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Sola Dosis Facit Venenum: Understanding Severity of TCA Intoxication

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PROVIDENCE Health & Services

INTRODUCTION

Tricyclic antidepressants (TCAs) have been mostly supplanted by SSRIs in the treatment of depression, however they remain a mainstay of chronic pain management.[1]

These medications carry significant risk of overdose and are found annually among the top 25 causes of poisoning fatalities.[2]

As polyvalent drugs, they act on multiple targets including antagonism of GABA, muscarinic receptors, alpha-1 adrenergic receptors, H1, and their primary mechanism of toxicity – blockade of cardiac fast sodium channels.

Suicide attempts with a TCAs carry a 70% fatality rate unless these patients reach a healthcare facility, in which cases the fatality rate drops dramatically to 3%.[3] As such, maintaining healthcare provider recognition and management of TCA toxicity is of lifesaving importance.

Here we describe a case report in which alcohol ingestion masked the severity of an accidental TCA overdose.

CASE HISTORY

Brief HPI: 68F presents with AMS

VS: T 96.8, HR 86, RR 20, BP 124/59, Sat 98% on RA.

1500 – last known normal
1545 – slurred speech, unsteady gait, consumed “at least one beer”
1600 – ground level fall, head injury, lost consciousness, EMS called.
Patient had bottle of 25mg amitriptyline in her purse, dispensed as 120 pills, with 80 pills remaining. Family denies recent changes to dose. Patient takes up to 35mg nightly for sleep and chronic pain.

PMH: COPD, diverticulitis, prediabetes, HLD, HTN, chronic pain. Remote history of treatment for depression with Prozac, poorly tolerated and DC’d.

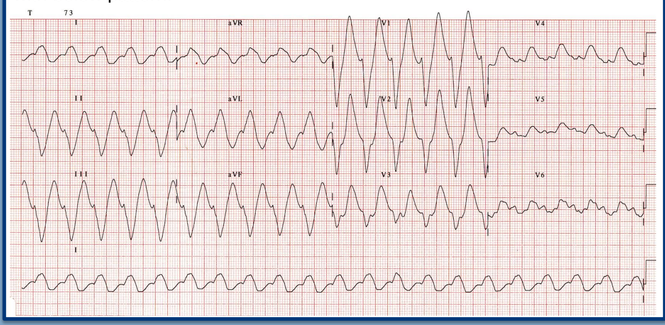
Medications: Amitriptyline 25mg PO nightly, Amitriptyline 10mg PO nightly, atorvastatin 40mg PO nightly, Nicorette gum 4mg PO PRN

Social: Drinks one 6-pack beer weekly, smokes 1ppd since her teens, denies other substance use.

PE: Unresponsive to verbal or tactile stimuli, 4cm bruise with swelling above the L eye without laceration or crepitus. Dry mucous membranes. Otherwise unremarkable exam.

Labs: Normal CBC, troponin, lactate. Mild hyponatremia and hypokalemia. eGFR of 50. Tylenol and aspirin both WNL. UDS is positive only for tricyclics. Alcohol level is positive at 217. ABG pH 7.3, CO2 51, O2 104.

Imaging and other studies: normal head CT, normal CXR. EKG QRS 110 with below pattern.



MANAGEMENT

1640 - Patient arrives in ED and is a triaged appropriately
1700 – EKG indicates widened QRS at 100ms.
1720 – Oregon Poison control contacted, discussed patient, fast facts provided for management guidance.
Poison control recommended blood gas and BMP q2 hours (Monitor for hyponatremia and hypokalemia)
1755 - Patient was intubated for GCS <8
1800 - Sodium bicarbonate drip started at 100cc/hr
1935 - Patient transferred to ICU based on the ADORA criteria - Antidepressant Overdose Risk Assessment
ANY of the following = high risk for seizure or VT/VF
- Arrhythmia
- QRS>100 (33% chance seizure)
- Conduction defects (such as new RBBB)
- GCS <14
- Seizure
- RR <8
- SBP <90
- R wave in aVR lead >3mm tall

