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Emergency Medicine Pharmacotherapy with Resuscitation (EMPoweRx) Conference

Pediatric Trauma Pearls

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Disclosures

No one involved in the development of the educational content has a relevant financial relationship to disclose.

Objectives

Outline

- Outline practice essentials for pediatric trauma response

Interpret

- Interpret pediatric-focused literature on the use of ketamine during rapid sequence intubation, specifically on its impact on intracranial pressure management in children with traumatic brain injuries

Compare and contrast

- Compare and contrast the efficacy of hypertonic saline versus mannitol in managing elevated intracranial pressure in pediatric trauma patients

Pediatric Trauma Statistics

- According to the American Academic of Pediatrics, fatal traumatic injuries have dramatically increased (overall fatality rate increased by 250% (P=0.0012) over the last decade
  - Dramatic increase in firearm injuries and poisoning injuries have driven this trend
    - Firearms: fatalities increased by 87.1% since 2011
    - Drug poisonings: fatalities increased by 133.3% since 2011
  - Top mechanisms of injury:
    - Firearm
    - Drowning
    - Suffocation
    - Drug poisoning
    - Machinery

Essentials for Pediatric Trauma Response

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Initial Management of Pediatric Patient

1. ATLS Primary/Secondary Survey: Airway, Breathing, Circulation
2. Mechanism of injury
    1. Blunt abdominal and thoracic trauma
    2. Traumatic brain injury
    3. Extremity and pelvic fractures
    4. Facial and eye injuries
    5. Dental injuries
    6. Penetrating injuries
    7. Spinal cord injuries
    8. Non-accidental trauma
3. Vital signs per age-based normal values:
    1. HR, BP, RR

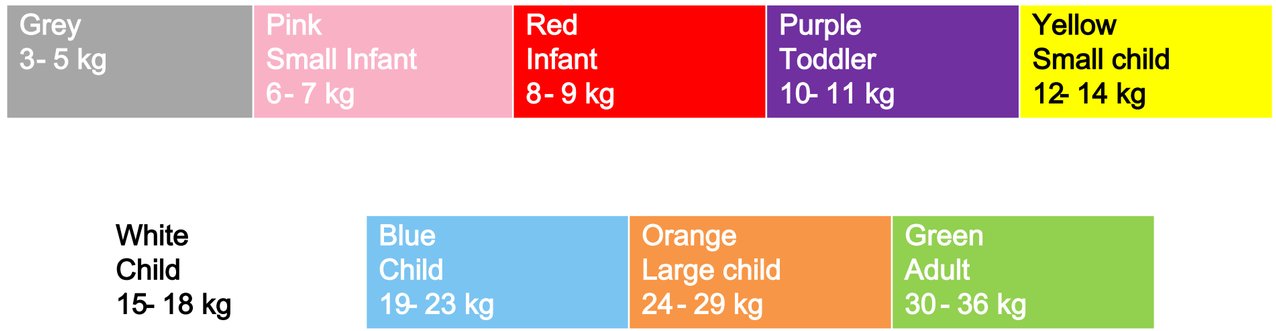
Normal Pediatric Vital Signs

Age Group	Heart Rate		Blood Pressure	Respiratory Rate
	Awake	Sleep		
Neonate	100-205	90-160	67-84	30-53
Infant (1-12 mo)	100-180	90-160	72-104	
Toddler (1-2 yo)	98-140	80-120	86-106	22-37
Preschooler (3-5 yo)	80-120	65-100	89-112	20-28
School age (6-9 yo)	75-118	58-90	97-115	18-25
Preadolescent (10-12 yr)	60-100	50-90	61-80	12-20
Adolescent (12-15 yr)			110-131	

PALS Pocket Reference Guide

Weight-based Dosing

- Simplify management of these patients by rounding to nearest reasonable weight
  - Remember: patient weight in these situations are likely estimated
  - Bed weights can lead to large errors in patient dosing in pediatrics
- Example of rounding scheme:
  - <10 kg: Round up to nearest 0.5 kg
  - 10-49 kg: Round up to nearest 1 kg
  - >50 kg: Utilize adult dosing
- Numerous resources to assist with development of pediatric dosing references
  - Broselow tape
  - Handtevy, SafeDose
  - EHR-generated patient specific code sheets
  - Excel-based code sheet generation



