THE USE OF DEXMEDETOMIDINE FOR EEG SEDATION IN CHILDREN WITH BEHAVIORAL DISORDERS

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NCT03799783 protocol

Background

Diagnostic and therapeutic procedures are often difficult to perform in pediatric population due to a low compliance. Electroencephalogram (EEG) recording represents a particular challenge. The child should be quiet for a medium-long time and an EEG registration during spontaneous sleep is often necessary for a complete assessment. Even if a dedicated environment and adequate preparation of both child and parents make it usually easy to be successfully performed, it could become difficult in children affected by behavioural disturbance, such as autism spectrum dis- order (ASD). It's known that children with ASD have a higher risk of epilepsy compared with the general population,so they more frequently need EEG recordings both while awake and while asleep. In such cases, the use of conventional sedative and hypno-inducing drugs to obtain an EEG both in wakefulness and sleep is definitely limited, taking into account that the majority of drugs modifies EEG pattern.In this context, Dexmedetomidine could represent an alternative solution. It is an emerging long-lasting α-2 agonist anxiolytic and sedative drug with analgesic effects,able to induce a para-physiologic sleep status with no significant interference on EEG patternsand possible but infrequent cardiovascular side effects (hypotension, hypertension, and bradycardia).In Italy, the use of dexmedetomidine in children outside the operating room was approved in 2016.Nevertheless, studies on its use for diagnostic and therapeutic procedures in special pediatric population are so far limited,and up to date guidelines and protocols in children are still missing.

The aim of the present is to evaluate the effectiveness and safety of intravenous dexmedetomidine in pediatric patients with behavioural disorders undergoing EEG recording.

Methods

Setting

This single-center prospective study will be carried out at the Department of Woman and Child's Health of Padova, a tertiary pediatric teaching hospital in Northern.

Study population

We will include all consecutive patients referred to our Pediatric Neurology and Neurophysiology Unit to perform a sleep-EEG after failing the usual local protocol based on parents' education, melatonin administration, and/or sleep deprivation according to the age of patient.

Inclusion criteria:

- age between 1 month and 15 years
- acute or chronic behavioural disorder
- American Society of Anesthesiologists (ASA) status of 1 or 2
- written informed consent by a parent or legal guardian.

Exclusion criteria:

- patients with failure to gain peripheral vein access, previous hypersensitivity re- action to dexmedetomidine
- contraindications to administration of dexmedetomidine (cardiac failure, cardiac arrhythmias, long QT syndrome, bradycardia, hypotension, use of betablockers or digoxin, uncontrolled arterial hypertension, recent stroke or intracranial bleeding, Moya-Moya syndrome)
- use of sedative drugs in the previous 8 hours
- presence of vomit or gastroesophageal reflux, and craniofacial abnormalities

Intervention

Each patient will be evaluated by a pediatrician involved in the study to verify inclusion and exclusion criteria and to assess clinical condition of the child, including fasting (6 hours for meals, 4 hours for breast milk, 2 hours for liquids). Sedation will be administered by a Pediatric Intensivist in an emergency equipped room. Equipment will be comprehensive of wall oxygen supply and devices for basic and advanced airway management, including bag masks, oropharyngeal airway, laryngeal mask airway and complete equipment for intubation, defibrillator, suction devices, and nasogastric tubes. Before each procedure, the pediatric intensivist will check each device to control its functioning. The pediatric intensivist will stay with the patient throughout the procedure, monitoring the parameters in order to anticipate and promptly treat any possible problem or complication. In the EEG room, an oxygen tank and emergency medical bag with all the equipment previously described was always present. Patients will finally get back to the ward or emergency department's room until complete recovery. Oxygen saturation, respiratory rate, heart rate, blood pressure, end tidal CO_2 ($EtCO_2$), and Pediatric Sedation State Scale (PSSS) score will be recorded continuously, every 5 minutes, from the beginning of the sedation until complete recovery, defined by NICE guidelinesas a complete return to presedation state.

An intravenous bolus of dexmedetomidine (2 mcg/kg over 10 minutes) will be administered, followed by continuous infusion (1-2 mcg/kg/hour), interrupted at the end of the procedure. The bolus may be repeated up to 3 times to reach the optimal target level of sedation, before starting the continuous infusion. The target level of sedation is defined as a score of 2 assessed by using the PSSS, corresponding to a child in a quiet state (asleep or awake), not moving during the procedure. If PSSS of 2 will not be achieved, despite the dexmedetomidine boluses and infusion, an additional sedative drug of the physician's choice will be administered, considering as a failed procedure for the study.

We will register time to falling asleep (onset time), to first awakening and to complete recovery after the procedure (offset time).

Duration

The study will last 18 months.

Outcome measures

Primary outcome: The primary outcome is to evaluate efficacy of dexmedetomidine, consisting in number of patients that reach a score of 2 five minutes after the infusion of dexmedetomidine assessed by the PASS (Pediatric Sedation State Scale)

Secondary outcome: The secondary outcome is to evaluate the safety of dexmedetomidine, consisting in adverse events immediately after dexmedetomidine infusion, according to the world SIVA classification recording tool.Hypotension and hypertension were defined as a decreasing or increasing of blood pressure of more than 25% as compared to baseline values measured before the administration of the drug or to age-specific normal valuesif the patients were particularly agitated before the procedure. The same definitions were used for bradycardia and tachycardia using heart rate values.

Statistics

Data will be registered in an Excel spreadsheet and analyzed with SAS 9.4 (SAS Institute Inc) for Windows. Quantitative variables will be reported as mean, standard deviation, median, interquartile ranges, minimum, and maximum values. Categorical variables will be expressed as number and percentage of subject in each category. Comparisons between groups will be conducted with Wilcoxon-Mann-Whitney test for quantitative variables, with Fisher's exact test for categorical variables. Spearman's rank correlation coefficient will be used to assess the correlation between quantitative variables. A P-value < .05 will be considered statistically significant.

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