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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
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Study website
https://warwick.ac.uk/fac/sci/med/research/ctu/trials/packman/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2020-000154-10

IRAS number
1003404

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
Paramedicine

Study type(s)
Treatment

Participant information sheet
This will be made available on the trial website

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 measure
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.

Secondary outcome measures
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

Overall study start date
16/04/2018

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

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 446; UK Sample Size: 446

Total final enrolment
458

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
England

United Kingdom

Study participating centre
West Midlands Ambulance Service NHS Foundation Trust
Millennium Point
Waterfront Business Park
Waterfront Way
Brierley Hill
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DY5 1LX

Study participating centre
Yorkshire Ambulance Service NHS Trust
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Sponsor type
University/education

Funder(s)

Funder type
Government

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

Results and Publications

Publication and dissemination plan
1. The protocol will be published via NIHR NETSCC
2. Planned publication in a high-impact peer-reviewed journal within 1 year of the end of the trial

Intention to publish date
15/12/2024

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?
HRA research summary			28/06/2023	No	No
Statistical Analysis Plan	version 1.0	14/06/2023	08/11/2023	No	No
Protocol article		24/11/2023	27/11/2023	Yes	No
Plain English results			07/04/2025	No	Yes
Results article		05/04/2025	07/04/2025	Yes	No
Statistical Analysis Plan	version 2.0	14/02/2024	07/04/2025	No	No