Treatment goal – alkalinize pH to 7.5-7.55, this reduces affinity between free drug and fast cardiac sodium channels, and prevents free drug from dissociating from circulating glycoprotein
- Bicarb drip for 8 hours
- While drip is running, repeat EKG, with plan to repeat EKG in 1 hour
- Criteria to d/c drip (all must be met)
- QRS<120
- HR <140
- R wave in AVR <3mm
- SBP >100

2015 – pH 7.33, CO2 48, O2 78
2125 – Sodium bicarbonate drip increased to 150cc/hr
2315 – pH 7.41, CO2 42, O2 100
0440 – ECG shows QRS <100ms

1hr EKG

QRS not increased by >10msec over prior EKG + SBP >100 → **Telemetry and observe until awake**

QRS increased to >10msec Or SBP <100 → **150mEq NaHCO3 + Restart bicarb drip**

0450 – pH 7.49, CO2 42, O2 66
0515 – Bicarb drip discontinued
0735 – ECG shows QRS continues to be <100ms
0835 – Passed SBT and extubated without complication
1225 – Multidisciplinary interview determines overdose was accidental
1300 – Discharged home in good condition with PCP follow-up in 3 days.

IF/THEN

- **If seizure occurs, treat with 150mEq of bicarb or benzodiazepines**
- **If hypotensive MAP<65, no contraindication to vasopressors**
- **Do not treat with physostigmine – associated with cardiac arrest**
- **Do not treat with phenytoin – antiarrhythmics generally worsen outcomes**

Disclosure Statement

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

DISCUSSION

TCA intoxication presents with a variety of symptoms ranging in severity from mild nausea and headache to seizure, respiratory distress, or fatal arrythmia.

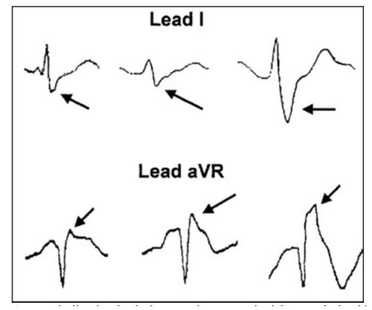
Our patient presented with lethargy, but the severity of her TCA intoxication was clouded by her combined alcohol ingestion. Understanding the magnitude of her TCA overdose represented a clinically relevant diagnostic target.

While the therapeutic drug concentration of TCAs is <300ng/ml and toxicity is generally observed >1000 ng/ml, toxicity does not correlate well with serum drug concentration.[4] Meanwhile several common drugs like diphenhydramine, cyclobenzaprine, carbamazepine, and quetiapine can register as false positives for a TCA on the UDS.

Instead, repeat EKGs to monitor QRS length and the presence of an R wave in lead aVR is the diagnostic mainstay. A study cited repeatedly in the relevant literature by Boenhart and Lovejoy found that a QRS >100 msec carried a 33% incidence in seizures, and a QRS >160 msec carried a 50% incidence of dysrhythmias.[5]

An amitriptyline level was eventually collected, it did not result until a day after the patient had recovered. The primary therapy was a bicarbonate drip which was titrated based on her QRS length, which eventually narrowed.

In these unique times of scarce medical resources, if a bicarbonate drip is not available, a sodium acetate drip may be used (but do NOT bolus sodium acetate).



Harrigan, 2001

KEY LEARNING POINTS

TCAs are common cause of overdose in the United States. Clinical presentation can vary greatly, and the most important sequelae include life-threatening tachyarrhythmia, seizure, respiratory failure, and coma.

The key diagnostic tool is an EKG with special attention toward the QRS, leads I, aVL, aVR, and intraventricular leads.

If the QRS is greater than 110ms, The mainstay of treatment is sodium bicarbonate with a goal to reduce the QRS to less than 100 MS and to alkalinize the blood to a pH of 7.5-7.55.

Do not waste time on quantitative serum TCA concentrations, as these are a poor predictor of systemic toxicity and can often take days to result. Instead, monitor intoxication severity with every 2 hours EKG, VBG, and BMP while treating with sodium bicarbonate.

As with any overdose situation, consider co-ingestion such as alcohol in this case, and be sure to contact local poison control authorities.

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