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Original Article

Comparison of ketamine/propofol (ketofol) and etomidate/fentanyl (etofen) combinations for procedural sedation and analgesia in the emergency department: An observational study

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ABSTRACT

Objectives: The primary aim of this study was to report the vital signs, hemodynamic parameters and pain scores of the patients who have received procedural sedation and analgesia (PSA) with either ketofol (combination of ketamine and propofol) or etofen (combination of etomidate and fentanyl) and compare the proportion of patients with airway or respiratory adverse events (AEs) requiring an intervention and calculate the relative risk of AEs with each combination.
Methods: This study is a prospective observational study with survey analysis. All patients received procedural sedation and analgesia (PSA) with either ketofol (combination of ketamine and propofol) or etofen (combination of etomidate and fentanyl) were prospectively observed. Vital and hemodynamic parameters and pain scores of the patients were recorded by automated equipment and visual analog scale (VAS) charts.
Results: 112 patients were enrolled, 55 received ketofol and 57 received etofen. All patients with a respiratory AE (n = 27) observed to receive a respiratory intervention. Respiratory AE rate and proportion of patient who required a respiratory intervention were significantly higher with ketofol (p = 0.0029). Overall AE rate, and rates of desaturation, emergence reaction were also significantly higher in ketofol group.
Conclusion: Etofen is a promising combination for the PSA of adult patients with lower respiratory AE and intervention rates and with better hemodynamic profile.

1. Introduction

Procedural sedation and analgesia (PSA) is defined as the technique of administering sedatives or dissociative agents with or without analgesics to induce an altered state of consciousness that allows the patient to tolerate painful or unpleasant procedures while preserving cardiorespiratory function.[1] American College of Emergency Medicine (ACEP) recommends propofol (A), etomidate (B), ketofol (B), ketamine (C) and alfentanil (C) for the PSA of adults with given levels of recommendations.[1]

The use of short-acting sedative agents such as propofol and etomidate for emergency department (ED) PSA has been widely accepted since shorter periods of impaired levels of consciousness created by those agents and less risk for respiratory adverse events (AE).[1] Also, the combination of ketamine and propofol (ketofol) has been one of the most studied of combinations because of the theoretical synergy of those agents.[1] Fewer respiratory AEs with

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and higher provider satisfaction was reported by ketofol compared to propofol.[2–4]

Etomidate is a non-barbiturate, non-benzodiazepine, imidazole derivate providing rapid onset of action, short duration of sedation, clinically insignificant hemodynamic alterations with minimal respiratory and hemodynamic effects.[5–8] The biggest disadvantage of etomidate is the associated myoclonus which is extensively described in 20–40% of patients.[5,8–10] Since, etomidate does not have any analgesic property, it has to be combined with an analgesic agent like fentanyl. However, to our knowledge, etofen (combination of etomidate and fentanyl) and ketofol has not been compared in PSA to date.

The primary aim of this study was to observe and compare the number and proportion of patients with airway or respiratory AEs requiring an intervention, and calculate the relative risk of adverse events with ketofol compared to etofen. Secondary aims were to compare the incidence of overall and non-respiratory AE rates, maximum changes in hemodynamic parameters, number and proportion of patients who received additional drug dose, duration of sedation, level of sedation, patient pain and physician satisfaction scores.

2. Methods

2.1. Study design and setting

This study is a prospective observational study with survey analysis which has been performed at the EM Department of a Level 3 Adult Trauma and Burn Center with an annual patient load of 500.000 in Turkey. Study protocol was examined and approved in by the Hospital Ethics Board (12/06/2012; B104ISM4340029/1009/49).

2.2. Selection of participants

All the patients who have been decided to receive PSA for the treatment of their isolated upper extremity orthopedic injuries in the procedure room by emergency physicians (EPs) and orthopedic surgeons (OS) have been enrolled for observation if they had an American Society of Anesthesiologists (ASA) physical status of two or less. Patients were excluded if they were below 16 years of age, had a known hypersensitivity to the study agents, were pregnant, already treated with analgesics or oxygen, or indicated to have surgery.