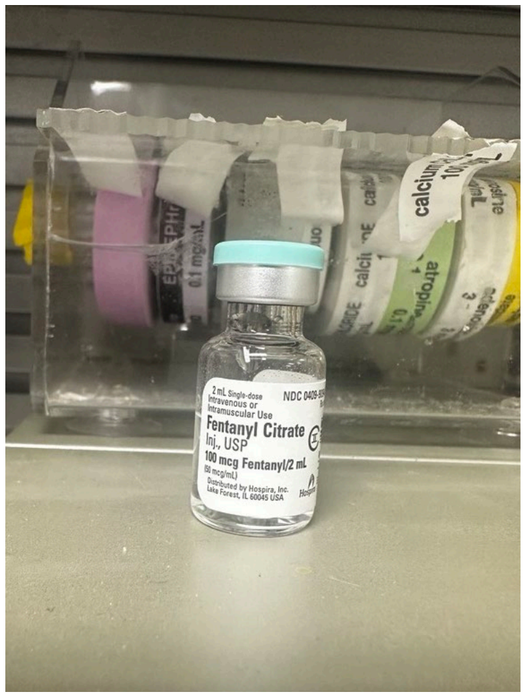
PALS Pocket Reference Guide

Initial Fluid Resuscitation

- Normal initial fluid volume: 20 mL/kg (max: 1,000 mL) of warmed normal saline or Lactated Ringer's
  - Can be repeated up to 60 mL/kg
- Transfusion of PRBCs should be considered if:
  - Hemodynamically unstable despite 20 mL/kg bolus of crystalloid
  - Hgb <7 if hemodynamically stable with ongoing concern for bleeding
  - Hgb 5-7 if no longer clinical concern for ongoing bleeding

Depending on facility, could meet criteria for activation of Massive Transfusion Protocol (MTP)

Volumes Too Small To Measure?



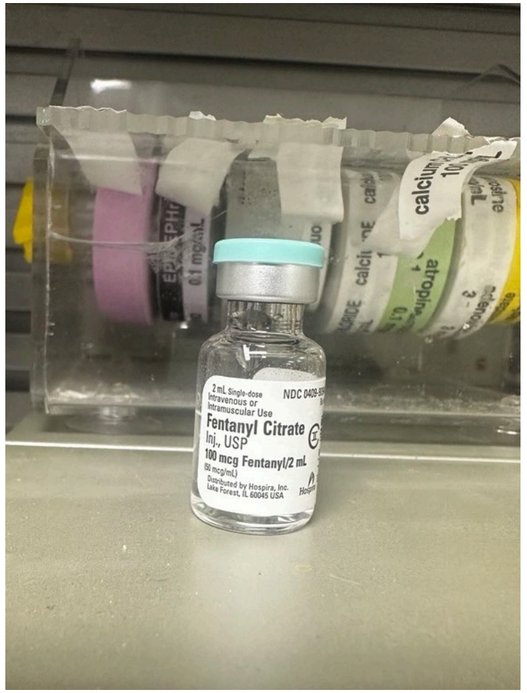
Example: A 6 day old female patient (3.5 kg) presented unresponsive to the ED and provider is requesting fentanyl as one of the sedation agents for intubation

Fentanyl 2 mcg/kg x 3.5 kg = 7 mcg

Fentanyl vial is 50 mcg/mL→ Volume needed is 0.14 mL

- Per ISO 7886-1, the minimum accurate measurement for a 1 mL syringe is 20% of its nominal volume: 0.2 mL
- **This volume is too small to accurately measure with a 1 mL syringe**

Volumes Too Small To Measure?



How can we dilute to make a measurable concentration and volume for this patient?

