Safety of etomidate administration for procedural sedation in elderly emergency department patients

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Abstract:
The aim of this study was to assess the effectiveness, safety and frequency of adverse drug reactions of etomidate use as a procedural sedative agent in the Emergency Department (ED), for elderly patients (age >70 years).
We conducted an observational study of a series of 145 consecutive patients above 70 years who received etomidate for painful orthopedic procedures.
Deep sedation was induced in 65 patients, moderate sedation was observed in 80 patients. Full recovery was achieved on average after 25 min in patients treated with fentanyl and on average after 20 min in patients treated without fentanyl administration. Adverse cardio-respiratory events were documented in 7 patients (4.82%). Desaturation < 94% was noted in 6 patients, bag-valve-mask ventilation in 1 patient. There were no signs of circulatory depression. One patient experienced nausea, and we observed one episode of anxiety. Myoclonic tremors were observed in 32 patients (22%).
Etomidate is a relatively safe and sufficient pharmacotherapeutic agent for procedural sedation in elderly people with minor adverse reactions. Short recovery time, lack of hemodynamic instability at lower doses, low frequency of adverse drug reactions provide optimal and safe conditions for procedural sedation in ED for elderly people.

Key words:
etomidate, elderly, adverse drug reactions, emergency department

Introduction

The broad spectrum of patients with emergent and painful conditions are treated every year in the emergency departments (ED). Some of these patients undergo unpleasant therapeutic or diagnostic procedures like: cardioversion, incision and drainage of abscesses, closed reduction of fractures and dislocation. These procedures must be performed with adequate analgesia and sedation to minimize pain and anxiety in order to improve quality of care and patients’ satisfaction [2, 7]. Adequate analgesedation facilitates performing interventional procedures. On the other hand, medicines which are used for sedation, may cause depression of the cardio- and respiratory system [6, 20]. The ideal agent for sedation in the ED should have rapid onset of action, short time of action, with a minimum cardiorespiratory adverse effects [11, 17].
Etomidate is a nonbarbiturate hypnotic that induces sedation through GABA receptors in the central nervous system (CNS). The onset of action is approximately 60 s after intravenous injection and duration of action is 5 to 15 min. These features together with lack of hemodynamic alteration made etomidate an attractive option for procedural sedation in the ED [2, 15]. The safety profile for etomidate in procedural sedation in the ED was confirmed in many studies [4, 7, 9, 16, 10, 21, 24]. Unfortunately, these studies did not assess safety and effectiveness of etomidate in elderly patients.

The aim of this study was to assess the effectiveness, safety and frequency of adverse drug reactions of etomidate use as a procedural sedative agent in the ED, for elderly patients (age >70 years).

Materials and Methods

We conducted an observational study of a series of consecutive patients who received etomidate for painful orthopedic procedures. This study was conducted in teaching ED, with approximately 50 000 ED visits per year, in a large urban hospital between January 1, 2005 and December 31, 2006.

Inclusion criteria for our study were: age above 70 years, orthopedic procedures performed within the department and procedural sedation with etomidate. Exclusion criteria: American Society of Anaesthesiologists Physical Assessment Score (ASA) greater than 2, known hypersensitivity to etomidate, necessity of additional muscle relaxant medicine administration in order to perform the procedure, lack of informed consent for sedation. We did not use any other sedative agent for this age group during the period studied.

Standard anesthetic preparations for safe conduct of sedation were applied, according to international standards [7, 14, 19]. Standard management of pain on admission to ED was administration of ketoprofen (1 mg/kg of body weight iv infusion) and tramadol (1 mg/kg iv infusion). Sedation started with the induction dose of etomidate 0.1 mg/kg followed by boluses of 0.05 mg/kg when needed. According to individual patients’ needs additional fentanyl (1 µg/kg) bolus was administered in order to achieve complete pain control.

Adverse respiratory events were defined as: oxygen saturation less than 94%, with oxygen supplementation 5 l/min, airway obstruction requiring supportive maneuvers, bag-valve-mask-assisted ventilation, need for endotracheal intubation. Adverse circulatory events were defined as: bradycardia < 50 beats/minute, arrhythmias, systolic blood pressure (SBP) below 100 mmHg or decrease in DBP > 30 mmHg as compared to pre-procedural parameters. Other adverse events included in the study protocol were: seizure, incomplete recovery, altered mental status, occurrence of myoclonic tremors. All adverse events were recorded in patient’s data sheet for final analysis.

