Local anaesthetic systemic toxicity following oral ingestion in a child: Revisiting dibucaine

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ABSTRACT
Dibucaine, a potent and toxic local anaesthetic, although currently withdrawn by the United States Food and Drug Administration for use as a spinal anaesthetic, continues to remain available in many over-the-counter topical formulations. Systemic toxicity following oral ingestion of local anaesthetics is rare. We report a case of accidental ingestion of dibucaine (ear drops) in a 7-year-old child who developed diplopia, giddiness, ventricular premature contractions and a right bundle branch block. We also present a brief discussion on the pharmacologic and toxicity profile of dibucaine, the Naranjo algorithm for assessing causality in case of adverse drug reactions and a review of current guidelines on the management of local anaesthetic systemic toxicity.

Key words: American Society of Regional Anesthesia guidelines, dibucaine, local anaesthetic systemic toxicity, Naranjo algorithm

INTRODUCTION
Dibucaine is a long-forgotten potent and highly toxic amide local anaesthetic. However, it is still available in many over-the-counter topical medications. The paediatric population is vulnerable with a few toxicity reports following exposure. We report a case of local anaesthetic systemic toxicity (LAST) following orally ingested dibucaine in a 7-year-old child.

CASE REPORT
A 7-year-old boy presented to the emergency paediatric services with a history of giddiness and diplopia, 3 h after he accidentally ingested around 10 ml of ear drops containing dibucaine 0.1% w/v [Figure 1]. The dose consumed was approximately 0.5 mg/kg. The child was receiving calcium supplementation for a hypopigmented macule on the face, and someone fed the child the ear drops, mistaking it to be calcium syrup. On presentation, he had an altered sensorium with an essentially normal cardiovascular and neurological physical examination. However, a 12-lead electrocardiogram (ECG) revealed a right bundle branch block (RBBB).

There was no history of seizures or difficulty in breathing and haemodynamics were normal. The child was immediately admitted in the Paediatric Intensive Care Unit, where continuous ECG monitoring was started with a cardioscope and gastric lavage was initiated. There were intermittent ventricular premature contractions evident on the cardioscope. Supportive treatment with continuous monitoring of vital signs continued. ECG was repeated every 6 h for monitoring. Intralipid 20% was kept at hand as an antidote but not administered as the arrhythmia was not associated with haemodynamic instability. After 72 h, the ECG reverted to a normal sinus rhythm following which the child was transferred to the ward and discharged home in healthy condition on the 5th day.
DISCUSSION

Dibucaine hydrochloride, also called cinchocaine, is an amino amide local anaesthetic which is ten times more potent than lignocaine. It is one of the most toxic local anaesthetics known. The drug made its appearance in clinical practice as an anaesthetic for spinal and epidural anaesthesia as early as 1929. The half-life of dibucaine hydrochloride is approximately 11 h. Concentration peaks 2 h after administration and declines to baseline within 48 h. The drug has a high toxic potential and adverse effects have been reported even at concentrations as low as 0.03%. Due to its high neurotoxicity and implication in affecting the cauda equina, it was withdrawn by the United States Food and Drug Administration as a spinal anaesthetic. However, it still continues to be available as a component in topical solutions (Dermacaine®, Nupercaine®, Nupercainal®, Otogesic®) for the treatment of minor burns, sunburns, cuts, scratches, haemorrhoids and in ear drop solutions.

Accidental ingestion of the drug in any of its formulations may be harmful. The first case of fatal poisoning with dibucaine was reported in 1955 in a 3-year-old child who accidentally ingested Nuporal® lozenges. They were being used by her mother for symptomatic relief of pain due to a sore throat. The total swallowed dose was approximately 0.8 mg/kg. The child succumbed after suffering severe respiratory and circulatory failure. Following this, three deaths with seizures and cardiac failure have been reported in the literature in toddlers who accidentally ingested small amounts of dibucaine. The oral acute toxicity dose in children has been expressed in terms of lowest lethal dose (50–74 mg/kg). In 2009, the first case of a child who survived a potentially fatal dibucaine-induced wide complex arrhythmia was reported. The drug also has a propensity to cause sensitisation causing allergic contact dermatitis and photosensitivity following exposure to solutions containing 0.1% dibucaine as the active ingredient. A case of severe anaphylaxis requiring cardiopulmonary resuscitation has been reported after spinal injection with 2 ml of 0.3% solution.

The systemic toxicity of individual local anaesthetics differs. Patient characteristics such as age, sex, body weight, the specific anaesthetic agent, total local anaesthetic dose (the product of concentration and volume), rapidity of diagnosis and adequacy of management may account for the variable clinical manifestations of toxicity. Lignocaine has more neurotoxic potential causing central nervous system (CNS) excitement such as auditory changes, circumoral numbness, agitation, seizures and/or CNS depression with coma and respiratory arrest. The more potent agents such as bupivacaine and dibucaine have greater cardiac toxicity, as they generate arrhythmias at lower concentrations. The ventricular dysrhythmias seen in LAST are due to a re-entry phenomenon slowing conduction speed. LAST has been classically described due to systemic absorption following regional blocks or due to accidental intravascular injection. However, with dibucaine, the literature has reported consistent toxicity after accidental oral ingestion in children. This may be attributed to the per kilogram ingested dose, which is higher in children.

The Naranjo Adverse Drug Reaction Probability Scale is commonly used to assess causality for adverse drug reactions [Table 1]. It consists of ten questions answered as either ‘yes’ or ‘no’ or ‘do not know’ with values (−1, 0, +1 or +2) assigned to each answer. With scores >9, the causality is considered definite. A score between 5 and 8 suggests the reaction is probable, between 1 and 4 possible and doubtful if the score is 0 or less. In our case, the child had a score of 7 suggesting that the reaction was probably due to dibucaine.

The American Society of Regional Anesthesia (ASRA) and pain medicine practice advisory have summarised current knowledge regarding the prevention, diagnosis and treatment of LAST. Supportive management of airway, respiratory and cardiovascular function takes precedence. Ventilation with 100% oxygen prevents hypoxia and subsequent acidosis. Seizures
should be controlled with benzodiazepines. If orally ingested, gastric lavage should be started. In case of cardiac arrest, standard advanced cardiac life support measures are to be rapidly instituted. Epinephrine and amiodarone are recommended for ventricular arrhythmias, whereas calcium channel blockers and vasopressin are to be avoided. For the potent, lipid-soluble local anaesthetics such as bupivacaine and dibucaine, lipid rescue therapy with 20% lipid emulsion is recommended in case of life-threatening arrhythmias. This acts as a ‘lipid sink’ which withdraws the anaesthetic from cardiac tissues, thus improving conduction. ASRA recommends an initial bolus of 1.5 ml/kg intralipid followed by an infusion of 0.25 ml/kg/min for at least 10 min after circulatory stability has been established. A repeat bolus or increasing the infusion to 0.5 ml/kg/min is recommended in case of failure of the initial dosing. Approximately 10 ml/kg for 30 min is considered the upper limit for initial dosing.

In our case, the RBBB did not cause haemodynamic instability and reverted to a normal sinus rhythm after 72 h of drug exposure. The half-life of oral dibucaine is not known; however, considering our case and the drug’s toxic profile, we recommend monitoring for signs of LAST for at least 3 days following exposure in a high dependency unit.

**CONCLUSION**

Dibucaine, although a long-forgotten local anaesthetic, still holds a potential for toxicity in the paediatric age group. Awareness of the presence of this drug in topical formulations and caution in storage is the key to preventing accidental hazards.

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**Conflicts of interest**

There are no conflicts of interest.

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