<u>Create a Fentanyl 10 mcg/mL syringe:</u>

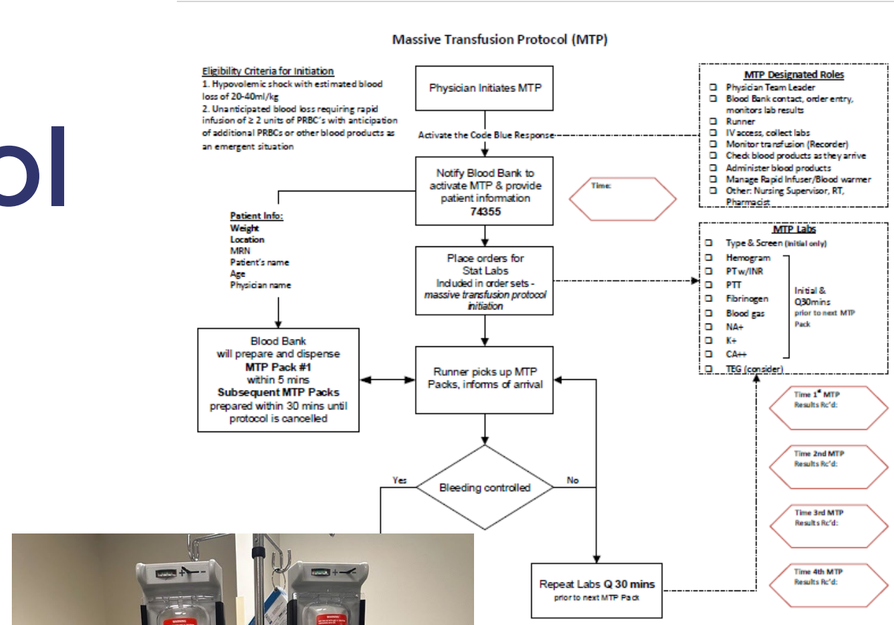
Use entire 2 mL vial (100 mcg) and dilute with 8 mL NS to a total volume of 10 mL

Using a syringe to syringe connector, you can draw up the patient specific dose from the stock syringe you created → 0.7 mL of 10 mcg/mL fentanyl solution = 7 mcg fentanyl

Some pediatric facilities utilize premade Fentanyl 10 mcg/mL syringes for RSI kits

Massive Transfusion Protocol

- Facility dependent on protocol
- MTP workflow helps coordinate as many resources as possible to manage emergency
- Pharmacy considerations:
  - Calcium chloride 10-20 mg/kg (max 1,000 mg) or Calcium gluconate 100 mg/kg (max 2,000 mg) over 5 minutes
  - Tranexamic Acid
    - Patients <40 kg: 25 mg/kg over 10 minutes, followed by 3 mg/kg/hr for 8 hours
    - Patients ≥40 kg: 1,000 mg over 10 minutes, followed by 1,000 mg over 8 hours
  - Cryoprecipitate
  - Factor VII 90 mcg/kg IV over 2-5 minutes



Physician Team Leader – Considerations

- ☐ Calcium Chloride is 10-20 mg/kg (max 1 gram) *or* Calcium gluconate 100 mg/kg (max 2 gram) IV over 5 min
- ☐ Tranexamic acid (TXA)
  - Consider MTP Pack #1
  - Consider in post-operative patients and trauma < 3 hours from injury
  - Patient < 40 kg (25 mg/kg over 10 minutes followed by: 3 mg/kg/hr. x 8 hours)
  - Patient ≥ 40 kg (1 gram over 10 minutes followed by: 1 gram over 8 hours)
- ☐ Cryoprecipitate (MTP Pack#3)
- ☐ TEG Hemostasis Profile
- ☐ Factor VII (MTP Pack#4) 90 mcg/kg IV over 2-5 min (Contact Pharmacy)

Monitor for potential complications

- Dilutional thrombocytopenia
- Coagulation factor depletion
- Hypocalcaemia
- Hyperkalemia
- Acid/Base disturbance
- Acute respiratory distress syndrome
- Transfusion reaction

Assessment Question

What trend has driven the increase in fatal traumatic injuries in pediatric patients?

A. Increased road traffic accidents
B. Increased firearm and poisoning injuries
C. Increased sports-related injuries
D. Increased high level falls

Assessment Question

What trend has driven the increase in fatal traumatic injuries in pediatric patients?

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Pediatric Airway Management

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Intubation Preparation

- Premedication selections are largely provider preference as no clear evidence exists
- Benefit of individual pre-medication should outweigh the risk of complicating RSI procedure
- Key step to pre-intubation procedure: Management of hypoxia and hypotension
  - Hypoxia is large predictor of imminent cardiac arrest in pediatric patients

Lidocaine

- 1 to 1.5 mg/kg IV
- Suspected to blunt rise in ICP during direct laryngoscopy by inhibiting cough reflex
- Can cause significant hypotension after administration

Atropine

- 0.02 mg/kg IV (maximum 1 mg)
- Consider use in infants <1 year of age, patients with septic shock, and patients receiving succinylcholine for paralysis

Huh JW, et al.