The statistical analysis of the results was performed by using nonparametric Fisher Exact Test, Mann-Whitney U Test and Spearman’s R Correlation Coefficient. For the analysis of the susceptibility to deep sedation and adverse drug reactions occurrence the odds ratio (OR) was calculated.

Results

During the study period, a procedural sedation with the use of etomidate was performed in 482 patients in all age groups. Out of this number 103 patients (21.36%) were aged 70–85 years, and 42 patients (8.71%) were above 85 years. Statistical analysis was done for these two groups.

Coexisting medical conditions in this group were: hypertension (58 patients – 40%), diabetes (8 patients – 5.51%), coronary artery disease (22 patients – 15.17%), congestive heart failure – NYHA II (9 patients – 6.20%), persistent atrial fibrillation (3 patients – 2.06%), alcoholism in 2 patients (1.37%). Etomidate was used for closed reduction of shoulder dislocation in 68 (46.89%) cases, closed reduction of hip dislocation in 10 (6.89%) cases, crural’s fractures and immobilization in 20 (44.44%) cases, antebrachial fractures and immobilization in 47 (32.41%) cases. All procedures lasted less than 10 min.

In 127 (87.58%) patients there was no need for additional doses of etomidate. Another dose was required in 18 (12.41%) cases. To improve pain control 57 patients (39.31%) received fentanyl (0.1 µg/kg) before procedure: 42 aged 70–85 years, and 15 above 85 years.
Etomidate induced deep sedation in 65 (44.82%) patients, moderate sedation was observed in 80 patients (55.17%). Deep sedation was observed in 25 patients who received additional dose of fentanyl, and 40 patients who did not (Tab. 1). There were no statistically significantly higher frequency of deep sedation among older patient (> 85 years) who did not receive additional dose of fentanyl or in both groups (with and without fentanyl administration) together. Only among patients who received the additional dose of fentanyl, deep sedation frequency was statistically significantly higher (p = 0.038) among older patients (odds ratio OR = 3.6, CI 1.07–12.03).

Adverse cardio-respiratory events were documented in 7 patients (4.82%). Decrease in saturation below 94% was noted in 6 patients, bag-valve-mask ventilation in 1 patient. None of those patients required endotracheal intubation, there was also no signs of circulatory depression. One patient experienced nausea, and in one episode of anxiety was observed (Tab. 3). Myoclonic tremors were observed in 32 patients (22%), 22 among patients between 70 and 85 years of age, and 10 > 85 years, but their duration was short and no cardio-respiratory emergency occurred. We did not perform a follow-up of the patients, thus the incidence of post myoclonic myalgia was not noted.

Summarized frequency of adverse drug reactions did not increase with age, only risk of myoclonic tremors was slightly higher in the older group (OR = 1.15, CI 0.5–2.66, NS), but without statistical significance (p > 0.1).

**Tab. 1.** Depth of sedation in correspondence to patients' age, cumulative doses of etomidate, and co-administration of fentanyl.

<table>
<thead>
<tr>
<th>Age</th>
<th>Number of patients</th>
<th>Depth of sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Single dose of etomidate</td>
</tr>
<tr>
<td>Without fentanyl</td>
<td>70–85</td>
<td>61</td>
</tr>
<tr>
<td>&gt; 85</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>With fentanyl</td>
<td>70–85</td>
<td>42</td>
</tr>
<tr>
<td>&gt; 85</td>
<td>15</td>
<td></td>
</tr>
</tbody>
</table>

Etomidate for sedation in elderly emergency department patients

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The initial dose of etomidate used in our study was a standard dose, recommended by guidelines [10, 21]. Only 18 patients needed a repeated dose. In the previous studies, authors reported that despite the fact that 0.1 mg/kg was recommended as an initial dose for procedural sedation the repeated dose was necessary for sufficient sedation [24]. Adequate pain control together with moderate sedation was sufficient to perform orthopedic procedures with patients’ satisfaction [2, 16, 24]. Our pain control protocol with ketoprofen or tramadol administered prior to specific management allowed for reduced doses of sedative agent. Adjunctive therapy with opioids is also advised [15, 24].

