Propofol and etomidate.
Are they also safe for patients with Brugada-Syndrome?

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24665

Source
NTR

Brief title
N/A

Health condition

Brugada-Syndrome, Propofol, Etomidate, Arrhythmia,

Sponsors and support

Primary sponsor: Universitair Ziekenhuis Brussel
Laarbeeklaan 101
1090 Jette
Belgium
Source(s) of monetary or material Support: Universitair Ziekenhuis Brussel
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Intervention

Outcome measures

Primary outcome

ECG changes. ST elevation of 1 or more mm which is described as type I, or coved.

Secondary outcome

N/A

Study description

Background summary

Introduction:

Since the first report of Brugada-Syndrome (BrS), and the increased screening of genealogical trees of patients with aborted sudden death or syncope, the incidence of diagnosis of BrS has increased noticeably. This implies that anaesthetists and critical care physicians will be confronted with those patients more frequently in the future.
Propofol is listed at the official website of Brugada-drugs (www.brugadadrugs.org) as a drug that should be avoided, with a recommendation of class IIb. (There is conflicting evidence and/or divergence of opinion about the drug, and the potential arrhythmic effect in BrS patients is less well established by evidence/opinion). This is based mostly on isolated case reports, with prolonged infusions, multiple drug infusions, intensive care comorbidity, confounding any possible conclusion.

It remains a fact that no prospective studies have been done yet to investigate the use of those commonly used anaesthetic agents in this relatively new disease. Knowing that propofol and etomidate are the most commonly used anaesthetic agents on daily basis, for paediatric and adult patients, it is only a matter of time that a patient with undiagnosed BrS is administered one of those anaesthetic agents. Therefore we believe that it is of outmost importance to investigate whether those agents can be used safely, with caution, or should be banned for those patients.

The pharmacokinetic profile of propofol favours its use. It has a very short onset of action and a short duration of action, with a half-life of 1 to 8 minutes. Moreover, it provides very fast recovery of anaesthesia. In fact, until now, there are no absolute contraindications for its use, unless a known allergy for the substrate, or its emulsion-vehicle (soya). Prolonged infusions of high doses of propofol have been associated with propofol-infusion-syndrome (PIS). It is a very rare entity of lactate acidosis, rhabdomyolysis, and heart-failure that can be fatal.

Etomidate is another frequently used hypnotic agent. It is an imidazole, with an initial half-life of 2,6 minutes. It reduces cerebral bloodflow, and is probably not neuroprotective. It has

been shown to increase ischemic parameters in cerebral ischemic zones. Although its use is more limited due to contraindications and known side-effects its administration is indicated in hemodynamic fragile patients. It has been proved to be more emetogenic and can cause thrombophlebitis. Prolonged infusions cause adrenal suppression by blocking cortisol-synthesis (11-beta-hydroxylase), increasing morbidity and mortality of intensive care patients. Some studies report that even a single-bolus can induce adrenal suppression.

Study purpose:

The purpose of this study is to investigate whether commonly used hypnotic agents, propofol and etomidate, are also safe for patients with BrS.

Study setup:

Prospective, randomized clinical trial, double-blind.

Study protocol:

Current medical practice requires patients that have a baseline electrocardiogram (ECG) defined as BrS, and patients that have been found positive for Ajmaline-test, to undergo an electrophysiological study (EPS). This procedure happens frequently under sedation or general anaesthesia to warrant comfort and safety of the patient, and assure that precise findings are acquired.

After obtaining eligibility with the patient profile (in- and exclusion criteria) and informed consent, patients are admitted to have an EPS. Electrolyte balance is checked preoperatively and corrected if needed. Induction of anaesthesia is achieved intravenously, randomly assigned, either with propofol, either with etomidate and maintained with an inhalation anaesthetic (Sevoflurane®). Continuous blood pressure, peripheral oxygen saturation, 12-lead ECG, and capnography are used to monitor our patients, in an operation theatre equipped with everything needed to assure a safe procedure. Defibrillator pads are attached to the patient through the perioperative period. The 12-lead ECG is monitored live by a cardiologist, and recorded. The anaesthetic agent will be injected slowly over 2 minutes, in a perfusion line with good flow. The dose will be calculated based on the body-weight of the patient. In case of obesity, with a body mass index (BMI) above 25, the ideal body weight will be used to calculate the required dose. Propofol will be given at a dose of 2mg/kg for adults and at 3mg/kg for paediatric patients. The dose used for etomidate will be 0.2mg/kg for adults and for children. ECG monitoring will go on for another 15 minutes after administration of the full-dose, (before starting the actual EPS), unless ECG changes occur that require abandoning further administration.

The criteria to abandon further administration are 30% prolongation of the QRS, or induction of ventricular arrhythmias, or any other rhythm disturbance that could compromise the safety of our patient.

The ECGs will be analysed by three cardiologists blinded for the anaesthetic agent. The ECG analysis will include QRS-duration, intraventricular conduction delays, PQ interval, QTc intervals, ST-segment elevation in V1 to V3.

Inclusion criteria:

All paediatric and adult patients that have been screened for BrS and were found positive before or after the Ajmaline-test are included.

Exclusion criteria:

Patients with a known allergy for soya are excluded from the study.

Patients with a supressed immune-status are excluded from the study.

Patients with a recent transient ischemic attack or cerebrovascular accident will be excluded from the study.

Power analysis:

A power analysis indicated that 2 groups of 39 subjects would be required to achieve a statistical power of 0.9 at an á-level of 0.05 and a standard deviation of 0.1mV to detect a difference in ST-segment elevation of 0.2mV.

Study objective

Propofol is safe for patients with Brugada-syndrome.

Study design

During and after induction of anaesthesia, during 5 minutes after induction of anaesthesia.

Intervention

Administration of propofol versus etomidate for induction of anaesthesia in patients screened for Brugada Syndrome.

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Eligibility criteria

Inclusion criteria

All paediatric and adult patients that have been screened for BrS and were found positive before or after the Ajmaline-test are included.

Exclusion criteria

1. Patients with a known allergy for soya are excluded from the study;

2. Patients with a supressed immune-status are excluded from the study;

3. Patients with a recent transient ischemic attack or cerebrovascular accident will be excluded from the study.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2012
Enrollment:	78
Type:	Anticipated

Ethics review

Positive opinion

Date:	28-02-2012

Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL3182
NTR-old	NTR3326
Other	MEC UZ Brussel : 2012/027
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A