Sedation

Drug	Use/MOA	Dosing	Onset	Half-Life	Pearls
Etomidate	Imidazole-derived sedative hypnotic Stimulates GABA receptors	0.3 mg/kg IV	15-45 sec	3-12 min	Ultrafast acting and quickly reduces cerebral metabolism No histamine release Minimal cardiovascular effects Myoclonus can occur
Ketamine	Non-competitive inhibitor (glutamate antagonist) of NMDA receptors in thalamocortical and limbic CNS Stimulates pulmonary beta-receptors	1-2 mg/kg IV 4-10 mg/kg IM	30 sec	5-15 min	Does provide analgesia Intense amnesia, cataleptic-like state Oral secretions Anticonvulsant activity Biphasic CV impact: negative inotropy preceding sympathomimetic activity
Midazolam	Fast acting BZD Agonist of GABAa	0.2-0.3 mg/kg IV or IM	60-90 sec (if administered with opioids) Up to 5 min alone	1-4 hours	Avoid in hemodynamic instability, HF, liver disease
Propofol	GABAa agonist Glycine agonist Nicotinic agonist M1 agonist	1.5 mg/kg IV	15-45 sec	5-10 min	Decreases ICP Mild bronchodilation NO analgesia Caution in HoTN

Stollings, et al; Vuyl J, et al

Paralytic Agents

Drug	Use/MOA	Dosing	Onset	Half-Life	Pearls
Rocuronium	Non-depolarizing NMB	0.6-1.2 mg/kg IV	1-2 minutes	30-67 minutes	Can reverse rocuronium utilizing sugammadex
Succinylcholine	Depolarizing NMB Binds to Ach receptors on motor end plate Depolarization= continuous stimulation	1-2 mg/kg IV (2 mg/kg in infants and children <2 years) 3-4 mg/kg IM (onset is delayed)	1-1.5 minutes	2-6 minutes	Can cause histamine release Muscle fasciculation Malignant hyperthermia (rapid release of Ca2+) Rhabdomyolysis Hyperkalemia (0.5-1 mEq/L increase)

Stollings, et al.

Succinylcholine in Pediatrics

- Succinylcholine administration has been associated with bradycardia and asystole when administered to children <5 years of age
- Succinylcholine has led to acute rhabdomyolysis, cardiac arrest, and death in otherwise healthy appearing pediatric patients due to undiagnosed skeletal muscle myopathy

Succinylcholine Contraindications				
Personal or familial history of malignant hyperthermia	Skeletal muscle myopathies	Known hypersensitivity to succinylcholine	Acute phase of major burns, multiple trauma, extensive denervation of skeletal muscle, or upper motor neuron injury	Severe hyperkalemia

Bisesi SA, et al.

Ketamine in Elevated ICP

Ketamine and ICP

CPP = MAP - ICP

- Originally suspected to cause uncontrollable ICP in patients
  - Found in early studies from the 1970s
  - Patients did not receive controlled ventilation
    - Hypoventilation leads to increased ICP due to increased cerebral blood volume
- Mechanism
  - Large vessel dilation from elevation in PCO_2 in non-ventilated patients
  - Small vessel constriction from nitric oxide synthase inhibition
- Multiple adult studies have shown that this effect does not have clinical impact
- Very few pediatric studies available

Zeiler, et al; Laws, et al; Morgan, et al

Effectiveness of ketamine in decreasing intracranial pressure in children with intracranial hypertension

Bar-Joseph G, Guilburd Y, Tamir A, Guilburd JN. Effectiveness of ketamine in decreasing intracranial pressure in children with intracranial hypertension. *J Neurosurg Pediatrics*. 2009;4:40-46.

Population	• 30 patients included aged 1-16 years • Included patients were patients with intracranial hypertension (ICP >18 mmHg) who did not respond to first-tier and second-tier measures
Study Design	• Group 1: Ketamine administered to prevent further ICP increase during distressing intervention (respiratory physiotherapy, endotracheal suctioning, bed linen or diaper change, and positional change) • Group 2: Ketamine administered as an additional measure to lower markedly elevated ICP

Effectiveness of ketamine in decreasing intracranial pressure in children with intracranial hypertension

