

Pediatric Use of Etomidate at UC Davis for Intubation (PEDI)

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Disclosure

- Presenters: Lara Barsoumian, Ailin Kim, Maki Usui, Victoria Yi
- No conflicts of interest

Learning Objectives

- To understand the pharmacology of etomidate
- To compare the use of etomidate and fentanyl/midazolam for pediatric intubation
- To evaluate various clinical markers used to measure adrenal suppression
- To highlight the challenges of detecting adrenal suppression in pediatric patients undergoing rapid sequence intubation (RSI)

BACKGROUND

Background - Comparison of RSI Medications

- At UCDMC, **etomidate** is the preferred agent in the ED, while **fentanyl and midazolam** are the preferred agents in the pediatric intensive care unit (PICU) for intubation.

	Etomidate	Fentanyl/Midazolam
PK/PD	Onset: 5-15 sec Duration: 5-15 min $t_{1/2} = 2.6-3.5$ h	Onset: Immediate / 3-5 min Duration: 0.5-1 h / <2 h $t_{1/2} = 2.4-21$ h (age-dependent) / 2.9-4.5 h
Concerns	Adrenal suppression associated with prolonged infusions of etomidate	<ul style="list-style-type: none">- Can cause hypotension and respiratory depression- Midazolam can cause hemodynamic instability at doses required for sedation- Fentanyl can cause chest wall rigidity

Current Literature

- Conflicting data in regards to **onset** of adrenal suppression and its **clinical significance**
 - As early as 1 hour and as late as 72 hours after single-dose etomidate
- **Challenge to define adrenal suppression** given the complexity of critically ill patients requiring intubation
- To date, studies have **defined adrenal suppression as:**
 - administration of corticosteroids post-administration of single-dose etomidate
 - or a significant decrease in cortisol or blood pressure individually
- Studies mainly in adult population, **limited in pediatric** population

METHODOLOGY

Study Design

- Retrospective cohort study
- 120 pediatric patients who received etomidate or fentanyl/midazolam for RSI at UCDMC
- January 1, 2015 to September 1, 2019

Inclusion	Exclusion
<ul style="list-style-type: none">■ Age > gestational age of 1 month and \leq 18 years old■ Received rocuronium or succinylcholine■ Received etomidate or fentanyl/midazolam for intubation	<ul style="list-style-type: none">■ PMH: TBI, stroke, diabetes, CKD, seizures, or status epilepticus■ Med Hx:<ul style="list-style-type: none">– Received steroids within 30 days of intubation– Taking anti-hypertensives or any medications that can affect adrenal axis■ Documented allergy to etomidate, fentanyl, or midazolam

Statistical Analysis

- Wilcoxon rank sum test was used to identify any statistically significant differences in baseline characteristics between the two groups.
- Fisher's exact test was used to test for a significant difference in the prevalence of clinically significant decrease in SBP and hypotension. P-value < 0.05 was considered significant.

Outcome Measures

- To evaluate the difference between etomidate vs. the combination of fentanyl and midazolam in the development of **clinically significant hypotension or decrease in SBP, a clinical marker for adrenal suppression, within 48 hours** immediately post-intubation in the pediatric population

Definitions	
Clinically significant decrease in SBP	2 consecutive SBPs that decreased by at least 20% from baseline (SBP prior to intubation)
Clinically significant hypotension	2 consecutive SBPs that were below the 5th percentile, according to the PALS definition of hypotension ⁵

- Additional clinical markers: sodium, potassium, glucose, creatinine, steroid use, vasopressor use, cortisol

