Toxicology in Trauma

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AROC, April 17, 2015
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Disclosures

• Paid speaker/consultant
• CSL Behring
• Kcentra, 4 factor PCCs

Objectives

• Discuss the impact of alcohol abuse as it relates to traumatic injuries
• Describe alcohol intoxication, withdrawal and its management
• Discuss the impacts of alcohol intoxication
Traumatic Injury And Alcohol

• Alcohol abuse is a highly salient risk factor for sustaining traumatic injury
• 44% recurrence rate and a 20% 5 year mortality

Traumatic Injury And Alcohol and Drugs

• Dischenger et al. followed a cohort of 27,399 trauma patients
• Toxicology positive patients had an almost double eventual death rate (1.9% vs. 1%; p < 0.001)
  – A longitudinal study of former trauma center patients: the association between toxicology status and subsequent injury. J Trauma. 2001;51:877-884

Traumatic Injury And Alcohol

• Rivara et al. Records of 2,578 trauma patients.
• Those acutely intoxicated with alcohol were 2.5X more likely to have recurrent injury in the following 18 months
• Chronic alcoholics were 3.5 times more likely to have recurrent injury in the following 18 months
  – The effects on alcohol abuse on readmission for trauma. JAMA 1993;270:1962-1964
Toxicology in Trauma

A Shifting Paradigm

• Despite the improvement in trauma care systems, death at the scene has remained approximately 50%.
• Efforts to decrease traumatic injuries associated with the use of alcohol is best achieved by a captive audience.
• Counseling and behavior modification should start in the inpatient setting.

A Shifting Paradigm

• There is little effort devoted to prevent recidivism.
• Brief alcohol counseling sessions have reduced recidivism by 50%.
Stages of Intoxication

- Sobriety
- Euphoria
- Excitement
- Confusion
- Stupor
- Coma
- Death

Stages of Intoxication

- Sobriety (.01 - .05%)
  - No apparent influence
  - Nearly normal behavior
  - Slight changes detected on cognitive testing
  - Subjective feeling of ethanol effects present

Stages of Intoxication

- Euphoria (.03 - .12%)
  - Mild euphoria, sociability, loquacious
  - Increased self confidence, diminished inhibitions
  - Decreased attention, judgment and control
  - Loss of efficiency in fine motor responses
Stages of Intoxication

- Excitement (.09 - .25%)
  - Emotional instability
  - Loss of inhibition and critical judgment
  - Impaired memory and cognition
  - Decreased sensory response, reaction speed and muscle coordination

Stages of Intoxication

- Confusion (.18 - .30%)
  - Exaggerated emotional states
  - Disturbed sensation and perception
  - Impaired pain sense, balance, coordination, gait, speech
Stages of Intoxication

- Coma (.35 - .50%)
  - Unconsciousness, anesthesia
  - Hypothermia
  - Cardiovascular and respiratory compromise
- Death (> .45%)
  - Self explanatory

Ethanol and Hypoglycemia

\[
\text{CH}_3\text{CH}_2\text{OH} \xrightarrow{\text{NAD}^+} \text{CH}_3\text{CH}_2\text{H} + \text{H}^+ + \text{NAD}^+
\]

\[
\text{CH}_3\text{CH}_2\text{H} \xrightarrow{\text{NAD}^+} \text{CH}_3\text{COH} + \text{H}^+ + \text{NAD}^+
\]

Increased NADH + H+/NAD+ ratio

Conversion of pyruvate to lactate consumes H+
Toxicology in Trauma

Pyruvate

\[ \text{H}_3\text{C} - \text{C} - \text{C}^\text{O} \]
\[ \downarrow \text{pyruvate} \]
\[ \text{H}_3\text{C} - \text{C} - \text{C}^\text{O} \]
\[ \text{O} \]
lactate

\[ +\text{NH}_2 \rightarrow \text{Alanine} \]
\[(\text{gluconeogenesis)} \]

1) Poor PO intake
2) Decreased glycogen reserves
3) Decreased substrate for glucose production

Ethanol Withdrawal

- Alcohol Withdrawal
  - Alcohol tremor
  - Alcohol hallucinations
- Alcohol Induced seizures
  - Delirium Tremens

Pathophysiology

- \( \text{GABA}_A \) is an inhibitory chloride channel
- Ethanol increases \( \text{GABA}_A \) tone by direct effect on chloride channel
- Ethanol also acts by indirectly potentiating \( \text{GABA}_A \) binding
- Chronic Ethanol ingestion results in down-regulation of \( \text{GABA}_A \) receptors
Pathophysiology

• The enzyme Phenylethanoamine-N-methyltransferase (PNMT) catalyzes the conversion of Norepinephrine to Epinephrine
• Epinephrine activates presynaptic $\alpha_2$ receptors, which inhibits norepinephrine release

Pathophysiology

• Ethanol increases PNMT activity
  – Increases epinephrine in the synapse
• Chronic ingestion of Ethanol down-regulates $\alpha_2$ receptors

Pathophysiology

• Withdrawal causes a decrease in PNMT activity
  – Results in decrease in Epinephrine levels
  – Loss of negative feedback results in increased sympathomimetic activity
Ethanol Withdrawal