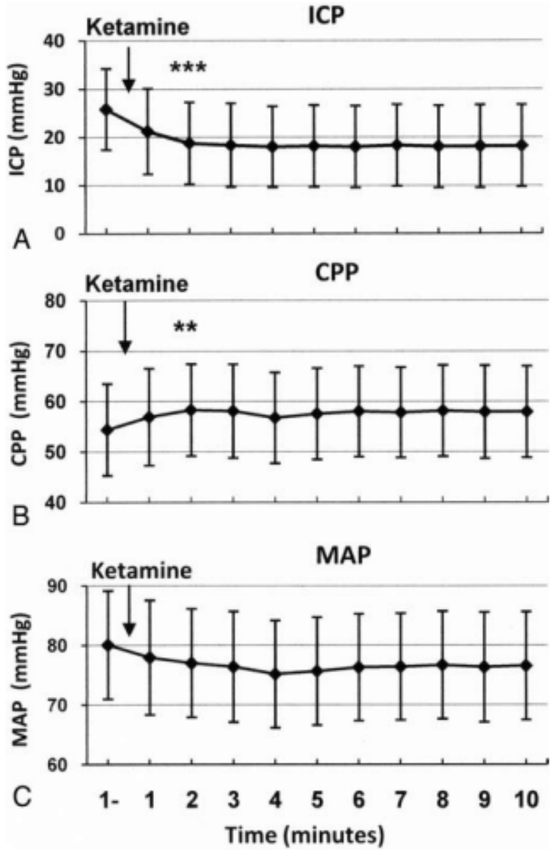

FIG. 1. Graphs showing ICP (A), CPP (B), and MABP (C; MAP) responses to ketamine administration in the entire study population (30 patients, 82 events). Intracranial pressure decreased by 30% within 2 minutes of ketamine administration. **p < 0.005, ***p < 0.001.

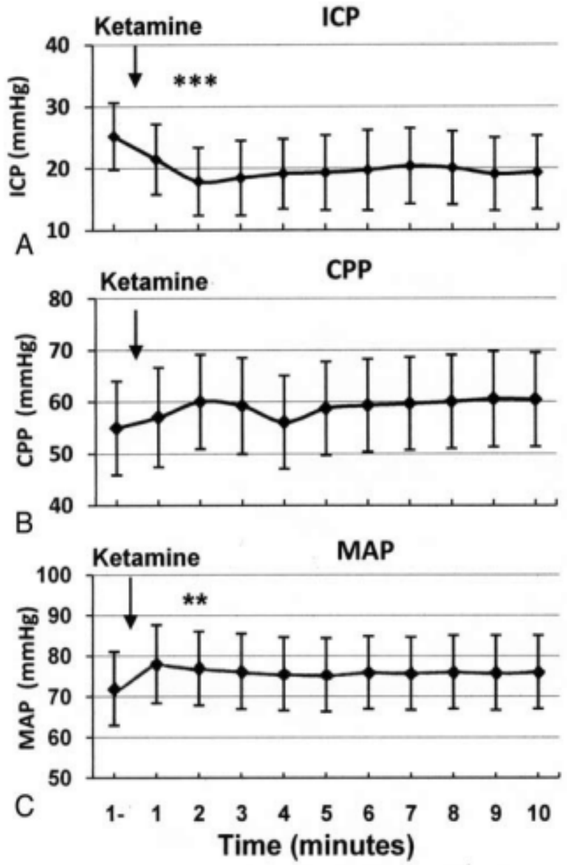

FIG. 2. Graphs demonstrating ICP (A), CPP (B), and MABP (C) responses to ketamine administration before a potentially distressing intervention in patients with intracranial hypertension (17 events, Group 1). Intracranial pressure decreased by ~ 20% within 2 minutes of ketamine administration and did not increase during the intervention. **p < 0.005, ***p < 0.001.

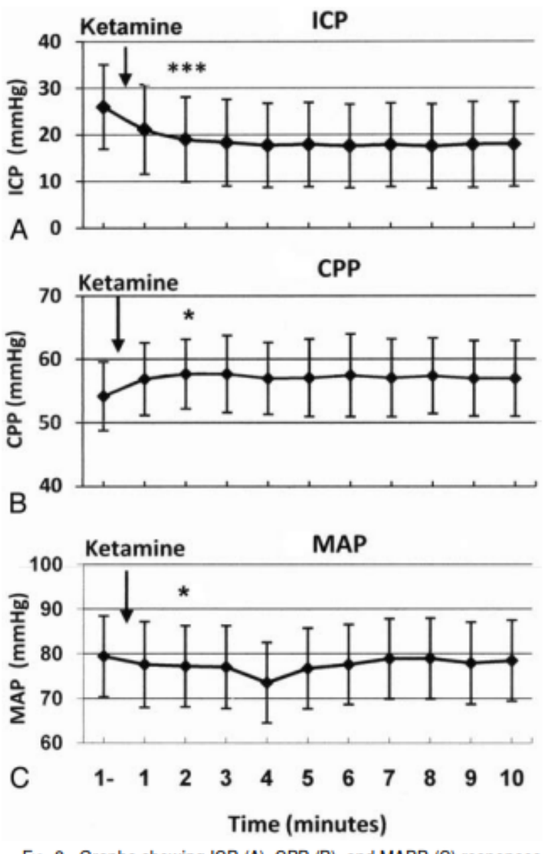

FIG. 3. Graphs showing ICP (A), CPP (B), and MABP (C) responses to ketamine administration in an attempt to lower markedly elevated ICP (65 events, Group 2). Intracranial pressure decreased by 33% within 2 minutes of ketamine administration. *p < 0.05, ***p < 0.0001.

