ISRCTN50308308 https://doi.org/10.1186/ISRCTN50308308

Safety and efficacy of analgesia-based sedation using remifentanil 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
Registration date 25/05/2004	**Overall study status** Completed
Last Edited 08/09/2008	**Condition category** Injury, Occupational Diseases, Poisoning

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Andreas Karabinis

Contact details
Intensive Care Unit
Genimatas General Hospital
Athens
Greece

Additional identifiers

Protocol serial number
USA30217

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

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Neurotrauma

Interventions
The study was designed to compare the safety and efficacy of analgesia-based sedation, using remifentanil, 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): remifentanil 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 remifentanil 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)
Remifentanil, fentanyl

Primary outcome(s)
Not provided at time of registration.

Key secondary outcome(s))
Not provided at time of registration.

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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)

ROR
https://ror.org/01xsqw823

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline (UK)

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

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