The Journal of the Association of Physicians of Tamil Nadu,
Vol. 1, Issue 1, English Quarterly, January – March 2022

Toxicology clinics-bench to bedside A Toxic Slumber

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A 13 years old male was brought to ED with a reduced level of consciousness. He is protecting his airway, has a respiratory rate of 15/min, a pulse rate of 70/min, and blood pressure of 85/35 mmHg. He is responsive to painful stimuli and has pinpoint pupils. His mother says that 5 of her 'sleeping tablets' are missing from her handbag. She thinks her son may have taken them while she was asleep, between 1 and 4 hours previously.

What agent is likely to have been ingested based on the clinical presentation?

Clonidine toxicity mimics opioid toxicity — it causes miosis, respiratory depression, and decreased level of consciousness. However, bradycardia and hypotension are more prominent.

Describe the toxicodynamics of Clonidine?

Clonidine is an alpha2 adrenergic agonist that primarily targets pre-synaptic receptors in the central nervous system and acts as a sympatholytic agent. It also increases endothelial nitric oxide production and decreases renin production.

CNS — miosis, sedation, ataxia, slurred speech, and respiratory depression. Severe toxicity may lead to coma and apnea.

CVS — initially transient hypertension (~20-50% of cases) may occur, but this progresses to bradycardia (as low as 20/min in adults) and hypotension.

Describe the toxicokinetics of Clonidine?

Absorption: Rapidly and completely absorbed with high bioavailability resulting in peak effects within 1-3 hours.

Distribution: large volume of distribution (3-6L/kg); 20-40% protein binding.

Metabolism: hepatic metabolism

Elimination: 50% is renally excreted unchanged; half-life of 6-24 hours.

What is the risk assessment in this case based on the information provided?

In this case, the ingestion is likely to have occurred 1-4 hours previously and involved 300 mcg of clonidine (15mcg/kg for a 20kg child). The dose-response relationship does not always strictly hold true, but as a general guide, the following can be expected:

- >10mcg/kg — sedation, bradycardia, hypotension
- >20 mcg/kg — potential for clinically significant respiratory depression, apnea, and coma.

The effects of clonidine are seen early, and the patient's current clinical condition matches the rest of the risk assessment.

What are the Differential Diagnoses?

- Alcohol toxicity
- Sedative drug overdose
- Electrolyte disturbances (hypercalcemia, hypernatremia)
- Meningitis
- Reye syndrome
- Stroke

Are there any antidotes that may be useful?

Naloxone may have a role.

The effectiveness of naloxone in reversing clonidine toxicity is controversial. If any effect is to be seen, high doses of naloxone may be needed. In adults, use naloxone cautiously in treating clonidine toxicity — you may aggravate underlying opioid withdrawal.

What are the main aspects of assessment and management in this case?

Providing airway and respiratory support

- Close observation in a monitored setting with the child in the recovery position (with suction available at the bedside) is sufficient.
- Consider naloxone (e.g. 100mcg IV every few minutes titrated to respiratory rate) in the event of apneas or significant respiratory depression, particularly if advanced airway and respiratory support are unavailable.

Provide circulatory support

- Bradycardia and hypotension are usually well tolerated.
- Specific treatment of bradycardia is generally unnecessary (e.g., atropine, pacing) unless significantly decreased end-organ perfusion.
- A fluid bolus (e.g., 10-20 mL/kg) normal saline can be given for symptomatic hypotension.

Investigations

- Perform an ECG — bradycardia is typical of clonidine ingestion; rule out evidence of cardiotoxicity from other agents.

What is the prognosis?

Clonidine is a relatively safe drug, and even at toxic doses, mortality is rare. Most morbidity or mortality arises from airway problems instead of cardiovascular issues, and the medication can be associated with CNS morbidity (depression) and cardiorespiratory compromise. Clonidine overdose generally results in good outcomes when adequately addressed.

What is the appropriate disposition?

Admit for supportive care in a monitored setting. Significant clonidine toxicity typically persists for up to 24 hours. Do not discharge at night.

Acknowledgments:

We thank Prof. P. Thirumalaikolandu Subramanian, M.D, for the critical review.

Reference:

1. Manzon L, Nappe TM, DelMaestro C, Maguire NJ. Clonidine Toxicity. In: StatPearls. Treasure Island (FL): StatPearls Publishing; July 26, 2021.