Effectiveness of ketamine in decreasing intracranial pressure in children with intracranial hypertension

Bar-Joseph G, Guilburd Y, Tamir A, Guilburd JN. Effectiveness of ketamine in decreasing intracranial pressure in children with intracranial hypertension. *J Neurosurg Pediatrics*. 2009;4:40-46.

Results	• Overall, ketamine led to ICP decrease of 30% ($p<0.001$) and CPP increase from 54.4 ± 11.7 to 58.3 ± 13.4 mmHg ($p<0.005$)
	• Group 1:
	  • ICP decreased significantly following ketamine administration
	  • ICP increased >2 mmHg during distressing intervention in only 1/17 events
	• Group 2:
	  • ICP decreased by 33% ($p<0.0001$) following ketamine administration

Conclusion	• Ketamine effectively decreased ICP and prevented ICP elevations during distressing interventions without lowering blood pressure and CPP • Ketamine is a safe and effective drug for patients with traumatic brain injury and intracranial hypertension • Alternative sedative and hypnotic agents decrease blood pressure and may potentially decrease CPP

Acute effects of ketamine on intracranial pressure in children with severe traumatic brain injury

Laws JC, Vance EH, Betters KA, et al. Acute effects of ketamine on intracranial pressure in children with severe traumatic brain injury. Crit Care Med. 2023;51(5):563-572.

Population	• Patients <18 years of age with sTBI who underwent ICP monitoring
	  ○ sTBI defined as persistent Glasgow Coma Scale ≤8 following injury
	• Patients underwent invasive mechanical ventilation to maintain arterial CO2 (37 +/- 2 mmHg)
	• 33 patients included:
	  ○ 22 patients received bolus doses of ketamine
	  ○ 127 doses analyzed
	  ○ Over 14,500 hours of ICP data analyzed

Study Design	• Retrospective, observational study • Patients received bolus doses of ketamine for sedation or as treatment for ICP crisis (ICP > 20 mmHg for >5 minutes)

Acute effects of ketamine on intracranial pressure in children with severe traumatic brain injury

