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Gabapentin in post-surgery pain

Submission date 05/06/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 05/06/2017	**Overall study status** Completed	
Last Edited 26/05/2022	**Condition category** Surgery	

Plain English summary of protocol

Background and study aims
Gabapentin is a medicine used to treat epilepsy and nerve pain. Recently, doctors have begun using gabapentin to treat pain after an operation with the intention of reducing the amount of other drugs needed while maintaining good pain relief. Opioid drugs, such as morphine, are the most commonly used drugs to control pain after surgery, but doctors want to try to reduce the amount of opioid drugs because they cause side effects, often delaying discharge from hospital and leading to slower recovery. There is uncertainty about whether adding gabapentin to the usual drug regimen (which includes opioid drugs) will result in good pain relief, fewer side effects overall and faster recovery after surgery. The aim of this study is to find out whether gabapentin reduces the amount of time patients stay in hospital after the operation, the amount of opioid medication they take, and to assess how gabapentin influences pain in hospital and four months after surgery.

Who can participate?
Adults who are undergoing non-emergency heart, lungs or abdominal surgery

What does the study involve?
Participants are randomly allocated into one of two groups. Those in the first group are treated with gabapentin one hour before surgery and for two days after surgery. Those in the second group are treated with an identical looking dummy pill (placebo) at the same timepoints. Pain levels are assessed by asking patients one, four and 12 hours after surgery and then twice a day until they are discharged from hospital. Patients are also followed up until discharge to find out if they have taken opioid pain killers, as well as to assess their quality of life after four weeks and four months.

What are the possible benefits and risks of participating?
There are no guaranteed benefits of participating, however those who receive the gabapentin may have fewer side effects from opioid drugs and may recover from surgery more quickly. The results from this study may help improve management of pain after surgery in the future. Risks of taking part in the study include the risks of side effects from gabapentin. The side effects of gabapentin are usually short lived and will stop when the medication is stopped. These side effects have only been observed in patients who take gabapentin over long periods of time (e.g. to treat epilepsy or long-term pain). Gabapentin is usually well tolerated and it is unlikely that these events will occur in this study where gabapentin is only taken for a short period of time.

Where is the study run from?
Trials Unit: Bristol Trials Centre (Clinical Trials and Evaluation Unit), Bristol (UK)
Sponsor: University Hospitals Bristol & Weston NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2017 to January 2023

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

Who is the main contact?
Professor Chris Rogers
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Study website
http://cteu.bris.ac.uk/gap

Contact information

Type(s)
Scientific

Contact name
Prof Chris Rogers

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Additional identifiers

EudraCT/CTIS number
2017-002078-38

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
SU/2016/6033

Study information

Scientific Title
Effectiveness, cost effectiveness and safety of gabapentin versus placebo as an adjunct to multimodal pain regimens in surgical patients: A placebo controlled randomised controlled trial with blinding (The GAP study)

Acronym
GAP Study

Study objectives
Gabapentin reduces opioid use after surgery and speeds up recovery, thereby reducing post-operative hospital stay compared to standard multimodal analgesia (usual care).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Yorkshire and the Humber – Sheffield REC, 23/11/2017, REC ref: 17/YH/0381

Study design
Multi-centre parallel group placebo-controlled pragmatic randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Pain management after surgery

Interventions
Participants are randomised in a 1:1 ratio to one of two groups by an authorised member of the local research team using a secure internet-based randomisation system ensuring allocation concealment.

Intervention group: Participants receive gabapentin 600 mg given preoperatively with the patient's premedication and 600 mg/day (300 mg in the morning and 300 mg in the evening) given postoperatively for two days following extubation (if applicable) within the multimodal analgesic regimens specified by local analgesic protocols.

Control group: Participants receive a placebo which will be taken at the same time points as the active tablet within the multimodal analgesic regimens specified by local analgesic protocols.

Patients in both groups are followed up at approximately four weeks and four months after randomisation for information on pain, adverse events, resource use and quality of life. this information will be collected via postal questionnaires and/or over the phone.

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome measure
Time from start of surgery to hospital discharge is measured by reviewing participant hospital notes at discharge.

