Ingested poisonings Anticholinergics and Cyclic Antidepressants (TCA)

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Outcomes

- At the completion of this lecture, the learner will be able to:
- Describe the incidence, morbidity and mortality of toxic emergencies (5-8.1)
- Identify risk factors predisposing to toxic emergencies (5-8.2)
- Discuss the pathophysiology of the entry of toxic substances (5-8.7)
- Discuss the assessment findings associated with various toxidromes (5-8.8)

Outcomes, cont.

- Correlate abnormal findings with clinical significance in patients with the most common poisonings (5-8.23)
- Identify the need for rapid intervention of a patient with a TCA toxic emergency (5-8.9)
- Discuss the management, in detail, of toxicologic emergencies (5-8.10)
- Review the contraindications and disadvantages of inducing vomiting and gastric lavage (5-8.17)

Anticholinergic Poisoning

Pharmacologic effects:

- Cholinergic blockade
  - Brain (Muscarinic ACh-blocker)
    - ALOC … seizures … psychosis
    - Respiratory depression
  - Peripherally (Nicotinic ACh-blocker)
    - CV
      - Arrhythmias
      - Tachycardia
      - BP ↑↓
    - Atropine - like
      - Skin, resp. GI, GU, "faucets shut"

Anticholinergics

Anticholinergic poisoning effects -

- Atropine-like :
  - Atropine OD mnemonic :
    - Blind as a bat
    - Mad as a hatter
    - Red as a beet
    - Dry as a bone
    - Hot as Hades

Anticholinergic OD Management

Goal : prevention of complications of :

- Brain
  - seizures
  - respiratory depression
- CV
  - BP ↓
  - arrhythmias

Management

- Much the same as for coma except that patient may be mistaken for stable
- All OD emergencies are potentially unstable
- C A B C D E / C O_2 M_3 E B I G
- Coma cocktail

Agents Causing Anticholinergic Syndrome (p.519-20)

- Anti histamines (diphenhydramine)
- Anti psychotics (chlopromazine)
- Atropine-like
  - Scopolamine
  - Jimsonweed
- Anti depressants (TCA)
- Anti nausea (promethazine)
- Anti spasmotics (Clidinium)
- Ophthalmics (Mydriacyl)
- OTCs : - Excedrin PM, Percogesic
  - Pamprin
  - Allerest

Treatment of Anticholinergic Syndrome

- Supportive. ABCs. COMEBIG
- R/O hypoxia
- R/O hypotension
- Be prepared for arrhythmias
  - avoid class 1A′s (Procainamide); ?? 1B′s + 1C′s
- Be prepared for seizures
- R/O hypoglycemia
- Charcoal. Gastric lavage
- Treat agitation with benzo.s

Cyclic Antidepressants (TCA)

Prescribed for :

- major depression
- OCD; panic; eating disorders
- ADD
- chronic pain syndrome
  - peripheral neuropathy
  - migraine headaches
- bedwetting

Toxicity

- Pharmacologic activities
  - narrow therapeutic window or index (tolerated dose / minimum curative dose)
  - therapeutic: 1-5 mg / kg / day
  - life-threatening: >10 mg / kg / dose
- Prescribing patterns of physicians
  - 2 months supply : > 8 x LD
  - huge prescriptions : morally equivalent to handgun dealer selling a handgun to a mentally ill patient

Toxicity

- > 4000 exposures annually
- > 24 deaths annually
- most often in young adults
- often associated with self-destructive behavior (“intentional”)
- toxicity : not necessarily related to drug overdose

Pathophysiology

Mechanism of action / injury :

- Anticholinergic effects
- SSRI, NE reuptake inhibition
- Sodium channel blockade
- Potassium channel blockade
- GABA-A blockade
- Alpha blockade

Pathophysiology, cont.

- Anticholinergic
  - atropine OD - like
- SSRI, and NE reuptake blocker
  - agitation, mydriasis, tachycardia, hyperreflexia, brief hypertension
- Sodium channel blocker,
  - Quinidine - like;
  - prolonged phase 0
  - prolonged PR , QRS ; also RAD (“R in aVR”)
- Potassium channel blocker
  - prolonged QT
- GABA-A blocker (central)
- Alpha blocker (peripheral)

Pathophysiology, cont.