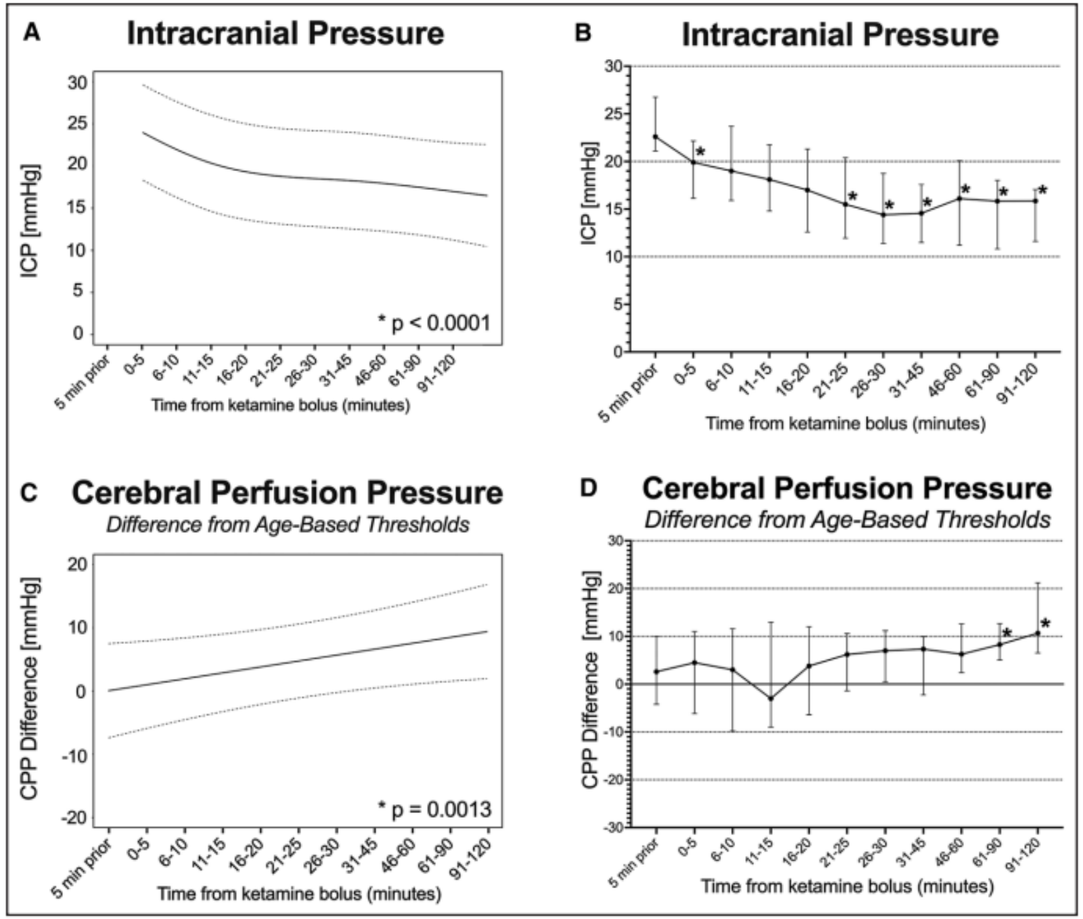

Figure 2. Intracranial pressure (ICP) and cerebral perfusion pressure (CPP) before and after ICP-targeted ketamine administration. ICP-targeted ketamine administrations were identified as those preceded by ICP greater than 20 mm Hg for greater than or equal to 5 min. For each ketamine administration, mean ICP and CPP were calculated for each epoch. **A** and **B**, Display restricted cubic splines modeling ICP and CPP, respectively. *Dotted lines* indicate 95% CIs. *Asterisks* denote significant trends over time by generalized least squares analysis "NS" denotes "not significant." **A**, ICP. **B**, Difference between CPP and age-based CPP threshold. **C** and **D**, ICP and CPP for individual epochs. Median values are displayed. *Error bars* denote interquartile range. *Asterisks* denote values significantly different from baseline (−5 to −1 min before ketamine doses) by multiple *t* tests with the Bonferroni correction.

Acute effects of ketamine on intracranial pressure in children with severe traumatic brain injury

Laws JC, Vance EH, Betters KA, et al. Acute effects of ketamine on intracranial pressure in children with severe traumatic brain injury. Crit Care Med. 2023;51(5):563-572.

Conclusion	• ICP bolus administration was not associated with increased ICP in children with sTBI • Ketamine administration for ICP crises was associated with a reduction in ICP

Assessment Question

How does ketamine affect intracranial pressure (ICP) in patients undergoing distressing interventions?

A. Increased ICP and decreases blood pressure
B. Decreases ICP without lowering blood pressure and cerebral perfusion pressure (CPP)
C. No effect on ICP
D. Only lowers blood pressure

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How does ketamine affect intracranial pressure (ICP) in patients undergoing distressing interventions?

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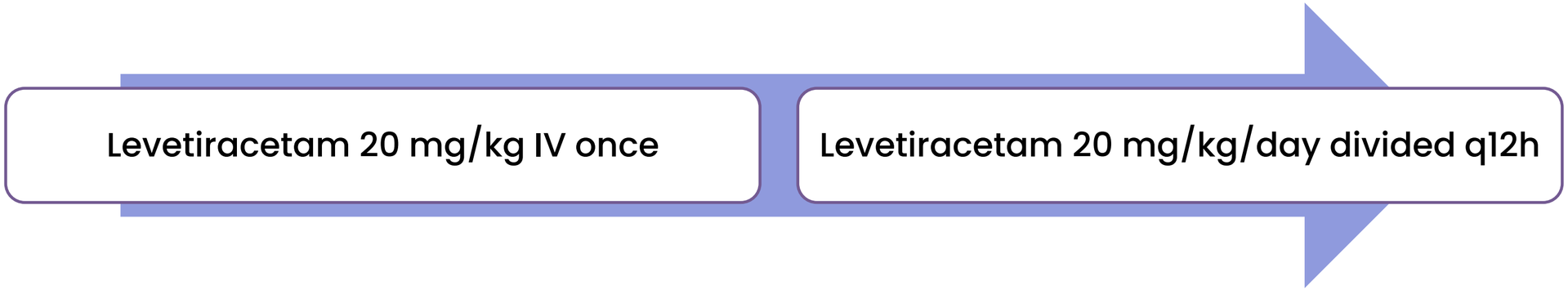
Traumatic Brain Injury (Seizure Prophylaxis and Hyperosmolar Therapy)