- Symptoms begin about 6 hours after a significant drop in Ethanol level (highly individualistic)
- Patient may not be confused or disoriented
- May occur with as little as 2 weeks of drinking

Ethanol Withdrawal

- May occur without clinical intoxication ever having occurred
- Symptoms peak and begin to resolve within 24 hours
- About 75% of patients experience mild withdrawal symptoms only

Ethanol Withdrawal

- Irritability
- Hyperreflexia
- Agitation
- Anxiety
- Hyper alertness
- Insomnia

- Tremor
- Mild disorientation
- Mood lability
- Tachycardia*
- Hypertension*
- Hallucinations*

* indicates worsening withdrawal
Alcohol Seizures

- Generalized Tonic/Clonic
- Brief, generalized seizure
- Short “post-ictal” period
- 90% within 7 - 48 hours of cessation
- About 50% of patients have more than one seizure, all within a few hours of each other
- If focal, it is almost always CNS pathology

Benzodiazepines

- Drug of choice
- Low Cost
- Increase the frequency of open GABA chloride channel
  - Sedative
  - Anticonvulsant
  - Anxiolytic

Treatment: Diazepam

- Rapid IV onset of 5 minutes
- Rapid redistribution
- Unlikely to cause airway compromise
- Active metabolites decreases need for re-bolus
- 40% propylene glycol by weight
Treatment: Diazepam

- IV load 10mg q15 minutes until sedation
- 25% of all patients will require 200mg+
- Will require more as alcohol is metabolized
- Patient will self taper with the metabolites

Treatment: Lorazepam

- Lorazepam has shorter half life and no active metabolites
- Symptom dosing requires more frequent dosing
- 80% propylene glycol by weight
- May result in inadequate treatment

Propylene glycol

\[ \text{NAD}^+ \xrightarrow{\text{ADH}} \text{NADH} + \text{H}^+ \]
Withdrawal Protocols

- The response to Alcohol withdrawal is highly individualistic
- Theoretically, a protocol should be able to be used successfully for all patients
  - Does not address individual differences
- My personal belief is that each patient should be treated individually with frequent assessments of treatment response

Urine Tests

- Drugs of abuse screen
  - Immunoassays that rely on drug-specific antibodies that bind either to drug in the patient’s sample or to known concentrations of “labeled” drug added to the sample
  - Many false positives and negatives

UDS

- Amphetamines
- Marijuana
- Cocaine
- Opiates
- TCA’s
- PCP
- Methadone
- BZD’s
Toxicology in Trauma

Toxicological Screening In Trauma

- 116 eligible patients over a six month period
- 93 enrolled, 27% had an ethanol level >80mg/dL
- Prevalence of 51% toxicology positive on initial screening 12 exclusions resulted in 35% confirmed drug screens

TD Carrigan et al.
J Accident and Emergency Medicine
2000;17:33-37

Toxicological Screening In Trauma

- Individual drug prevalence:
  - 13% Cannabinoids
  - 11% Codeine
  - 8% Morphine
  - 6% Amphetamine
  - 6% Benzodiazepines
  - 3% Cocaine
  - 1% Dihydrocodeine
  - 1% Methadone

TD Carrigan et al.
J Accident and Emergency Medicine
2000;17:33-37
Testing For Substance Abuse In Trauma Patients

- Retrospective review of longitudinal data
- Patients 15 – 50 years old admitted for traumatic injuries from 1998 – 2003
- Outcome measures: Drug and alcohol testing and results
- Results: Half of the admitted patients were tested for alcohol use

London et al. Archives of Surgery, 142 (no.7) July 2007

Testing For Substance Abuse In Trauma Patients

- Half of those patients had positive results
- 36.3% of patients were tested for drug use, of those 46.5% had positive results
- No significant trends in alcohol testing and results
- Compared to 1988, patients are less likely to be tested for drugs and are more likely to have positive results

London et al. Archives of Surgery, 142 (no.7) July 2007

Drug and alcohol use among adolescent blunt trauma patients: Dying to get high?

- Comparison of ISS, hospital course and outcomes between patients with a positive toxicology screen and those without
- Trauma registry 2000 – 2005
- 9.3% positive toxicology screens (40% canannaboids, 30% alcohol, 23% polysubstance, 3% amphetamines, 3% cocaine, 1% barbituates)

Draus et al. Journal of pediatric surgery 2008: 43, 208 - 211
Drug and alcohol use among adolescent blunt trauma patients: Dying to get high?

- Mean age 17.2 years
- Toxicology positive patients had a lower glasgow coma scale, higher ISS, required more emergency operations, length of stay was longer, functional independence measure scores were lower and mortality rate was higher

Draus et al. Journal of pediatric surgery 2008: 43, 208 - 211

Summary

- The inconvenient marriage of Toxicology and Trauma is a recipe for the continued prosperity of both subspecialties
- Alcohol appears to be the most offensive agents involved in traumatic injuries and is the most objectively supported
- Less clear is the contribution of illicit drugs as it relates to traumatic injuries

Summary

- Efforts should be made to counsel inpatients that suffered traumatic injuries that abuse drugs or alcohol
- Trauma physicians should be familiar with both intoxication and withdrawal of illicit substances