RESULTS

Baseline Characteristics

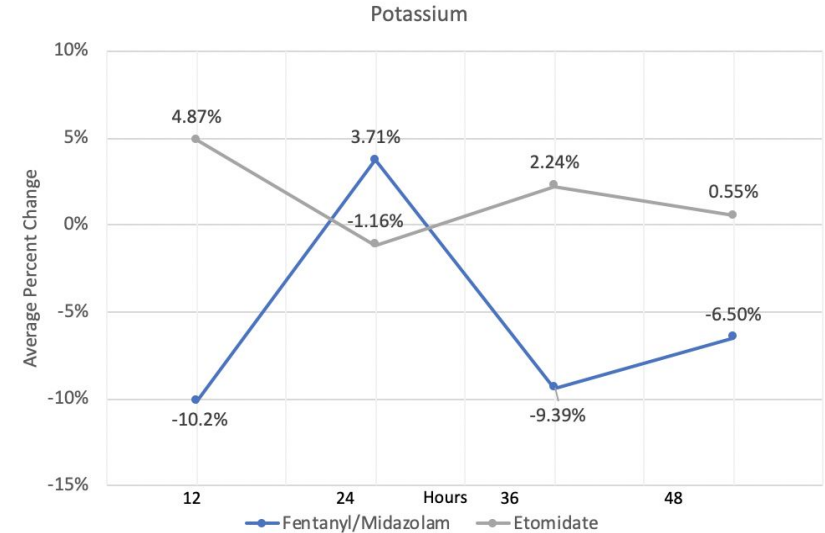
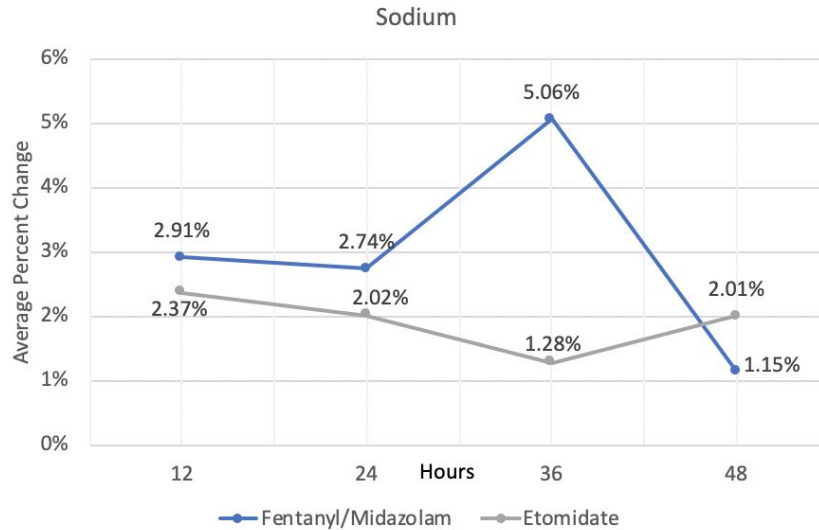
Characteristic	Etomidate (N = 52)	Fentanyl/Midazolam (N = 29)
Age (years) - median (IQR)	3.13 (1.59-14.9)	0.91 (0.35-5.59)
Sex - no. (%)		
Female	21 (40.4)	13 (44.8)
Male	31 (59.6)	16 (55.2)
PIM2 Score - mean \pm SD	14.8 \pm 21.3	12.4 \pm 19.9
Chief Complaint of Admission - no. (%)		
Bronchiolitis	2 (3.85)	8 (27.6)
Cardiac arrest	0 (0)	2 (6.90)
Pneumonia	3 (5.77)	2 (6.90)
Seizure	7 (13.5)	0 (0)
Sepsis	2 (3.85)	0 (0)
Substance Ingestion	8 (15.4)	0 (0)
Trauma	23 (44.2)	1 (3.45)
Other	7 (13.5)	16 (55.2)
Hypotensive at Baseline - no. (%)	2 (3.85)	2 (6.90)
Death during Admission - no. (%)	2 (3.85)	7 (24.1)

