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Case Report

Pediatric Neem powder poisoning: a report of two cases and a review of toxicity mechanisms

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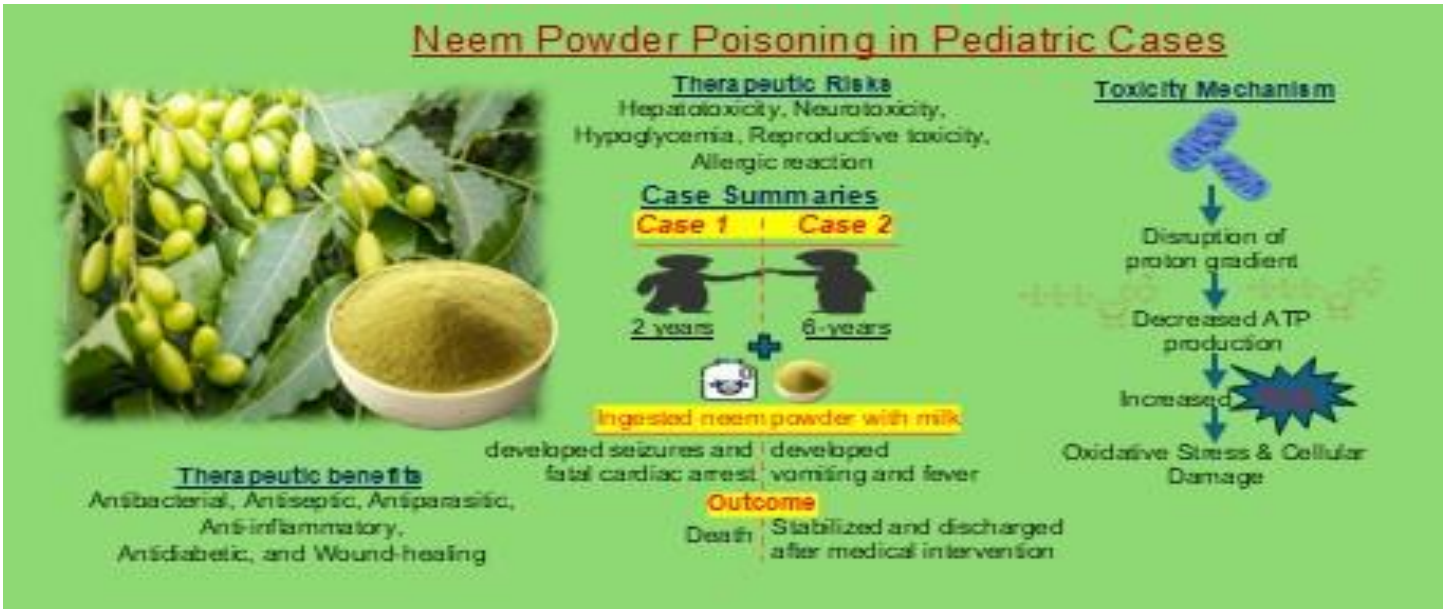
ABSTRACT

Neem (Azadirachta indica) is a plant known for its wide array of therapeutic properties, derived from its diverse phytochemical makeup. Despite its medicinal benefits, neem can pose significant toxicity risks, especially in children. This report presents two pediatric cases of neem powder poisoning. The first case involves a two-year-old boy who ingested neem powder with milk, resulting in seizures and fatal cardiac arrest. The second case describes a six-year-old boy who experienced vomiting after consuming neem powder with milk. Prompt medical intervention, including gastric lavage and supportive care, led to his stabilization and discharge. Neem's toxicity is attributed to compounds like azadirachtin, which disrupt mitochondrial function, leading to symptoms such as seizures, vomiting, and hepatic stress. These cases highlight the importance of recognizing the potential dangers of neem and underscore the need for public health education and regulatory oversight to prevent such adverse outcomes in pediatric populations.