Sodium channel blockade

- made worse by:
  - acidosis
  - hyponatremia
- results in :
  - pump failure
    - shock
  - arrhythmias
    - wide QRS
    - Torsades de pointes (TdP)
    - heart block
  - if QRS > 0.10 sec. :
    - increased risk for seizures
    - increased risk for arrhythmias

TCA Treatment Goals

- usual ABCs / COMEBIG
- treat acidosis
- prevent hyponatremia
- treat pump failure and shock
- prevent / treat arrhythmias
- prevent / treat seizures

TCA Treatment - acidosis and hyponatremia

- Treat acidosis / prevent hyponatremia
- Treat “the monitor”
  - if QRS > 0.10 sec. :
    - hyperventilation
    - Na^+ bicarbonate
      - sodium bicarbonate dose is mistakingly listed as “1-2 mg” IV
      - this should be 1-2 mEq / kg

TCA Treatment - Alkalinization

$NaHCO_3$ treatment :

- mechanism of action
  - increased binding of drug
  - forces sodium through sodium channels
  - decrease is sodium blockade
  - improves cardiac conduction
  - improves cardiac contractility (?)
  - improves nerve conduction (?)
- goal: pH: > 7.50

TCA Treatment - Seizures

TCA seizures treatment:

- treat aggressively
  - if seizures occur :
    - will increase drug level, which will
    - increase drug toxicity
  - RSI if necessary
- Benzodiazepines - drugs of choice
  - Valium 10 mg IV

TCA Treatment - Shock

- NS volume resuscitation
- Sodium bicarbonate
  - if shock is unresponsive to fluid therapy
- Dopamine: may actually drop pt's BP (see below)
- Norepinephrine
  - direct alpha
  - more effective than Dopamine (patient is catecholamine depleted)
- pure beta agents (Dobutamine, Isoproterinol)- contraindicated: these cause unopposed beta stimulation

TCA Treatment - Arrhythmia

- Sodium bicarbonate 1 mEq / kg
- Lidocaine 1.5 mg / kg
- TdP: Mg^{++} 2 gm IV
- avoid Type 1 A's (Procainamide)
  - prolonged refractory period [vulnerable]
- what about 1B′s (Lidocaine) + 1C′s
  - all 1′s: - depress phase 0 (conduction)
    - depress phase 4 (automaticity)
- Mg^{++} - may help cardiotoxicity (ATP-pump,…)

TCA Treatment Algorithm

- Is there trauma? If yes, immobilize C spine
- Is there a gag? If no, ET
  RR: 30
- Is breathing adequate (rate and volume)?
  Assist > 20 / min.
- Is there a pulse ? If no, CPR
  Is there perfusion? Support BP
- C O M E B I G
  - Initial baseline EKG
  - D / T / N - as warranted

TCA algorithm, cont.

- NG tube
  - gastric lavage (after airway is secured)
  - activated charcoal 1 g / kg
    - consider multi dose activated charcoal
- (Ipecac contraindicated)

TCA algorithm, cont.

Sodium bicarbonate 1-2 mEq / kg

- for Q R S > 100 milliseconds
- for shock
- for arrhythmias

TCA algorithm, cont.

- for a arrhythmias
  - as above ($NaHCO_3$)
  - Lidocaine 1.5 mg / kg IV
  - Mg^{++} for TdP : 2 g
- for shock
  - NS 10 mL / kg increments
  - $NaHCO_3$
  - ? Dopamine > mg / kg / min
  - Norepinephrine 1 mic. / min
- for seizures
  - Lorazepam 2 mg/m in., up to 0.1 mg / kg (or Diazepam 5 mg IV)
- PMH, OPQRST, AMPLE, PE;
  collect all pill bottles before leaving the house

Summary

We have discussed ：

- incidence, morbidity, + mortality of TCA toxicologic emergencies
- assessment findings associated with anticholinergic toxidromes
- need for rapid intervention in TCA toxic emergencies
- clinical significance, pathophysiology, and signs and symptoms of TCA overdose
- management algorithm, in detail, of TCA OD
  - contraindication of inducing vomiting