Primary Outcome

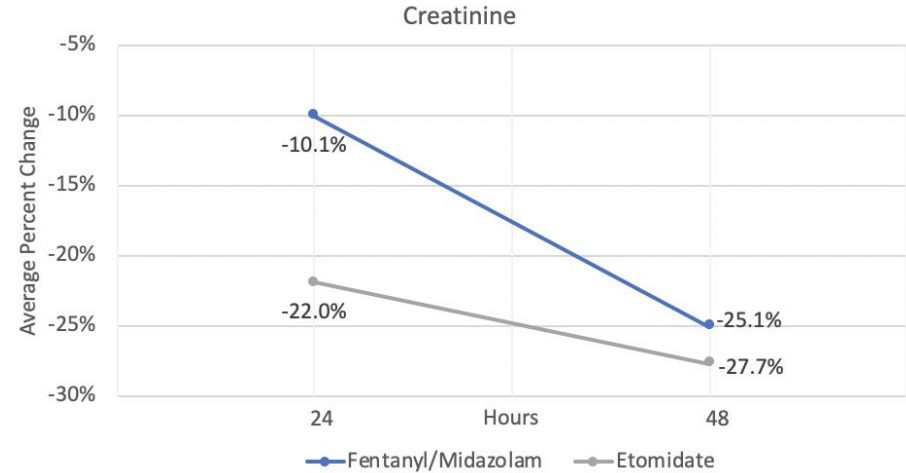
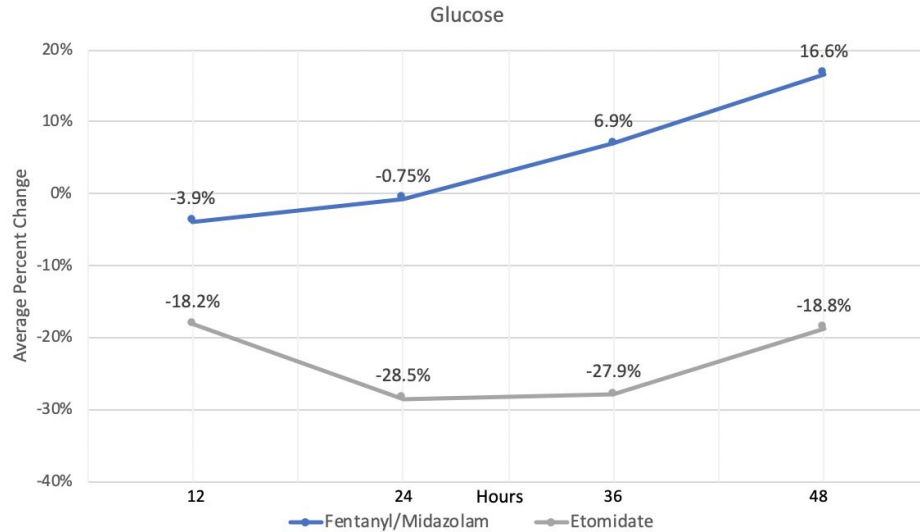
- SBP measurements every 4 hours within a 48-hour period after intubation were recorded for 80 pediatric patients.

Prevalence	Etomidate (N = 51)	Fentanyl/Midazolam (N = 29)	p-value
Clinically significant hypotension - <i>no. (%)</i>	3 (5.88)	6 (20.7)	0.0653
Clinically significant decrease in SBP - <i>no. (%)</i>	19 (37.3)	12 (41.4)	0.8125

Exploratory Findings



Exploratory Findings



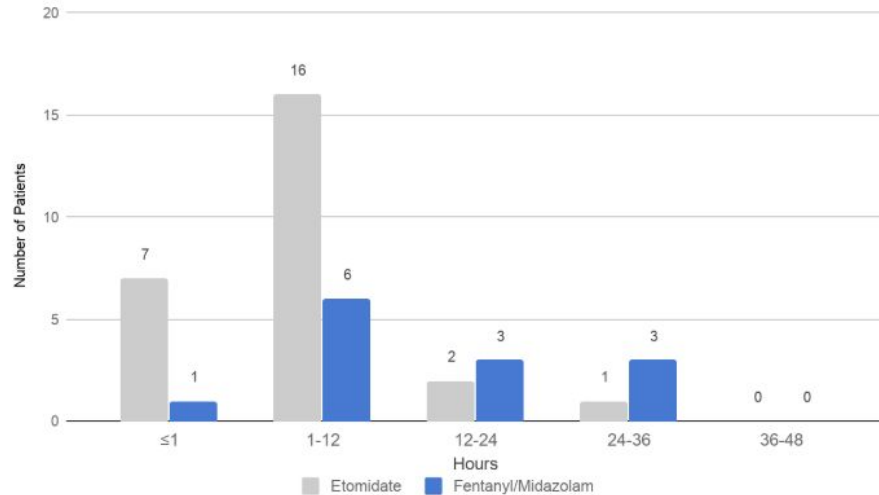
Exploratory Findings

	Etomidate (N = 52)	Fentanyl/Midazolam (N = 29)
Steroid Use - no. (%)	11 (21.2)	9 (31.0)
Vasopressor Use - no. (%)	5 (9.62)	4 (13.8)