Seizure Prophylaxis

- Infants and children have a lower seizure threshold
- Prophylactic treatment is suggested to reduce post-traumatic seizures within 7 days
- No evidence based preference between levetiracetam and phenytoin
  - Only two included studies in the Clinical Guidelines with large patient variation
- Wide dosing variations depending on treating facility
- Levetiracetam is typically easier to administer and well tolerated



Kochanek et al

Hyperosmolar Therapy

- In the evidence included in the 2019 Pediatric Traumatic Brain Injury guidelines, hyperosmolar therapy administered in the emergency department had no significant effect on patient outcomes
- The Fourth Edition of the adult TBI guidelines inform the pediatric guidelines with studies comparing HTS to mannitol
- Evidence that influenced these guidelines were based only on studies with 121 and 169 patients

Kochanek, et al.

Comparison of Intracranial Pressure Measurements Before and After Hypertonic Saline or Mannitol Treatment in Children with Severe Traumatic Brain Injury

Kochanek PM, Adelson PD, Rosario BL, Hutchison J, Ferguson NM, et al. Comparison of intracranial pressure measurements before and after hypertonic saline or mannitol treatment in children with severe traumatic brain injury. *JAMA Netw Open*. 2022;5(3):e220891.

Population	• 1018 screened pediatric patients, 518 included for analysis
	  • 339 patients treated with HTS boluses
	  • 105 patients treated with mannitol boluses

Study Design	• Observational comparative effectiveness research analysis using data from the Approaches and Decisions for Acute Pediatric TBI Trial (ADAPT) • Inclusion criteria: birth to 18 years of age at time of injury, diagnosis of TBI, ICP monitor used as part of standard care, and Glasgow Coma Scale (GCS) score of 8 or lower at time of monitor placement

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Results	• Decrease in mean ICP
	  • HTS: 1.03 mmHg (P<0.001)
	  • Mannitol: 0.20 mmHg (P=0.44)
	• Increase in mean CPP
	  • HTS: 1.25 mmHg (P<0.001)
	  • Mannitol: 1.20 mmHg (P=0.009)
	• Unadjusted analysis
	  • HTS associated with larger observed association with ICP than mannitol
	• Adjusted analysis
	  • Observed associations of the 2 agents were not different
	• Osmolar load
	  • 1.88 times higher for 3% HTS, but maximum serum osmolarity observed was lowest in patients that only received HTS

Comparison of Intracranial Pressure Measurements Before and After Hypertonic Saline or Mannitol Treatment in Children with Severe Traumatic Brain Injury

Kochanek PM, Adelson PD, Rosario BL, Hutchison J, Ferguson NM, et al. Comparison of intracranial pressure measurements before and after hypertonic saline or mannitol treatment in children with severe traumatic brain injury. *JAMA Netw Open*. 2022;5(3):e220891.

Conclusion	• Bolus of 3% HTS was associated with reduced ICP and increased CPP, whereas mannitol was only associated with increased CPP • After adjustment for confounders, both agents were associated with decreased ICP and increased CPP • During increased ICP periods, 3% HTS was associated with greater improvements than mannitol

Assessment Question

In the context of the 2019 Pediatric Traumatic Brain Injury Guidelines, what was the conclusion regarding hyperosmolar therapy administered in the emergency department?

A. It significantly improved patient outcomes
B. It has no significant effect on patient outcomes
C. It was found to be more effective than other alternative treatments
D. It is only effective in adults

Assessment Question

In the context of the 2019 Pediatric Traumatic Brain Injury Guidelines, what was the conclusion regarding hyperosmolar therapy administered in the emergency department?

A. It significantly improved patient outcomes
B. It has no significant effect on patient outcomes
C. It was found to be more effective than other alternative treatments
D. It is only effective in adults

Summary

- Prevalence of fatal pediatric traumas have steadily increased, highlighting the importance of pediatric readiness at non-pediatric healthcare facilities
- Utilization of pediatric resuscitation dosing tools and familiarization with pediatric pharmacy practice can help improve outcomes
- Emerging evidence on the use of ketamine in traumatic brain injury has highlighted the usefulness in the care of trauma patients despite years of contraindication
- The ADAPT trial in pediatric patients with traumatic brain injury has showed improved quality of evidence in the use of hyperosmolar therapy since the release of the 2019 Pediatric Trauma Guidelines

Resources

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Any questions/comments?