamine is superior to morphine for the management of acute severe pain from traumatic injury treated by NHS paramedics.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 01/09/2020, West of Scotland Research Ethics Committee (Ward 11, Dykebar Hospital, Grahamston Road, Paisley, PA2 7DE, UK; +44 (0)141 3140212; wosrec1@ggc.scot.nhs.uk), ref: 20 /WS/0126

Study design

Randomized; Both; Design type: Treatment, Drug, Health Economic

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Analgesia

Interventions

Participants are randomized on a 1:1 basis between ketamine and morphine, stratified by ambulance services. Specially prepared, sequentially numbered treatment packs containing identical ampoules of either morphine (comparator) or ketamine (intervention) will be provided to each ambulance service. Numbered study drug packs in a pre-randomized sequence, will be carried by participating ambulance paramedics. Participants will be randomised by opening the pack.

The study drug can be administered by the intravenous (IV) or intraosseous (IO) routes. Paramedics will dilute the ampoule of study drug with 9 ml of 0.9% sodium chloride in a 10 ml syringe. (Syringe 1).

Syringe 1 will be administered by slow IV/IO injection over 4 to 5 minutes. Titrate to effect (up to the full 10ml being administered) aiming to give the minimal effective dose.

Paramedics will observe the participant for at least 5 minutes for effect. If pain is not relieved after syringe 1 has been administered, they prepare a second syringe by diluting a further ampoule of study drug with 9 ml of 0.9% sodium chloride in a 10 ml syringe (Syringe 2).

They administer 2 ml aliquots from Syringe 2 by slow IV/IO injection every 5 minutes and repeat further 2 ml aliquots every 5 minutes until adequate pain relief is achieved.

If after adequate pain relief is achieved the person experiences breakthrough pain, further 2 ml aliquots may be administered every 5 minutes.

The maximum dose that can be administered under this protocol for ketamine is 30 mg (two ampoules) and for morphine is 20 mg (two ampoules).

Participants will be followed up for 6 months.

Intervention Type

Other

Phase

Phase III

Primary outcome(s)

Effectiveness of pain relief from randomisation to arrival at hospital as measured by Sum of Pain Intensity Difference (SPID) score (using a 0-10 numerical rating scale); Timepoint(s): Arrival at hospital.

Key secondary outcome(s))

- 1. Effectiveness of pain relief and overall patient experience from randomisation to arrival at hospital measured using the following at baseline:
- 1.1. Total Pain Relief (TOTPAR) score
- 1.2. Time to perceptible analgesia
- 1.3. Time to meaningful analgesia
- 1.4. Time to peak analgesia
- 1.5. Duration of analgesia
- 1.6. Requirement for rescue analgesia
- 1.7. Proportion of patients with a pain intensity score below 4/10 (0-10 numerical rating scale (NRS)) on arrival at hospital

- 1.8. Vital signs (temperature, blood pressure, pulse rate, respiration rate)
- 1.9. Patient Global Impression of Change on arrival at hospital
- 2. Incidence of side effects and adverse events measured by recording side effects and adverse events at baseline to 30 days post IMP administration:
- 2.1. Airway: vomiting, aspiration, advanced airway management
- 2.2. Respiratory: desaturation, need for ventilatory support
- 2.3. Cardiovascular: arrhythmia, hypotension and hypertension
- 2.4. Neurologic: sedation, excitatory movements, adverse behavioural reactions
- 2.5. Other: allergic reaction, serious unexpected serious adverse reactions
- 3. Resource use measured by recording the following information at baseline and from hospital data:
- 3.1. Ambulance job cycle time (scene arrival to arrival at hospital)
- 3.2. Number of ambulance resources (technicians, paramedics, doctors and vehicles) in attendance
- 3.3. Cumulative IMP doses administered
- 3.4. CT scan use
- 3.5. Hospital or ICU admission
- 3.6. Length of stay ED, ICU, Hospital
- 4. Longer-term outcomes measured using the following at 3 and 6 months post-randomization:
- 4.1. Chronic pain measured using BPI-SF
- 4.2. Health-related quality of life measured using EQ-5D-5L and CSRI
- 4.3. Cost-effectiveness expressed in terms of incremental cost per quality-adjusted life-year (QALY) gained using EQ-5D 5L and CSRI

Completion date

30/11/2023

Eligibility

Key inclusion criteria

- 1. Age ≥16 years
- 2. Patient reports a pain score ≥7/10 on a 0-10 NRS following acute traumatic injury
- 3. Vascular access obtained
- 4. Determined by a paramedic to require IV morphine or equivalent

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

16 years

Sex

Αll

Total final enrolment

Key exclusion criteria

- 1. Known or suspected pregnancy
- 2. Unable to articulate severity of pain using the 0-10 NRS
- 3. Lack of capacity due to a reason other than pain
- 4. Ketamine or opioid analgesia prior to randomisation
- 5. Contraindication to either ketamine or morphine*
- 6. Patient declines participation
- 7. Known prisoner

Date of first enrolment

11/11/2021

Date of final enrolment

31/05/2023

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

West Midlands Ambulance Service NHS Foundation Trust

Millennium Point Waterfront Business Park Waterfront Way Brierley Hill United Kingdom DY5 1LX

Study participating centre

Yorkshire Ambulance Service NHS Trust

Trust Headquarters Brindley Way Wakefield 41 Business Park Wakefield United Kingdom WF2 0XQ

Sponsor information

Organisation

University of Warwick

Funder(s)

Funder type

Government

Funder Name

NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR128086

Results and Publications

Individual participant data (IPD) sharing plan

All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		05/04/2025	07/04/2025	Yes	No
Protocol article		24/11/2023	27/11/2023	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results			07/04/2025	No	Yes
Statistical Analysis Plan	version 1.0	14/06/2023	08/11/2023	No	No
Statistical Analysis Plan	version 2.0	14/02/2024	07/04/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes