

# **A Prospective Study To Evaluate The Drug Etomidate For Sedation To Facilitate Essential Procedures In The Pediatric Emergency Department**

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## **A. Background**

Pain and suffering are frequently encountered in the Emergency Department. In the recent past, the field of conscious sedation grew from the desire of physicians to safely and more efficiently treat this pain in carrying out essential emergency procedures such as the reduction of fractures and joint dislocations, complex laceration repair and foreign body removal. Interestingly, while the overall use of effective analgesia in the Emergency Department has grown tremendously, the pediatric population continues to receive less analgesia for painful procedures than the adult population (1). Much of this discrepancy arises from the myth that analgesia is unsafe and not necessary in children. However, it is clear that children do feel pain in a similar manner to adults and that sedation and analgesia can ameliorate this suffering. When used in a controlled setting by physicians trained in the procedure, sedation can provide a tremendous benefit for the patient and the patient's family with little risk of harm (2).

Many agents are currently available for the induction of sedation. However, the search for more efficacious agents with less undesired side effects has prompted continued investigation of newer sedatives and analgesics. In 1983, the drug etomidate was approved for use in the United States as a induction agent and for maintenance of sedation (3). Etomidate is currently used extensively by anesthesiologists, critical care specialists and emergency medicine physicians for the induction of sedation for endotracheal intubation (4). agent has also been used widely by anesthesiologists for sedation of both adult and pediatric patients for the performance of painful procedures. Multiple investigators have found the drug to be an excellent agent for induction of sedation with a documented safety record when used in a controlled environment by physicians skilled in sedation and airway management (5,6,7,8). Many guidelines have been formulated by professional societies to cover the sedation of children for painful procedures. This research protocol will adhere to the guidelines written by the American College of Emergency Physicians (ACEP) in 1995 on sedation of children in the emergency department (9). This document is the most applicable of all current guidelines to the realities of procedures in the emergency setting. The definition of sedation as outlined in this document is "A controlled lessening of the patient's awareness of the environment and/or pain perception while maintaining stable vital signs, an independent airway and adequate spontaneous respirations".

## **B. Purpose**

This study will investigate the efficacy of etomidate to achieve a state of sedation as defined above for the performance of essential painful emergency procedures in the monitored setting of the Pediatric Emergency Department by physicians skilled in sedation and airway management. The results of the study will allow a better understanding of the pharmacodynamics of etomidate and its potential for use in the Pediatric Emergency Department.

## **C. Study Design**

1. Prospective/ Convenience sample

## **D. Description of Study Subjects and Method of Recruitment**

**a. Inclusion Criteria:**

- All patients 2-18 years of age presenting to the Columbia- Presbyterian Medical Center (CPMC) Pediatric Emergency Department with a condition clinically necessitating sedation are eligible for the study. Conditions for which sedation is normally utilized include, but is not limited to, reduction of fractures and dislocated joints, complex laceration repair and lumbar puncture.
- Prospective patients will be examined by an Attending Emergency Physician. Only those patients meeting the criteria for the American Association of Anesthesiologists physical classification I and 2 will be eligible for the study 10. This restricts the study to normally healthy subjects and those with only mild systemic disease and no functional limitations (an example of the latter would be a child with diabetes mellitus currently under good control).
- The presence of a reliable adult who will be able to observe the patient for a time period of at least twelve hours after discharge from the emergency department.

**b. Exclusion Criteria:**

- Pregnancy
- History of difficulties with anesthesia or known allergies to opiates or etomidate
- Anatomical attributes predisposing to a potential difficult airway
- A time period less than three hours between the patient's last intake of solid foods and the sedation procedure. For intake of liquids, a time period less than two hours.
- A need for the patient to be outside the monitored setting of the emergency department for any time during the entire sedation procedure or postprocedure monitoring
- Pain medications taken within the previous six hours besides ibuprofen or acetaminophen
- Use of alcohol or illegal drugs within twenty four hours of the sedation procedure

**E. Patient Identification and Enrollment**

All pediatric patients who meet the above study criteria will be identified by physicians in the pediatric emergency department. An Attending Pediatric Emergency Medicine Physician assessor will examine the patient and decide on the need for an emergency procedure and the use of sedation and analgesia. If a sedation procedure is clinically indicated and the patient meets the study criteria, the patient and their caretakers will be approached for enrollment in the study. The informed consent form and the risks and benefits of the study will be fully explained to the patients and their guardians. Only after obtaining informed consent will entrance into the study proceed.

