Prospective Observational Evaluation of a New Protocol for Adult Procedural Sedation With Ketamine-propofol in a 1 on 4 Ratio at the Emergency Department of a Tertiary Hospital

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Introduction

Procedural sedation is the monitored use of sedatives and/or analgesics in a patient who must endure a short painful or frightening procedure, bringing the patient into a sedative state while retaining his spontaneous breathing and respiratory reflexes. Examples of these procedures are cardioversion, repositioning of a shoulder luxation or incision of a skin abscess, and these are frequently performed at the emergency ward. An easy and unambiguous protocol for procedural sedation was composed at the emergency department of the University Hospital of Ghent applicable for nearly all patients and procedures. This protocol included recommendations for necessary monitoring such as continuous electrocardiogram, intermittent blood pressure measurements, oxygen saturation and capnography, as well as safety precautions for standby medications or medical devices for hemodynamic and airway control. As sedative drug a mixture of ketamine and propofol ("ketofol") in a 1 on 4 ratio was selected based on the available literature. Both ketamine and propofol are known to neutralise each other's undesirable effects and ketamine adds an analgesic quality. Ketofol has proven effective and safe in studies and is non-inferior to propofol. Though it is most often used in a 1 on 1 ratio, both pharmacological and clinical studies favour a 1 on 4 ratio.

This protocol became the hospital's golden standard for procedural sedation and an adult patient in need of procedural sedation, who agreed the informed consent for procedural sedation was treated according to this protocol. Patients with an American Society of Anesthesiologist physical status classification system status of III or more, with an anticipated difficult airway or intoxicated patients were discussed with the anaesthesiology department to decide the feasibility of sedation in the emergency ward setting. Pregnant patients were excluded.

Associated to this newly implemented protocol, an observational prospective study was associated to verify the safety and effectivity, and to score the physicians satisfaction. A separate informed consent was obtained for participation in the study to permit inclusion of patient and procedural data into a registry. Data was registered by the physician responsible for the sedation in a questionnaire. The investigators hypothesized the protocol with ketofol in a 1 on 4 ratio would be safe and effective and would serve to facilitate procedural sedation by emergency physicians.

Selection for Procedural Sedation

Inclusion criteria:

- 18 years or older
- American Society of Anesthesiologists physical status score I and II
- American Society of Anesthesiologists physicial status score III and III if after consultation with anaesthesiologist department sedation is deemed safe at the emergency department
- Intoxicated patients if after consultation with anaesthesiologist department sedation is deemed safe at the emergency department

Exclusion criteria:

- Pregnancy
- Known allergy to propofol or ketamine
- Expected procedure of more than 15 minutes

Informed consent is obtained for performance of procedural sedation at the emergency department

Specifics of protocol procedural sedation

Who:

- 1 emergency physician or resident, responsible for sedation, who has had at least 6 months experience at the anaesthesiology department.
- 1 medical doctor for performance of procedure
- 1 emergency nurse

How:

The participant was brought to a zone where advanced life support could be optimally administered and where all necessary drugs and materials for treatment of complications are present. Oxygen saturation, continuous electrocardiogram, intermittent blood pressure measurement (every 2 minutes) and capnography were applied. An intravenous line of minimum 20 gauge was inserted with crystalloid infusion. The participant was placed in semi-recumbent position and was given oxygen for at least 3 minutes through a non-rebreather mask unless contra-indications like risk of CO_2 retention applied.

Ketofol 1 on 4 was prepared by mixing 1ml of ketamine (50mg) and 20ml of propofol (200mg) in a single syringe up to a total volume of 21ml. It was administrated as a loading dose of 1ml/10kg, corresponding to 0,952mg/kg propofol and 0,238mg/kg ketamine, and followed by a stepwise titration in aliquots of 0,5ml/10kg every 1 to 2 minutes until desired depth of sedation was achieved. Subsequent aliquots of 0,5ml/10kg were given every 3-5 minutes to retain the desired depth of sedation. The loading dose was halved for participants above the age of 65.

The participant was observed for complications or cardiorespiratory interventions by the sedating physician until he was fully awake. Thirty minutes after the awakening, the participant was questioned for his remembrance and perception of the sedation and procedure. He was observed for complications until discharge, which was possible if no clinical remnants of sedating drugs were noticeable and minimum one hour after awakening, and if accompanied by responsible person.

Selection for observational study

Patients who undergo procedural sedation according to protocol of ketofol in a 1 on 4 ratio, and who sign a separate informed consent for approval of registration of characteristics of sedation.

Registration of outcomes

Is done by the sedating physician during and after the sedation, until participant leaves the emergency department.

Results are registered in a segment of the electronic patient file which can be retrieved later by the investigator.

Outcomes

Primary Outcome Measures:

1. Respiratory complication or intervention
   - Complication: desaturation (< 92%), apnea (absent end-tidal CO2 for > 15s and no breathing movements), hypoventilation (respiratory frequency < 8 /minute), airway obstruction (absent end-tidal CO2 for > 15s and breathing movements), laryngospasm (partial or complete airway obstruction, not responding to airway repositioning or introduction of naso- or oropharyngeal cannula), aspiration due to vomiting
   - Intervention: airway repositioning (head tilt or chin lift), pain stimulus for breathing stimulation, introduction of naso- or oropharyngeal cannula, positive pressure ventilation, introduction of laryngeal mask or endotracheal tube
2. Hemodynamic complication or intervention
   - Complication: hypotension (systolic blood pressure less than 90mmHg, or drop of 10% of systolic blood pressure)
   - Intervention: fluid bolus given, use of inotropes

Secondary Outcome Measures:

1. Success of procedure
   - sedation adequate for performing procedure (yes/no)
2. Amnesia
   - amnesia of the procedure by the participant (yes/no)
3. Agitation or hallucination
   - Agitation during or after sedation (yes/no)
   - Hallucination during or after sedation (yes/no)
     - If hallucination: Pleasant / neutral / unpleasant
4. Duration of sedation
   - Time from start of sedation till completely awake, expressed in minutes
5. Satisfaction sedating physician
   - Satisfaction of the sedation with the current protocol, score on a five point scale (++ / + / + - / - / - -)

Other Pre-specified Outcome Measures:

1. American Society of Anesthesiologist physical status classification status participant
   - American Society of Anesthesiologist physical status classification status I, II, III of IV
2. Age of participant
   - Age of participant in years
3. Type of procedure
   - Reduction of luxation or fracture (shoulder, ankle/foot, hip, elbow, other … (possibility to fill in))
   - Abscess incision
   - Cardioversion
   - Chest drain placement
   - Other: … (possibility to fill in)

Statistical Analysis

Data will be reported by descriptive statistics (Microsoft Excel Versie 2013: Microsoft Corporation, Redmond, WA, USA). Categoric values will be reported as frequencies with 95% confidence interval. Ordinal data will be reported as median with interquartile range and total range. Continuous data will be reported as mean with 95% confidence interval and as median with interquartile range and total range.

No other statistical analysis will be made.

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