2.3. Data collection

All demographic information (age, sex, weight, comorbid diseases) were gathered and recorded before the procedure. At the beginning of the PSA, baseline values of the following hemodynamic parameters, and pain and sedation scores of the patients were recorded by automated equipment, visual analog scale (VAS) charts and EPs: end-tidal CO_2 capnography ($ETCO_2$), systolic [SBP] and diastolic blood pressure [DBP], mean arterial pressure [MAP], heart rate [HR], respiratory rate [RR], peripheral oxygen saturation [pSO_2], Ramsay Sedation Score and VAS. All monitors have been set to automatically measure and record all hemodynamic parameters at every 5 min until the patients were recovered to the baseline alertness and sedation score, which were also recorded at the same time intervals. According to the departmental PSA protocol, patients with Ramsay score of 1–3 were re-evaluated for the need for an additional dose of treatment. Since the design was observational, EPs decided this need by themselves without a strict supervision.

All PSA procedures have been attended by an EP, an EM resident, and an EM nurse. Orthopedic procedures have been performed by OSs. The sole responsibility of the OS was the reduction and splinting. All other patient related medical interventions and evaluations have been performed and monitored by EPs. All the data and adverse events were recorded by the EM nurses and researchers.

Maximum recorded increase and decrease of each hemodynamic parameter during PSA have been obtained from the electronic records of the automated equipment. Pain intensity of each patient was evaluated by using a 10-cm long VAS chart before and after the PSA that had marks of 0 for no pain and 10 for worst possible pain. After the PSA was finished and patients were recovered to the baseline alertness and sedation score, OSs were asked to evaluate their satisfaction using a 10-cm long VAS chart which was marked by 0 for very unsatisfied and 10 for completely satisfied.

According to previous research, cardiopulmonary arrest, desaturation (defined as pSO_2 below 94%), myoclonus (rhythmic, shock-like muscle contractions), emergence reaction (unpleasant dreams or hallucinations when emerging from the dissociative state), vertigo (dizziness), nausea, cough and dysrhythmia (any rhythm other than patient's primary rhythm) were selected as AEs and the presence of those AEs were selectively sought and documented during the PSA.

2.4. Interventions

According to the written departmental protocol for PSAs, ketofol was given as 0.75 mg/kg IV bolus of ketamine and propofol, etofen was given as 0.15 mg/kg IV bolus of etomidate and 0.15 μg/kg fentanyl as the initial dose. Repeated doses of 0.375 mg/kg of ketamine and propofol were given in every 3 min and 0.1 mg/kg of etomidate was administered in every 2 min as needed to achieve and maintain adequate sedation. Patients in whom the above protocols were violated were excluded.

2.5. Outcome measures

Our primary outcome measure was the number and proportion of patients with airway or respiratory AEs requiring an intervention. Respiratory AEs were predefined as desaturation ($pSPO_2$<94%), apnea (cessation of respiration for more than 6 s on waveform capnography), respiratory depression (clinical evaluation), airway obstruction (complete absence of waveform) and aspiration (clinical evaluation). Respiratory interventions have been predefined and grouped as airway maneuvers (repositioning and airway opening maneuvers), maneuvers plus nasal oxygen administration (addition of supplemental oxygen), bag-mask-valve administration and any other airway intervention (intubation). Indications for each of those interventions have been clinically evaluated according to ACLS guidelines.

Secondary outcome measures were also predefined as any observed non-respiratory AE, the maximum recorded change in each hemodynamic parameter during the PSA, additional drug need, sedation duration (from the beginning of the first dose to the time full alertness has been gained), sedation levels, and patient pain and physician satisfaction scores.

2.6. Sample size estimation and power analysis

The sample size was estimated using the respiratory AE rates reported at previously published articles (22%–38%) for ketofol.[2,3,11] We estimated a sample size of 49 to find at least 20% difference between groups with an alpha value of 0.05 and power of 0.80. Therefore we enrolled 55 patients (49 + 10%) for each group.

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