Secondary outcome measures
1. Opioid consumption in the period from surgery until hospital discharge is measured by reviewing participant hospital notes at hospital discharge
2. Acute post-operative pain is assessed using the visual analogue scale (VAS) completed at 1, 4 and 12 hours post-surgery and then twice daily to discharge
3. Adverse health events from randomisation to 4 months including side effects of medication (e. g. nausea; vomiting; pruritus; sedation; confusion) and on-going pain are assessed by reviewing participant hospital notes throughout their hospital stay and at discharge, as well as phone calls with the participants at 4 weeks and 4 months after randomisation
4. HRQoL measured using the EQ-5D 5 level questionnaire and Short-form (SF) 12 completed at baseline and at follow-up at approximately 4 weeks and 4 months after randomisation
5. Resource use to 4 months is measured by reviewing participant hospital notes and completion of Resource Use Questionnaires during the hospital stay, at 4 weeks and 4 months
6. Chronic pain is measured using the brief pain inventory (BPI) at baseline and at 4 months after randomisation

Overall study start date
01/06/2017

Completion date
31/01/2023

Eligibility

Key inclusion criteria
Current inclusion criteria as of 18/01/2019:
1. Over 18 years of age
2. Undergoing non-emergency surgery:
2.1. Cardiac (surgery on the heart and great vessels carried out via midline sternotomy)
2.2. Thoracic surgery (open or minimal access surgery on the lungs and surrounding tissues)

2.3. Abdominal (open or minimal access surgery within the abdominal cavity)
3. Expected to stay in hospital at least until day 2 after surgery (day 0 is day of surgery)
4. Expected to be able to swallow during the time of the study intervention

Previous inclusion criteria:
1. Over 18 years of age
2. Undergoing non-emergency surgery:
2.1. Cardiac (surgery on the heart and great vessels carried out via midline sternotomy)
2.2. Thoracic surgery (surgery on the lungs and surrounding tissues)
2.3. Abdominal (open or laparoscopic surgery within the abdominal cavity)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
1180

Total final enrolment
1196

Key exclusion criteria
Current exclusion criteria as of 18/01/2019:
1. Taking anti-epileptic medication(s)
2. Allergy to gabapentin
3. Already taking gabapentin or gabapentanoids
4. Rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose galactose malabsorption
5. Planned epidural analgesia
6. Intended use of any gabapentanoids in the peri-operative analgesic protocol other than the study medication (this includes but is not restricted to: pregabalin, enacarbil gabapentin, 4-methylpregabalin and phenibut)
7. Known renal impairment (for such patients, estimated glomerular filtration rate (eGFR)
8. Weight <50kg
9. Inability to provide written informed consent to participate in the trial
10. Unwilling to participate in follow-up
11. Prisoners
12. Enrolled in another clinical trial and: a) the patient is currently taking an investigational medicinal product as part of the other trial; or b) co-enrolment is not permitted by the other trial; or c) co-enrolment would be burdensome for the patient

Previous exclusion criteria:
1. Expected to have a minimum length of hospital stay of less than 2 days

2. Taking anti-epileptic medication(s)
3. Allergy to gabapentin
4. Planned epidural analgesia
5. Intended use of any gabapentanoids in the peri-operative analgesic protocol other than the study medication (this includes but is not restricted to: pregabalin, enacarbil gabapentin, 4-methylpregabalin and phenibut)
6. Known renal impairment (for such patients, estimated glomerular filtration rate (eGFR) <30ml /min/1.732)
7. Weight <50kg
8. Inability to provide written informed consent to participate in the trial
9. Unwilling to participate in follow-up
10. Prisoners
11. Already taking gabapentin or gabapentanoids
12. Rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose galactose malabsorption
13. Currently taking an investigational medicinal product as part of another clinical trial

Date of first enrolment
24/04/2018

Date of final enrolment
20/05/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospitals Bristol & Weston NHS Foundation Trust
Bristol Royal Infirmary
Marlborough Street
Bristol
United Kingdom
BS2 8HW

Study participating centre
University Hospitals Southampton NHS Foundation Trust
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Musgrove Park Hospital
Parkfield Drive
Taunton
United Kingdom
TA1 5DA

Study participating centre
Basildon University Hospital
Nethermayne
Basildon
United Kingdom
SS16 5NL

Study participating centre
Blackpool Victoria Hospital
Blackpool Teaching Hospitals
Whinney Heys Road
Blackpool
United Kingdom
FY3 8NR

Study participating centre
Royal United Hospital
Royal United Hospital NHS Trust
Bath
United Kingdom
BA1 3NG

Study participating centre
Liverpool University Hospitals NHS Foundation Trust
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Sponsor information

Organisation
University Hospitals Bristol NHS Foundation Trust

Sponsor details
Research and Innovation
Level 3, Education Centre
Upper Maudlin Street
Bristol
England
United Kingdom
BS2 8AE

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
31/01/2024

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from the CTEU team on bristol-cteu@bristol.ac.uk. Please also note that anonymised data will be provided on request for ethically approved research. All such requests could be subject to a small charge to cover the costs of preparing the files and associated documentation.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v3.0	25/05/2018	18/01/2019	No	Yes
Protocol article	protocol	20/11/2020	15/01/2021	Yes	No
HRA research summary			28/06/2023	No	No