Keywords: Pediatric Neem powder poison, *Azadirachta indica*, Mitochondrial function, Hepatic stress, Supportive care, Public health education

INTRODUCTION

Neem, also known as Azadirachta indica, is a plant with a varied phytochemical makeup that provides a wide range of therapeutic qualities. These phytochemicals, which include limonoids, flavonoids, phenols, catechins, gallic acid, polyphenols, nimbins, azadiractin, and nimbidin, have been shown to have antibacterial, antimalarial, anti-inflammatory, and anti-cancer properties [1-3]. Neem has also been proven to have neuroprotective properties, which could reduce the burden of neurodegenerative illnesses [1]. Furthermore, the plant's high content of catalase, peroxidase, polyphenol oxidase, and ascorbate peroxidase enzymes, along with its other phytoconstituents, contribute to its versatile pharmacological activities, including anticancer, antidiabetic, antioxidant, antimicrobial, and antimalarial effects [3]. These findings highlight the potential of Neem as a valuable source of natural products for the development of medicines and industrial medicinal products [4]. However, sialin, picrin, azadirachta, nimbin, nimbinin, nimbidin, and nimbidol are toxic compound present in the Neem [5, 6]. We described two paediatric cases of Neem powder poisoning in a two-year-old boy that resulted in convulsions and fatal cardiac arrest, as well as a six-year-old boy who vomited and was stabilised with supportive treatment before being discharged.

CASE PRESENTATIONS

Case 1

A two-year-old male child was presented to the emergency room in an unconscious state. Upon examination, the patient exhibited no pulse, no respiration, and a flat line electrocardiogram (ECG). Cardiopulmonary resuscitation (CPR) was administered, but the patient was subsequently pronounced dead. The patient's medical history revealed that he had ingested Neem powder with milk in the morning, and developed a seizure approximately 30 minutes post-ingestion.

Case 2

A six-year-old male patient was brought to the emergency department Adichunchanagiri hospital and Research Centre (AH & RC), Karnataka, India, with complaints of 2-3 episodes of vomiting since morning which was a sudden in onset and non-projectile in nature. Food particles were present in vomit; however, they were not biliary, blood-tinged, or odorous. Patient had no history of abdominal pain, fever, headache or altered sensation. Patient was apparently normal until the day before, vomiting started after consumption of Neem powder mixed in milk.

On arrival, his vitals were normal with temperature of 96.1° F, heart rate 96 bpm, respiratory rate 18 cycle per minutes, SpO_2 96%, capillary refilling time was less than 2 seconds, and blood pressure 110/70 mmHg. On examination, bilateral air entry and heart sound was present, no added sound were detected, and was conscious and oriented with date and time. Patient was 15 kgs with up-to-date immunization history and development. Stomach wash was performed and the gastric lavage sent for the toxicological test. The patient was symptomatically treated with IV fluids DNS at ½ maintenance, injection Pantoprazole 15 mg (1mg/kg/dose), injection ondansetron 1.25 mg (0.15mg/kg/day). Laboratory investigation shows the elevation in white blood cells (WBC), neutrophilia, and erythrocyte sedimentation rate (ESR), elevated SGOT (AST), and blood urea. In gastric lavage, was common organophosphates was found negative (Table 1).

Table 1: Laboratory parameters and its reports

Parameters	Reports
Total White Blood Cell	18860 Cells/cumm
Neutrophils	83%
Lymphocytes	12%
Eosinophils	1%
Monocytes	3%
Basophils	1%
ESR	21 mm/hrs.
Red Blood Cell Count	4.92 × 10^6/microliter
Platelet Count	4.36 × Lakhs/cumm
Packed Cell Volume	35.20%
Mean Cell Volume	71.6 Fl
Mean Corpuscular Haemoglobin (MCH)	21.4 Pg
Mean Corpuscular Haemoglobin	34.00%
Haemoglobin	12 gm/dl
CRP Quantitative	6.3
Total Bilirubin	0.4 mg/dl
Direct Bilirubin	0.2 mg/dl
Indirect Bilirubin	0.2 mg/dl
Total Protein	7.9 g/dl
Serum Albumin	4.2 g/dl
Serum Globulin	3.7 g/dl
A/G Ratio	1.1
SGOT(AST)	55 U/L
SGPT(ALT)	17 U/L
Alkaline Phosphatase	219 U/L
Blood Urea	23 mg/dl
Creatinine	0.5 mg/dl
Sodium	142 Mmol/L
Potassium	4.4 Mmol/L
Chloride	102 Mmol/L
Gastric lavage toxicology	Organophosphates not present

The patient was diagnosed as a Neem powder poisoning with acute gastroenteritis (MLC). Patient was admitted under pediatric department for observation. Symptomatic treatment was given to patient, as the patient is clinically and hemodynamically stable, he was discharged on after 3 days with the advice to have plenty of oral fluids and syrup ondansetron (5ml twice a day for 2 days) and tablet lansoprazole 15mg once a day for 3 days. Danger signs were explained to the attendees and asked to review after four days.

