

DEXTROMETHORPHAN INDUCED SEVERE RESPIRATORY DEPRESSION IN CHILDREN: A CASE SERIES

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Received : 20/12/2025
Received in revised form : 01/02/2026
Accepted : 14/02/2026

Keywords: *Dextromethorphan, Respiratory depression, FDCs, Cough.*

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DOI: 10.47009/jamp.2026.8.1.193

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (1); 1013-1015



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ABSTRACT

A cough may be either a normal physiological reflex having protective mechanism for the airways and lungs or a viral respiratory tract infection. Cough receptors are mainly situated in the larynx, tracheobronchial tree, pharynx and are mediated by rapidly-adapting (irritant) A-delta fibers and C-fibers. Antitussive agents suppress dry irritating cough which are available as Over the counter drugs. Dextromethorphan is commonly used over-the-counter antitussive but it should not be given in children less than 4 years of age. Here, we present a case series of fatal adverse effect of severe respiratory depression caused by cough syrup containing dextromethorphan in 4 children which were admitted in pediatric intensive care unit (PICU) of Dr. Sushila Tiwari Hospital, Haldwani, in which 2 did not survive and 2 were discharged successfully after recovery. The aim of this case series is to focus the severe and fatal side effect of self-medication of cough syrup containing Dextromethorphan given to 4 children less than 2 years of age.

INTRODUCTION

The most common symptom in pediatric age group which occurs due to viral infections or self-limiting factor is cough and antitussives are the most commonly used treatment approach as they are easy to administer.^[1] Antitussives act centrally in CNS to raise the threshold of cough centre as well as reducing tussal impulses peripherally in respiratory tract. It has been classified in two groups Opioids and Non-Opioids and Mostly non opioids are preferred as they are less addictive among which Dextromethorphan is the most commonly used drug.^[2]

Dextromethorphan (3-methoxy-N-methylmorphinan) also known as “DXM” a synthetically produced prodrug which is available as Over The Counter (OTC) cough and cold preparation.^[3] It was approved by the US Food and Drug Administration in 1958 as a nonprescription drug to suppress cough and is now marketed throughout the world. Dextromethorphan (d-3-methoxy-N-methylmorphinan) is the d-isomer of the codeine analogue levorphanol, Its antitussive activity

is based on actions on σ -opioid receptors. Dextromethorphan is metabolized by CYP2D6 in parts. It causes blockade of N-methyl-D-aspartate (NMDA) receptors and inhibition of glutamate excitotoxicity. Dextromethorphan and its major metabolite, dextrorphan, also block the NMDA receptor at high doses, which produces effects similar to other dissociative anesthetics such as ketamine, nitrous oxide, and phencyclidine. Its potency is nearly equal to that of codeine. In therapeutic dosages, its antitussive effects persist for 6-8 hours. Its toxicity is low, but extremely high doses may produce CNS depression, respiratory depression, sedation, dizziness, drowsiness, dissociative hallucinations and ataxia. The drug is marketed for over-the-counter sale in liquids, syrups, capsules, soluble strips and lozenges or in combinations with antihistamines, bronchodilators, expectorants and decongestants.

When DXM was used as recommended dosing levels, it causes minor adverse effects if any but poisoning with dextromethorphan can occur if it is used in single large dose without doctor's

recommendation below 4 years of age. Side effects of dextromethorphan at normal therapeutic doses can include body rash, itching, nausea, vomiting, drowsiness, dizziness, sedation, confusion, A rare side effect is respiratory depression.^[4]

As per the F.No 28025/52/2025-SAS.II/EMR, DGHS, MoH&FW, GOI, Nirman Bhavan, New Delhi, Dt:03/10/2025 cough and cold medications should not be prescribed or dispensed to children under 2 years and these are generally not recommended below 5 years of age.^[5]

In this case series we report 4 interesting cases series of serious adverse effects of cough syrup containing Fixed dose combination of dextromethorphan hydrobromide 15 mg with chlorpheniramine maleate 2 mg and phenylephrine hydrochloride 5 mg consumed by children less than 2 years of age. All the 4 children developed severe respiratory depression after ingestion of 5 ml of cough syrup.

Case 1 – Eleven months old male neonate brought to emergency with history of fever, cold & cough since 3 days, breathing difficulty associated with 2-3 episodes of vomiting, tonic posture and gasping. During admission in emergency patient had an episode of convulsion which was tonic in nature followed by worsening of condition. Parents gave history of taking self-medicated cough syrup from local pharmacy store and was immediately rushed by the parents to emergency department of Dr. Sushila Tiwari Government hospital, Haldwani. On arrival in the emergency showing poor response, bag and mask ventilation was started with 100% O₂, patient was intubated and put on ventilator. He was diagnosed as case of severe bronchopneumonia and respiratory failure. Patient was managed with oxygen support and treatment was started as per the standard treatment guidelines for such cases. The child was stable and discharged.