**F. Procedures****a. Initial Clinical Evaluation**

- a) The prospective patient will undergo a complete history and physical. The findings will be fully documented in the medical record and those patients deemed appropriate candidates will be selected.
- b) Mobilization of appropriate staff and resources will then be carried out. A Pediatric Emergency Physician skilled in sedation and airway management or Anesthesiology Attending will be present during the entire procedure. In addition to the Pediatrics or Anesthesiology Attending and the physicians performing the emergency procedure, a physician or nurse experienced in sedation will be present as an independent observer to continually monitor the patient's vital signs and to look for any potential difficulty with the case. The procedure will be carried out in the Pediatric Emergency Department where the highest level of monitoring is possible and equipment for airway control and cardiovascular resuscitation is immediately available.

- c) Secure intravenous access will be obtained.
- b. Sedation Procedure**
- a) In adhering to the guidelines of the ACEP document on sedation, the patients will be monitored closely during the sedation procedure. Supplemental oxygen will be given to each patient during the sedation and pulse oximetry will be continuous and recorded every five minutes. Heart rate, respiratory rate and blood pressure will be monitored every minute and recorded every five minutes. One full set of vital signs will be recorded immediately before the procedure and any abnormal value will be investigated and corrected before proceeding with the sedation.
  - b) Each patient will then receive pretreatment with fentanyl at a dosage of one microgram per kilogram given intravenously slowly over two minutes to attain optimal analgesia during the procedure.
  - c) One minute after the pretreatment dose of fentanyl, sedation with etomidate will commence. Etomidate will be given intravenously as a titratable drip at a dose of twenty micrograms per kilogram per minute with maximum dose of eight milligrams per minute. The drug will be terminated once an adequate level of sedation as determined by the attending physician supervising the procedure has been reached.
  - d) The emergency procedure for which the sedation has been employed will then be performed.
  - e) The patient will be monitored closely during the procedure and will be treated immediately to correct any abnormal vital signs.
- c. Post Procedure Monitoring**
- a) Each patient will be monitored closely in the sedation area until the individual has returned to an alert and oriented state with stable and acceptable vital signs.
  - b) Patients will then be monitored in the Emergency Department for a period of one hour. Upon discharge, it will be ensured that a reliable adult will observe each child for any post procedure complications for a period of twelve hours.
  - c) Patient's families will then be contacted by telephone within seventy two hours to assess their experience with the sedation procedure and to learn of any post procedure complications.

## **G. Data Analysis**

### **a. Assessing the efficacy of etomidate.**

This study will attempt to quantify the degree of sedation achieved by fentanyl and etomidate at the time of the performance of the emergency procedure using a behavioral scale system defined below. A baseline behavior score to be used for comparison will be taken prior to the sedation procedure at the time of IV insertion. The total dose of etomidate given to each patient will be recorded for each set of behavior scores. The following timeline illustrates these points:

- Need For Sedation
  - Medical Evaluation
    - Patient Selection
      - Informed Consent
      - Monitored Setting
- Vital Signs
- IV Placement (A)
- Etomidate / Fentanyl
- Sedated State

- Performance of Essential Emergency Room Procedure (B)
- Post Procedure Monitoring
  - A At the time of IV placement, the clinical response of the child will be graded on the following scale:
    - Cooperative
    - Responds to IV placement with a verbal or physical response such as crying that stops after completion of the procedure
    - Uncontrolled crying before, during and after IV placement
  - B At the time of the performance of the painful emergency procedure, the degree of sedation will be assessed by the following behavior score:
    - Drowsy / Asleep. Eyes closed, may respond to stimulation but accepts the procedure passively.
    - Relaxed. Lying with eyes open, readily accepts intervention.
    - Anxious. Verbally or nonverbally seeks support but accepts intervention reluctantly.
    - Upset. Tearful, may be clinging to parent, considerable effort required to achieve compliance with the intervention.
    - Agitated. General loud or high pitched cry, requires considerable physical restraint, strongly refuse intervention.

#### H. Assessing the effect of etomidate on physiological parameters:

Scores will be assigned to grade the effect of etomidate on vital signs using the following scale. Scores will be assigned every five minutes from the time of administration of sedation until full recovery. All scores are given as change from baseline vitals taken before sedation.

A Blood Pressure	2 Less than 20 min change
	1 20- 40 min change
	0 Greater than 40 min change
B Heart Rate	2 Less than 20 beats/min change
	1 20-40 beats / min change
	0 Greater than 40 beats / min change
C Respiratory Rate	2 Less than 5 breaths / min change
	1 5-10 breaths / min change
	0 Greater than 10 breaths / min change
D Pulse	2 96-100 % oxygenation
Oxygenation	1 92-96 % oxygenation
	0 Less than 92 % oxygenation
E Airway	1 Able to maintain airway without assistance
	0 Requires assistance to maintain airway

#### a. Assessing the incidence of side effects of etomidate

The incidence of the known side effects of myoclonus (muscle shaking) and nausea /vomiting will be graded using the following scores. Scores indicate the presence of these effects at any time during the sedation and recovery period.

