CYCLIC ANTIDEPRESSANT OVERDOSE

Purpose

The Georgia Poison Center may be contacted for assistance in the management of ingestions of cyclic antidepressants and related pharmaceuticals. This document outlines the basic approach which should be followed in these circumstances, unless extenuating factors dictate otherwise. If the SPI believes that extenuating circumstances may exist, medical backup should be consulted promptly.

Background

Death from cyclic antidepressant (CA) overdose is most commonly caused either by a cardiac arrhythmia, asystole, and/or by intractable seizure activity.

Asymptomatic EKG changes are the most common clinical finding. Medical management involves predicting the serious complications and mitigating them with antidotal care when appropriate. There are two pharmacokinetic properties which are particularly important here. First, these drugs are rapidly absorbed; the onset of toxicity is usually rapid. Second, these drugs recycle through the gut.

Observation

All patients who have had an overdose of cyclic antidepressants, or who are strongly suspected of having done so, should be under medical observation for at least 6 hours following ingestion.

During that time:

1. All should be given charcoal, at least 30 g PO for adults and 1 gm/kg for patients less than 30 kg in weight.

2. All should have a 12 lead ECG, and the QRS and QTc duration should be recorded in the chart as soon as possible after arrival in the ED. This should be repeated again within 2 hours and again at 6 hours after the initial ECG. As long as QRS remains without widening at the end of 6 hours, then no further ECG monitoring is likely to be required.

3. A urine drug screening test for TCAs is not clinically helpful.

If, at the end of 6 hours, the patient has been asymptomatic other than sinus tachycardia that has resolved, then related symptoms are unlikely to develop.

4. Psychiatric evaluation should be carried out and treatment undertaken as appropriate.

5. Any patient with alteration in mental status, any patient who develops one or more of:

- QRS complex longer than 100 msec in adults (or the upper limit of age-based normal in pediatric patients), and/or
- elevated QT corrected for heart rate (QTc) (440 msec for pediatric patients, 460 msec for adult males, or 470 msec for adult females), and/or
- an R-wave amplitude in lead aVR greater than 3 mm, and/or
- an R:S ratio in lead aVR greater than 0.7

should be admitted to the ICU and placed on a cardiac monitor for at least 24 hours of observation. These patients should have intravenous access established and antidotal therapy (serum alkalinization) considered in conjunction with consultation with a toxicologist.

Patients who have not developed arrhythmias or seizures after 24 hours without alkalinization therapy are very unlikely to do so and can be released from the ICU.

Therapy

1. Decontamination

Gut decontamination should be considered in all CA overdoses. Seizures are a complication of CA overdose and the risk of aspiration must be weighed against the benefit of decreased gut absorption. If the patient becomes obtunded after charcoal has been administered, airway protection should be considered to prevent aspiration of charcoal. Activated charcoal dosing should follow standard protocols. Multidose activated charcoal and whole bowel irrigation may be of benefit in select cases and the decision for its use should be made in consultation with a toxicologist.

2. Serum alkalinization

If the patient has any EKG signs associated with cardiac effects of CA poisoning (prolonged QRS duration, large R in lead aVR, increased R:S ratio), then serum alkalinization should be implemented.

A. Patients should receive 8.4% sodium bicarbonate in sufficient quantity (2-6 mEq/kg or 1-4 amps) over 10 minutes to reverse EKG manifestations of CA poisoning (see above).

B. After these loading boluses of sodium bicarbonate have been administered, serum alkalinization should be continued (with either further intermittent boluses or an alkalinizing infusion) after consultation with a toxicologist.

A sodium bicarbonate infusion can be administered by mixing 3 ampules (150 mEq) of 8.4% sodium bicarbonate in 1L of D5W and infusing at a rate of 1-2x maintenance.

Serum pH should be checked frequently (often hourly), by VBG or ABG, and should not be increased beyond 7.55 – 7.60 to avoid complications of excessive alkalinization. This adjustment of pH may be supplemented by mechanical hyperventilation simultaneously, but hyperventilation is likely to be less effective than administration of sodium bicarbonate, and should usually be considered as a secondary method. If excessive alkalemia is experienced with inadequate clinical response, then hypertonic saline

may be considered in consultation with a toxicologist.

3. Seizure management
About 1/3 of patients with a QRS duration greater than 100 msec will seize.

A. If seizures occur while alkalinization is being implemented, then administer a benzodiazepine anticonvulsant, such as diazepam 0.1 mg/kg or 10-20 mg IV.

B. If seizures continue, anticonvulsants (generally including diazepam, lorazepam, and/or barbiturates) should be rapidly given in sufficient quantity to stop the seizure activity.

C. Phenytoin should be avoided as it may worsen cardiovascular toxicity.

4. Ventricular dysrhythmia management
A. If arrhythmias occur, re-bolus sodium bicarbonate and ensure the serum pH is at least 7.50.
B. The next step is to then use lidocaine for ventricular dysrhythmia, 1 mg/kg IV under cardiac monitor control.
C. If ventricular dysrhythmia persists or asystole occurs, since many cyclic antidepressants are lipid soluble, lipid rescue should be strongly considered and the continued use of external cardiac compressions for a prolonged period should be encouraged. Consult medical toxicology backup as soon as possible for further assistance. Patients have made a full recovery after 5 and 8 hours of cardiac compression.

5. Hemodynamic support
A. If hypotension occurs, the patient's intravascular volume status should be assessed, and if appropriate, rapidly corrected.
B. Dopamine or norepinephrine are initial choices for vasopressor therapy.
C. If dopamine is chosen with initial success but later fails to correct hypotension, norepinephrine should be instituted in its place. (Catecholamine depletion at receptor sites occurs in severe TCA poisoning, and may render dopamine and dobutamine ineffective in these situations.)

D. If initial choices are unsuccessful at maintaining an adequate blood pressure, either epinephrine or high-dose insulin euglycemic therapy should be considered in conjunction with toxicologist consultation. Lipid rescue therapy may also be considered in cases of refractory hypotension.

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