

Safety and efficacy of analgesia-based sedation using remifentanyl versus standard hypnotic-based regimens in intensive care unit (ICU) patients with brain injuries: a randomised, controlled trial

Submission date

24/05/2004

Recruitment status

No longer recruiting

☐ Prospectively registered

☐ Protocol

Registration date

25/05/2004

Overall study status

Completed

☐ Statistical analysis plan

☒ Results

Last Edited

08/09/2008

Condition category

Injury, Occupational Diseases, Poisoning

☐ Individual participant data

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

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Contact details

Intensive Care Unit

Genimatas General Hospital

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

Study information

Scientific Title

Study objectives

To compare the safety and efficacy of analgesia-based sedation with conventional hypnotic-based sedation in patients with brain injuries requiring sedation during mechanical ventilation.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Not provided at time of registration.

Study design

Randomised controlled trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Neurotrauma

Interventions

The study was designed to compare the safety and efficacy of analgesia-based sedation, using remifentanyl, with conventional hypnotic-based sedation in patients with brain injuries requiring sedation during mechanical ventilation. Patients were randomised on a 2:1:1 basis to receive either an analgesia-based treatment regimen or a hypnotic-based treatment regimen:

1. Analgesia-based treatment regimen (n = 84): remifentanyl was initiated and titrated to provide optimal sedation and analgesia before the addition of a hypnotic agent, according to a predefined dosing algorithm

2. Hypnotic-based treatment regimen: patients received the opioid fentanyl (n = 37) or morphine (n = 40) and a hypnotic agent for analgesia and sedation which were administered simultaneously and then titrated to response

For all three treatment groups, on days 1 - 3 the hypnotic agent was propofol, on days 4 - 5 propofol was substituted with midazolam.

Patient monitoring:

All patients were intensively monitored throughout the study. Baseline Glasgow Coma Score (GCS), SAS, Pain intensity (PI), mean arterial pressure (MAP) and heart rate (HR) were recorded prior to the administration of study drugs. When available, intra-cranial pressure (ICP) and cerebral perfusion pressure (CPP) were also recorded. SAS, PI, MAP, HR, ICP and CPP were then recorded at the time of any changes in study drug infusion rates or bolus dosing and at 10 minute intervals afterwards until adequate SAS/PI scores were attained. Once target SAS and PI scores were attained, haemodynamic monitoring was performed at 1 - 4 hour intervals. In addition, haemodynamic parameters were recorded at the start of down-titrations of study drugs for neurological assessment of patients and when the assessments were completed. The SAS, PI, MAP, HR, ICP and CPP were also recorded at the start of and at the time of adequate transitioning from propofol to midazolam at the end of day 3 and if a patient was extubated before day 5 of the study treatment period. These parameters were also recorded at the start of the final transition to an alternative analgesia/sedation regimen at the end of study day 5, at 20 min intervals after each down-titration of the remifentanyl infusion as part of this process, at 30 and 60 min after the termination of the infusion and at final transition to an alternative opioid.

Patients were continuously assessed for the occurrence of adverse events until 24 hours after permanent discontinuation of the study drugs or until ICU discharge if this occurred earlier. Serious adverse events were defined as adverse events that resulted in any of the following outcomes: death, life-threatening event, prolongation of hospitalisation, a disability/incapacity. Important medical events which did not result in death or were not life-threatening, were considered serious adverse events when, based upon appropriate medical judgement, they jeopardised the patient and required medical or surgical intervention to prevent one of the outcomes listed above.

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

Remifentanyl, fentanyl

Primary outcome measure

Not provided at time of registration.

Secondary outcome measures

Not provided at time of registration.

Overall study start date

01/01/2004

Completion date

31/12/2004

Eligibility

Key inclusion criteria

1. Acute, severe neurological insult/injury
2. Elective or emergency neurosurgery
3. Aged 18 - 80 years
4. Weighed less than or equal to 120 kg
5. Admitted into the ICU within the past 24 hours, were intubated and were expected to require mechanical ventilation for 1 - 5 days

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

161

Key exclusion criteria

1. Had or were likely to require:
 - 1.1. Long-acting (or continuous administration of) neuromuscular blocking drugs to facilitate mechanical ventilation during the study period
 - 1.2. Barbiturate administration prior to or during the study period
 - 1.3. Epidural block during the maintenance or extubation phases of the study
2. Failed to demonstrate signs of recovery/responsiveness within 6 hours of stopping any analgesia/sedation regimen in use at the time of screening for study entry
3. Likely to require a tracheostomy with spontaneous ventilation within five days of starting study drug treatment
4. Suffered severe, associated traumatic injury, had a neurological condition that might affect the ability to assess their Sedation-Agitation Scale (SAS) score, were admitted for status epilepticus, had moderate or severe renal impairment (predicted creatinine clearance of less than 50 ml/min)
5. History of allergy to opioids, benzodiazepines, propofol or of alcohol/drug abuse
6. Pregnant or lactating women

Date of first enrolment

01/01/2004

Date of final enrolment

31/12/2004

Locations**Countries of recruitment**

Austria

Belgium

Germany

Greece

Netherlands

Spain

Study participating centre

Intensive Care Unit

Athens

Greece

Sponsor information

Organisation

GlaxoSmithKline (UK)

Sponsor details

Greenford Road

Greenford

United Kingdom

UB6 OHE

Sponsor type

Industry

ROR

<https://ror.org/01xsqw823>

Funder(s)

Funder type

Industry

Funder Name

GlaxoSmithKline (UK)

Alternative Name(s)

GlaxoSmithKline plc., GSK plc., GSK

Funding Body Type

Government organisation

Funding Body Subtype

For-profit companies (industry)

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Results	01/08/2004		Yes	No