A Myoclonus	2 Absent
	1 Present, but does not interfere with the procedure
	0 Present and interferes with the procedure
B Nausea	2 Absent
Vomiting	1 Mild nausea, one or less episode of vomiting
	0 Greater than two episodes of vomiting

#### b. Assessing the perception of the sedation by the patient and their family

Patients and their lies will be asked to grade their perception of the efficacy of the sedation in ameliorating pain and anxiety. These perceptions will be elicited at the time of full recovery and just before discharge from the emergency department.

Perception	3 Excellent
	2 Good
	1 Fair
	0 Unacceptable

### **I. Study Duration**

The study will continue until data have been collected from thirty sedation procedures. Each patient's participation will end with the telephone follow-up interview.

### **J. Study Drugs**

Two drugs will be used in this study. Fentanyl will be used to a analgesia and etomidate will be used to provide sedation.

#### **a. Fentanyl**

Fentanyl is an opiate analgesic commonly used in the CPMC Pediatric Emergency Department. Fentanyl has the advantage over other currently used analgesics in providing potent pain relief with a short duration of effect quantified as 20-30 minutes making it an excellent choice for short procedures (11,12). In this protocol, the drug will be used as pretreatment to etomidate in a dosage of one microgram per kilogram given intravenously slowly over two minutes. This dosage is small compared to the commonly used dosages of three to five micrograms per kilogram. This lower dosage should provide adequate analgesia for each patient while minimizing the incidence of side effects (13). Fentanyl has also been proven to decrease the incidence of myoclonus observed with use of etomidate (14,15). Adverse side effects of fentanyl are primarily related to rapid infusion of the drug or the use of high dosages ( greater than five micrograms per kilogram) (16). These side effects include low blood pressure and respiratory difficulties.

#### **b. Etomidate**

Etomidate is a carboxylated imidiazole chemical with powerful sedation properties licensed in 1982 by the FDA for use as a sedative (3). The duration of action after a single dose of etomidate is short with return of consciousness in 5-14 minutes reflecting the rapid redistribution of the drug to inactive tissues (4). These pharmacokinetic features of the drug make it attractive for use in Emergency Department sedation procedures that most often demand only a short period of drug effect. The drug has a cardiovascular supportive effect that avoids the hypotension commonly seen with other sedative agents (3,4,5,17). Furthermore, etomidate has only a low rate of respiratory complications. A recent study at Memorial Sloan Kettering that used etomidate to sedate 101 children for painful procedures found the risk of respiratory events to be less than 2% (5). The majority of these complications involved only a minimal fall in blood oxygenation that was quickly reversed by the administration of supplemental oxygen with very few patients requiring assisted ventilation by bag valve mask. No adverse outcomes were observed as the result of these respiratory events. In the Memorial study, etomidate was given as a single dose bolus injection at the start of the sedation procedure. As an added safety feature, this study would employ the drug as a titratable intravenous infusion that can be quickly adjusted to the clinical status of the patient in providing an optimal level oiseda'tion. When compared to etomidate, sedation drugs currently used in the CPMC Pediatric Emergency Department such as versed and large doses of fentanyl have as great a risk of respiratory depression and a greater risk of causing low blood pressure (5 6 8,17,18,19,20). Other side affects of etomidate include myoclonus, nausea and vomiting.

### **K. Risks and Benefits**

1. Respiratory insufficiency and resulting low levels of blood oxygen are the most serious risks with the use of etomidate. These events will be by the use of supplemental oxygen on every patient, the employment of a titratable infusion of the drug that can be quickly turned off and by the extremely close monitoring of the patient by an attending physician skilled in airway management with respiratory assistance devices at the bedside. As discussed above, previous studies have found the drug to have a very low risk of adverse effects and a safety profile equivalent or better than the sedative drugs currently used in the CPMC Pediatric Emergency Department.
2. The benefit to the patients enrolled in the procedure is the improved control of pain and suffering caused by essential emergency procedures in the emergency department. The benefit to caretakers will be the decreased stress of seeing their children endure pain and suffering during the procedures.

#### **L. Confidentiality of Study Data**

All study data will be coded without personal identifiers and stored in computer files and printouts accessible only to the investigators.

#### **M. Location of Study**

The study will be performed only in the CPMC Pediatric Emergency Department. No enrolled patient will leave this monitored setting at any time during the study until full return of consciousness and acceptable vital signs have returned.

#### **N. Compensation and Costs for Subjects**

Patients who would be included in this study will be a selected population of individuals for whom sedation with the standard agents now employed in the CPMC Pediatric Emergency Department would be utilized. The additional cost of etomidate on top of the standard charge for a sedation procedure would be negligible.

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