ISRCTN01173443 https://doi.org/10.1186/ISRCTN01173443

Midazolam, propofol used alone or sequentially for long-term sedation in critically ill, mechanically ventilated patients

Submission date
25/02/2014

Recruitment status
No longer recruiting

Registration date
03/03/2014

Overall study status
Completed

Last Edited
15/05/2015

Condition category
Other

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

Plain English summary of protocol

Background and study aims
Currently, drugs like midazolam and propofol are the most commonly used for sedation in intensive care units (ICU). The two drugs are equally safe and effective for short-term sedation. However, each drug has side effects when used for long-term sedation. Considering the limitations associated with these drugs when used alone, our study will find out whether the sequential use of midazolam and propofol in the long-term sedation of critically ill, mechanically ventilated patients can reduce the side effects.

Who can participate?
Intubated adult patients who are expected to receive long-term (>3 days) mechanical ventilation on admission to the ICU.

What does the study involve?
Participants are randomly allocated to receive midazolam (group M) , propofol (group P), or sequential use of both (group M-P). In each group, sedation quality is assessed and the nurses continuously monitor the sedation depth and adjust the dosages of the drugs accordingly. According to our local sedation procedure, the sedation scores are recorded every 4 h (or more frequently when indicated) by the nursing staff. All the participants are managed with a daily interruption of continuous sedation daily, from the next day after enrolment. At the end of the study, we will find out the clinical effects, safety and cost of midazolam, propofol and their sequential use for long-term sedation in critically ill mechanically ventilated patients.

What are the possible benefits and risks of participating?
The main benefits to patients sedated with midazolam and propofol sequentially are as follows: first, compared with midazolam, the sequential use of midazolam and propofol may reduce the incidence of agitation after stopping sedation, and lead to a faster recovery, shorter mechanical ventilation time and lower total ICU cost; second, the drugs may cost less and incidence of low blood pressure is lower compared with propofol alone. The main benefits to the patients treated with propofol are faster recovery and shorter mechanical ventilation. Midazolam used for patients may decrease the risk of low blood pressure and high fat level in the blood. The risks

for patients sedated with midazolam are that it may cause acute withdrawal syndrome and delay recovery from drug accumulation, and may be associated with the risk of cardiovascular depression. The use of propofol may be associated with a risk of high fat level in the blood and cardiovascular depression, propofol infusion syndrome, and higher drug cost. There are no other anticipated risks for participants.

Where is the study run from?
The study is run from the West China Hospital of Sichuan University, China.

When is the study starting and how long is it expected to run for?
The study started in March 2010 and ran until September 2011.

Who is funding the study?
West China Hospital of Sichuan University (China).

Who is the main contact?
Professor Yan Kang, Kangyan_5626@hotmail.com
Yongfang Zhou, zyfmg@163.com

Contact information

Type(s)
Scientific

Contact name
Prof Yan Kang

Contact details
Guoxue Road 37
Chengdu
China
610041

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Midazolam, propofol used alone or sequentially for long-term sedation in critically ill, mechanically ventilated patients: a prospective, randomized study

Study objectives
We hypothesise that the sequential use of midazolam and propofol in long-term (>3 days) sedation may be useful and could reduce adverse effects for critically ill mechanically ventilated patients, compared with midazolam or propofol alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West China Hospital Sichuan University Clinical Trials and Biomedical Ethics Committee, 28/12 /2009, approval number: 2009 approval (57)

Study design
Single-centre prospective randomized study

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 the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Mechanical ventilation

Interventions
All the patients received continuous intravenous fentanyl for analgesia with bolus dosage of 1-2 ug/kg and maintenance dosage of 1-2 ug/kg/h. Patients allocated to the midazolam group (group M) were treated with an infusion bolus of 0.03-0.30 mg/kg and continuous infusion of 0.04-0.20 mg/kg/h, with the dosage adjusted to achieve the desired level of sedation. Patients allocated to the propofol group (group P) received an infusion bolus of 0.50-3.00 mg/kg and continuous infusion of 0.50-3.00 mg/kg/h with the dosage adjusted to achieve the desired level of sedation. Patients allocated to the sequential use of midazolam and propofol group (group M-P) first received midazolam by the same method as in group M. When patients met the sequential criteria, midazolam was switched to propofol, which was administered at the maintenance dosage of 0.50-3.00 mg/kg/h. To meet the sequential criteria patients passed the spontaneous breathing trial (SBT) safety screen. Starting with the next day after enrollment, all the patients were managed with a daily interruption of continuous sedation and the spontaneous breathing trial (SBT) protocols daily.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Midazolam, propofol

Primary outcome measure
To determine the recovery and extubation time, which were defined as the time from the cessation of sedation until awakening and extubation

Secondary outcome measures
To determine the cost of sedation, the primary monetary pharmaceutical costs of sedation and total ICU costs (including ICU therapy and sedation) were calculated. After patients were transferred out of ICU, their recollection of mechanical ventilation-related events (rolling over, suction, and endotracheal tube stimulation and pain) were recorded using a questionnaire. The patients responded from the following options: (A) unbearable memory, (B) bearable memory, and (C) no memory.

Overall study start date
01/03/2010

Completion date
30/09/2011

Eligibility

Key inclusion criteria
Intubated patients (>18 years old) who were expected to receive long-term (>3 days) mechanical ventilation on admission to the ICU within West China Hospital of Sichuan University between March 2009 and September 2011

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Total 105-135 patients

Key exclusion criteria
1. Known or suspected allergy to propofol or midazolam
2. Suspected pregnancy

3. Gross obesity
4. Hyperlipemia
5. Moribund state
6. History of alcoholism or intake of anti-anxiety drugs or hypnotics
7. Chronic renal failure
8. Coma by cranial trauma or neurosurgery or unknown etiology or status epilepticus
9. Unwillingness to provide informed consent by patients or their authorized surrogates following ICU admission

Date of first enrolment
01/03/2010

Date of final enrolment
30/09/2011

Locations

Countries of recruitment
China

Study participating centre
Guoxue Road 37
Chengdu
China
610041

Sponsor information

Organisation
West China Hospital of Sichuan University (China)

Sponsor details
Guoxue Road 37
Chengdu
China
610041

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/007mrxy13

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
West China Hospital of Sichuan University (China)

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	16/06/2014		Yes	No