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Methylnaltrexone for the treatment of opioid induced constipation

Submission date 25/03/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 25/03/2015	**Overall study status** Completed	
Last Edited 25/04/2023	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
The drug methylnaltrexone is approved for use in the palliative/end of life care setting for treating constipation caused by opioid drugs. We believe that the use of methylnaltrexone for patients taking opioids will be of even greater benefit for people being treated in intensive care. Opioid drugs are used for the sedation and pain relief required for critically ill patients to tolerate mechanical breathing assistance. Unfortunately, there are considerable side effects including pruritus (itching), suppression of the immune system and most clinically relevant gastrointestinal (bowel) dysfunction. This leads to digestive problems, constipation leading to stomach bloating, a large immobile stool volume in the bowel (faecal impaction) and infection. There are several case reports supporting use of methylnaltrexone in intensive care , and we have used the drug successfully at Hammersmith Hospital. We have published a study showing that a significant number of critical care patients do suffer from opioid induced constipation despite standard treatment given to prevent this. Those patients that were treated with methylnaltrexone opened bowels within 24 hours, a result not achieved with standard therapy. There were also some benefits in the feeding and digestion of food and mortality (death rate) although these were not statistically significant. We now want to carry out a full trial to further investigate whether the drug methylnaltrexone does alleviate constipation caused by opioid drugs for critical care patients.

Who can participate?
Adults (aged at least 18) sedated with opiods and requiring mechanical breathing assistance.

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 receive methylnaltrexone following 48 hours of opioid induced constipation. Those in group 2 receive a placebo following 48 hours of opioid induced constipation. All participants are then followed up every day to assess, among other things, relief of constipation, tolerance of feeding, infection and mortality.

What are the possible benefits and risks of participating?
Methylnaltrexone has been shown to ease constipation in patients with cancer. It would be anticipated that critically ill patients would benefit too. In addition, there is the possibility of

additional advantages in more effective feeding, and reversal of some of the detrimental immune effects of opioids. However, at the moment, we do not know if Methylnaltrexone definitely has these benefits or that the side effects will still be rare in this group of patients, which is why we are doing this study. We cannot guarantee taking part in the study will benefit a participant directly but if this study shows a benefit, then it might help improve the treatment of people with constipation and gut dysfunction in the future. There is little additional risk from taking part in this study, as Methylnaltrexone is very safe with few side effects (nausea, diarrhoea, flatulence, dizziness), and no serious adverse effects have been reported. Only very small quantities of extra blood samples will be collected, usually from existing lines, so there is no extra discomfort.

Where is the study run from?
Imperial College of Science, Technology and Medicine (UK)

When is the study starting and how long is it expected to run for?
May 2015 to February 2018

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

Who is the main contact?
Miss Aisha Anjum

Contact information

Type(s)
Scientific

Contact name
Miss Aisha Anjum

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Additional identifiers

EudraCT/CTIS number
2014-004687-37

IRAS number

ClinicalTrials.gov number

NCT00672477

Secondary identifying numbers
18502

Study information

Scientific Title
Use of methylnaltrexone for the treatment of opioid induced constipation & gastroIntestinal stasis in intensive care patients

Acronym
MOTION

Study objectives
The aim of this study is to investigate whether the drug methylnaltrexone alleviates constipation caused by opioid drugs for critical care patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London - Harrow, 30/12/2014, ref: 14/LO/2004

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Critical care; Subtopic: Critical care; Disease: All Critical care

Interventions
Methylnaltrexone (Relistor): Opioid antagonist
Placebo: Normal Saline
Study Entry : Registration and One or More Randomisations

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome measure
Time to significant rescue-free laxation (stool volume of greater than 100 ml) following randomisation; Timepoint(s): Daily

Secondary outcome measures
1. Average number of bowel movements; Timepoint(s): Daily
2. Escalation of opioid dose due to antagonism/reversal of analgesia and sedation; Timepoint(s): Daily
3. Incidence of Clostridium difficile infection: PCR or Toxin positive; Timepoint(s): Daily
4. Incidence of diarrhoea; Timepoint(s): Daily
5. Incidence of positive microbiology blood cultures; Timepoint(s): Daily
6. Incidence of ventilator associated pneumonia (VAP), defined by the Clinical Pulmonary Infection Score; Timepoint(s): Daily
7. Mortality; Timepoint(s): At 28 days, ICU discharge and hospital discharge
8. Requirement of prokinetics (10mg Metoclopramide tds, 250 mg Erythromycin qds); Timepoint (s): Daily
9. Requirement of rescue laxatives, defined as 1/2 sachet Picolax (5 mg Sodium Picosulphate), 2 Glycerin suppositories (4-g mould); Timepoint(s): Daily
10. Toleration of enteral feeds (assessment of % of patients achieving full target enteral feeding); Timepoint(s): Daily
11. Gastric Residual Volume (measured every 4 hours and totalled over 24 hours); Timepoint(s): Daily

Overall study start date
01/03/2015

Completion date
28/02/2018

Eligibility

Key inclusion criteria
1. Males and females at least 18 years of age
2. Following ICU admission, sedated with opioids and requiring invasive ventilator support
3. Scheduled for continuous infusion/administration of opioid analgesics for at least a further 24 hours
4. Constipated (not opened bowels for a minimum 48 hours following ICU admission)
5. Access for enteral administration of medications and nasogastric tube feeds
6. Initiation of nasogastric tube feeds
7. Patient weight of 38-114 kg (this allows pre preparation of drug with either 8 mg or 12 mg)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 84; UK Sample Size: 84; Description: 84 patients across the three General Intensive Care Units within Imperial College Healthcare NHS Trust.

Total final enrolment
84

Key exclusion criteria
1. Known to be pregnant
2. Patients with end stage renal failure requiring dialysis on admission
3. Diarrhoea on admission
4. Abdominal surgery within 8 weeks prior to ICU admission
5. Presence of Ileostomy or colostomy
6. Mechanical gastrointestinal obstruction
7. Suspected acute surgical abdomen
8. History of Crohn's disease or ulcerative colitis
9. On palliative care or not expected to survive more than 12 hours
10. Severe chronic hepatic impairment (Child Pugh Class C)
11. Suspected hepatic encephalopathy
12. Known to have received another IMP within 30 days or currently in another interventional trial that might interact with the study drug or previously enrolled into MOTION

Date of first enrolment
01/09/2015

Date of final enrolment
15/07/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

Imperial College of Science, Technology and Medicine
ICCH Building
59 North Wharf Road
London
United Kingdom
W2 1LA

Sponsor information

Organisation
Imperial College London

Sponsor details
Joint Research Compliance Office
Charing Cross Hospital
Fulham Palace Road
London
England
United Kingdom
W6 8RF

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/041kmwe10

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

Publication and dissemination plan
Plan to publish study protocol by September 2015. Plan to publish main study results in December 2018.

Intention to publish date
31/12/2018

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Parind Patel (p.patel@imperial.ac.uk/parind.patel@nhs.net).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	13/07/2016		Yes	No
Basic results		29/05/2018	08/06/2018	No	No
Basic results			21/04/2019	No	No
Basic results			23/07/2019	No	No
Other publications	post-hoc analysis	01/11/2016	23/07/2019	Yes	No
Results article		03/02/2020	25/04/2023	Yes	No
HRA research summary			28/06/2023	No	No