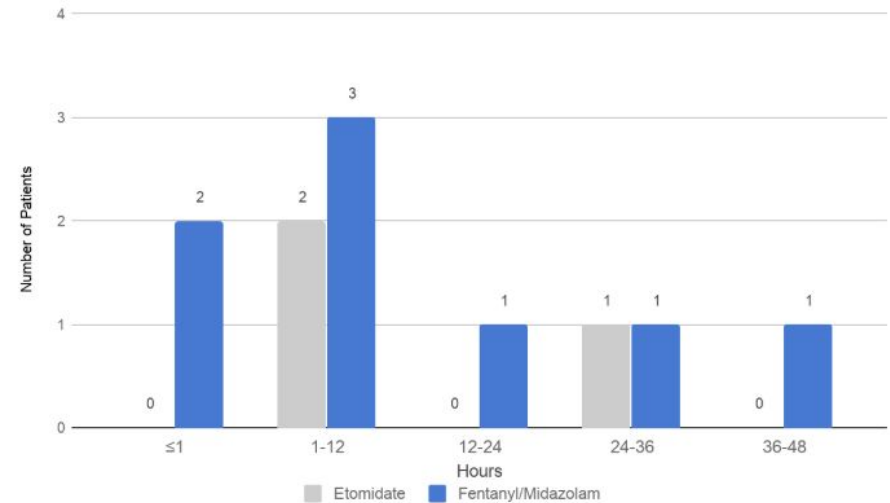
	Etomidate (N = 52)	Fentanyl/Midazolam (N = 29)
Cortisol Labs - no. (%)	4 (7.69)	3 (10.3)
Cortisol level (mcg/dL) - <i>median (IQR)</i>	6.55 (3.5-229)	9.4 (8-28.9)
Time (hrs) from intubation to cortisol lab draw - <i>median (IQR)</i>	11.3 (3.75-23.3)	69.0 (35.5-71.0)

Exploratory Findings

Time to Clinically Significant Decrease in SBP



Time to Clinically Significant Hypotension



DISCUSSION

Key Findings

- **No statistically significant difference** in the prevalence of clinically significant decrease in SBP or hypotension between fentanyl/midazolam and single-dose etomidate for intubation.
 - However, there was a large difference in the rate of hypotension between the two groups.
- Exploratory findings show **conflicting evidence** on the association of etomidate with adrenal suppression

MAY NOT be associated

- Average change in **Na** did NOT decrease from baseline
- Average change in **creatinine** did NOT increase from baseline
- **Less prevalence of vasopressor and steroid use** in the etomidate group compared to fentanyl/midazolam
- Median **cortisol level was within normal limits** in both groups

MAY be associated

- Average change in **glucose** ↓ from baseline
- Overall average change in **K** ↑ from baseline

Implications

- Complexity of these dynamic, critically ill patients requiring intubation proved to be a challenge
- Evaluating adrenal suppression using multiple clinical markers in addition to hypotension

Limitations

- Study did **NOT achieve power** due to **small sample size**.
 - There is insufficient evidence to reject the null hypothesis.
 - Higher statistical power is needed to further evaluate if single-dose etomidate is truly not associated with adrenal suppression.
- However, despite the non-significant p-value, the large effect size suggests further research is needed to determine if fentanyl/midazolam is associated with hypotension.
- Evaluation of the exploratory findings would benefit from being evaluated through a **prospective** rather than a retrospective study.

Recommendation

- **The outcome of our study neither confirms nor denies the association of etomidate with hypotension, which we used as a marker for adrenal suppression.**
- There is a need to further investigate adverse events associated with etomidate to establish its safe use for intubation in pediatric patients.

References

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Questions?