Case 2- Eight-month-old male neonate brought to emergency department of Dr. Sushila Tiwari Government Hospital in unconscious state with up rolling of eyeball with history of cough, cold and fever on/off since 1 month, vomiting 1 episode. There was history of giving one dose (5ml) of self-medicated cough syrup containing Chlorpheniramine maleate 2mg, Dextromethorphan Hydrobromide 15 mg, Phenylephrine Hydrochloride 5 mg which was purchased from local pharmacy store. After 3-4 hours of self-medication of Cough syrup patient developed symptoms of breathlessness. It was diagnosed as a case of severe bronchopneumonia and respiratory failure. Patient was intubated and put on bain circuit and vitals were continuously monitored and shifted to PICU. The child was managed with oxygen support, IV fluids and standard treatment guidelines. The child recovered and was discharged successfully

Case 3: Two-year-old male neonate brought to emergency in unconscious state with history of ingestion of FDC of cough syrup containing Chlorpheniramine maleate 2mg, Dextromethorphan Hydrobromide 15 mg, Phenylephrine Hydrochloride 5 mg after which he had developed altered sensorium

followed by unconsciousness. He was then brought to hospital in gasping condition. He was immediately intubated and put on ventilator, shifted to PICU at DR. Sushila Tiwari Government Hospital, Haldwani. He was diagnosed as case of bronchopneumonia with respiratory failure shock with right upper lobe collapse and Disseminated Intravascular Coagulation (DIC) with shock. Treatment was immediately started with oxygen support and followed all the standard treatment guidelines under all supportive care. Despite of all treatment measures and close monitoring patient could not be revived and expired. Case 4: A male neonate of eleven-month-old presented in emergency at Dr. Sushila Tiwari Hospital, Haldwani with history of high grade fever since 1 day, cough and cold since 3 days along with breathing difficulty since 4 hours with tonic posturing at time of presentation. Patient was immediately put on bag and mask ventilation and intubated, catheterized and Ryle's tube inserted and shifted to PICU. He was diagnosed as a case of severe Bronchopneumonia with respiratory failure and meningitis. He was monitored continuously and despite of all standard treatment protocols patient was monitored strictly but could not be revived and expired.

All the adverse drug reactions were serious and were entered in vigiflow and reported to Pharmacovigilance Programme of India, Indian Pharmacopoeia Commission, Ghaziabad within 7 days. The causality was found to be certain as per WHO UMC Causality Assessment Scale.

DISCUSSION

The most common approach to provide relief from the symptoms like cough, cold, allergies and respiratory infections in pediatric age group are cough syrup as they are easy to administer. However recently concerns have arisen regarding their safety and quality as it is available as OTC drug. Cough syrups typically contain a combination of active ingredients like dextromethorphan (suppressant), guaifenesin (expectorant), and antihistamines (e.g., chlorpheniramine, diphenhydramine) to target dry or productive coughs.

In this case series all the patients had history of self-medication of cough syrup for cough and fever which contains Chlorpheniramine maleate 2mg, Dextromethorphan Hydrobromide 15 mg, Phenylephrine Hydrochloride 5 mg from local pharmacy store without doctor's consultation and prescription. All patients developed severe respiratory depression within few hours of intake of syrup. The cough syrup contains high doses of dextromethorphan which produced severe adverse effects in children causing respiratory depression. Few studies reported similar findings.

In a study done by Seltzer et.al a case of 1 year 11-month-old male child presented with complaints of Vomiting, progressive lethargy and respiratory

failure after receiving dextromethorphan containing cough syrup.^[6]

As per the studies done by Paul IM et al a single dose of dextromethorphan resulted in mild adverse effects such as hyperactivity, nausea, dizziness, nervousness after acute ingestion.^[7]

As per study done by Henretig F et al,^[8] in 3 children aged 1 month to 4 years, dose of 5-21 mg/kg resulted in moderate to severe symptoms like lethargy, coma, ataxia, mydriasis and dystonia.

A study done by Devlin KM et al,^[9] 5 children of age 2-4 years who ingested unstated doses of extended-release dextromethorphan polistirex suspension exhibited one or more symptoms of urticarial, lethargy, nystagmus, tachycardia.

In another study done Iglesias Platas et al,^[10] (2002) by a 20-month-old boy developed mydriasis, hypotonia, blank stare after ingestion of 150 mg (11.5 mg/kg) of an unspecified Dextromethorphan product. Many researchers reported that within 30 to 120 minutes of ingestion of Dextromethorphan containing preparation the adverse effects occurred.^[4]

Therefore, patients with Dextromethorphan poisoning should be closely monitored for vital signs as well as respiratory cardiovascular and neurological status. Supportive and symptomatic relief should be provided. As per Indian Academy of pediatrics (IAP) standard treatment guidelines 2022, evidence-based medicine does not support cough syrups but its availability and rampant prescriptions in the real world, pediatricians can take a middle path by prescribing antitussives like dextromethorphan above 4 years of age as a single night time dose (0.5 mg/kg) or levodropropizine 1–2 mg/kg dose once or twice, apart from honey.^[11]

CONCLUSION

This case series highlights life threatening adverse reactions after ingestion of OTC cough syrup. According to Directorate General of Health Science, Ministry of health and Family Welfare, Government of India, to ensure the rational drug use and patient safety the prescribing and dispensing of cough syrups should be done judiciously as most acute cough in children often resolve without pharmacological intervention. Cough and cold medications should not be prescribed and dispensed under 2 years and not recommended below 5 years of age and if used it should follow careful clinical examination, and close supervision and appropriate dosing should be adhered strictly. The first line approach should be non-pharmacological measures including adequate hydration rest supportive measures. It is important to

make parents aware about harmful effects of self-medication of OTC cough syrup. Cough persisting beyond 2 weeks needs proper evaluation. Cough remedies must be used with caution and only to relieve the discomfort caused by cough, not to “cure” cough.

It is recommended that dose of cold and cough syrup for pediatric age group should contain specific instruction for pharmacist and parents in which it can be used.^[5] Further the public may also be sensitized regarding adherence to prescription before prescribing any drugs.

ACKNOWLEDGEMENT

We are highly grateful to Pharmacovigilance Programme of India, Indian Pharmacopoeia Commission, Ghaziabad for their support, guidance and contribution towards patient safety. We are also highly obliged to the patients who gave us consent for publication.

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