We noted no circulatory instability, even in patients older than 85 years. Desaturation occurred in 7 patients, and was managed non-invasively. A well-oxygenated patient desaturates only if apnea is prolonged, and all our patients received supplemental oxygen via oxygen mask during sedation. Use of fentanyl did not increase the risk of desaturation [5]. Kim’s study revealed that desaturation occurred specially in people receiving an adjunctive agent, like benzodiazepines [15]. Based on the analysis of the previous reports and his own study, Vinson recommended adequate oxygenation and lower doses of etomidate to prevent desaturation, especially in the elderly [24].

Etomidate has very little muscle relaxant features [15], but no sign of airway obstruction occurred in our study, and only one patient (> 85 year) required bag-valve-mask ventilation.

We did not observe vomiting. Only one patient experienced nausea, without further sequels. Since all orthopedic procedures had to be performed as soon as possible to avoid complications [7], the fasting time before sedation was in our patients shorter than 6 h. International guidelines indicate that recent food intake is not a contraindication for procedural sedation, but should be taken into account and no deep sedation is advised in those cases [7, 13, 19].

Myoclonus is a neurologic condition characterized by sudden, abrupt, brief, involuntary, jerk-like contractions of a muscle or muscle group. They are probably caused by drug-induced disinhibition of extrapyramidal activity and may be provoked by a stimulus, e.g. emergency procedure. The incidence is lower with oil-soluble etomidate solution and with titrated doses, presumably because depression of cortical activity caused by large doses precedes depression of subcortex. Transient myoclonic twitches occur frequently during the use of etomidate and according to some reports as often as in 20 to 45% of patients [23]. Benzodiazepines are the primary symptomatic treatment. No treatment is necessary, however, unless respiratory insufficiency occurs [21]. In our group 32 patients (22%) experienced myoclonic tremors. No specific

Tab. 3. Adverse drug reactions during procedural sedation with etomidate, corresponding to patients age

<table>
<thead>
<tr>
<th>Age</th>
<th>Desaturation (number of patients)</th>
<th>Bag-valve-mask ventilation (number of patients)</th>
<th>Nausea (number of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without fentanyl</td>
<td>70–85</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt; 85</td>
<td>1</td>
<td>1 (2 min of ventilation)</td>
</tr>
<tr>
<td>With fentanyl</td>
<td>70–85</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt; 85</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Discussion

Orthopedic manipulations are one of the most frequently performed painful procedures in the ED. The frequency of bone fractures and dislocations increase in elderly patients [3]. Safe and efficient manipulations are possible only under proper sedation [7]. Procedural sedation refers to a technique of administering sedatives or dissociative agents with or without analgesics to induce a state that allows the patient to tolerate unpleasant procedures while maintaining cardiorespiratory function [12, 14, 19].

Rapid onsets, short time of action, cardiorespiratory stability are those features of etomidate, which make it an attractive agent for the use in ED, especially for elderly patients. It was considered to be a safe rapid sequence intubation agent [1, 18, 22]. Further studies evaluated usefulness of etomidate for procedural sedation, compared to other sedative agents [8–10, 16, 21, 24]. Deep sedation was observed in 65 (44.82%) of our patients, what is definitely lower compared to results of other studies [15, 16, 21, 24]. Most of the adverse reactions of etomidate, which occurred in previous studies, referred to people above 70 years and sedation level was deeper, than in our group. However, we were able to successfully perform necessary orthopedic procedures in our patients. Higher frequency of deep sedation among older (> 85) patients in our study could be related rather with use of fentanyl than etomidate.

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management was necessary, since the episode did not compromise their cardio-respiratory functions.

**Conclusion**

According to our study, etomidate is a relatively safe and sufficient pharmacotherapeutic agent for procedural sedation in elderly people with minor adverse reactions. Short recovery time, lack of hemodynamic instability at lower doses, relative low frequency of adverse drug reactions during the use of etomidate, provides optimal and safe conditions for procedural sedation in ED for elderly people.

**References:**


**Received:**