DISCUSSION

Neem (*Azadirachta indica*) is renowned for its medicinal properties but can pose significant toxicity risks, particularly when ingested, as illustrated by two contrasting pediatric cases. Case 1 depicts a tragic outcome where a two-year-old child ingested Neem powder mixed with milk, subsequently experiencing seizures and progressing to cardiac arrest despite resuscitative efforts, highlighting the potential for rapid and fatal toxicity associated with Neem ingestion in young children. Conversely, case 2 presents a six-year-old

child who developed vomiting shortly after ingesting Neem powder in milk. Early recognition and intervention, including gastric lavage and supportive care with intravenous fluids and antiemetics, led to stabilization and discharge with symptomatic treatment, underscoring the critical role of prompt medical management in mitigating Neem toxicity.

Neem's toxicity is primarily attributed to its bioactive compounds, including azadirachtin, sialin, picrin, nimbin, nimbinin, nimbidin, and nimbidol [5, 6]. These compounds exhibit diverse biological activities but can disrupt cellular functions. Studies have demonstrated that azadirachtin interferes with mitochondrial bioenergetics, disrupting the proton gradient essential for ATP production [7]. This disruption can lead to symptoms such as fatigue, muscle weakness, and nausea. Furthermore, research has shown that azadirachtin affects the mitochondrial membrane potential, leading to decreased ATP synthesis and increased production of reactive oxygen species (ROS), which can cause oxidative stress and cellular damage [8]. This mechanism was evident in our patient's elevated SGOT levels, indicating hepatic stress. Additionally, neem's impact on cellular oxygen utilization can induce cytotoxic hypoxia, characterized by metabolic acidosis and hyperpnea. Cytotoxic hypoxia occurs when cells are unable to utilize oxygen efficiently, despite its availability. The metabolic acidosis observed in Neem poisoning cases is a consequence of the accumulation of lactic acid, a byproduct of anaerobic metabolism, which occurs when oxygen-dependent cellular respiration is compromised. Hyperpnea, or increased breathing rate, is a physiological response to metabolic acidosis as the body attempts to expel excess carbon dioxide and normalize blood pH levels [9].

In pediatric cases, the severity of Neem toxicity can be heightened due to the smaller body mass and developing organ systems of children. Case reports have documented instances of Neem oil poisoning in children, presenting with symptoms such as vomiting, drowsiness, tachypnea, and seizures. In severe cases, Neem toxicity can lead to encephalopathy, liver dysfunction, and even death [10, 11]. In case 1, we observed the rapid onset of symptoms and fatal outcome which are indicative of a severe disruption of essential physiological functions, possibly due to mitochondrial dysfunction and cytotoxic hypoxia caused by bioactive Neem compounds. The immediate seizure post-ingestion could be linked to the interference of azadirachtin with mitochondrial bioenergetics, leading to energy depletion and subsequent neuronal hyperexcitability and collapse. In line with case 1, *Sundaravalli et al.*, and *Sinnaih et al.*, reported the death of 10 and 13 individuals, respectively, exhibiting metabolic acidosis and toxic encephalopathy [11, 12]. WBC and ESR elevations indicate an inflammatory response and elevated SGOT levels indicate liver involvement, potentially because of oxidative stress and cellular damage brought on by neem's bioactive compounds in case 2, which is consistent with cases revealed by *Bethesda et al.,* where Neem toxicity resulted in hepatotoxicity [13].

The management of our case involved prompt symptomatic treatment, including hydration and symptomatic treatment, is critical for managing Neem toxicity, and gastric lavage was not recommended, consistent with guidelines and case studies on the subject. Ensuring patients are monitored for delayed or recurring symptoms is vital. Our patient was discharged with instructions for follow-up, aligning with best practices in pediatric care.

These cases of Neem toxicity highlight the importance of recognizing the potential dangers of traditional remedies and the need for public health education and regulatory oversight. The findings and management strategies in this case are consistent with existing literature, emphasizing the critical role of healthcare providers in identifying and managing Neem poisoning to prevent adverse outcomes and ensure patient safety.

Consent for Publication

Written consent was obtained from the caretaker for the publication.

Conflict of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper

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