

Paracetamol-induced Liver Disease among Children in India: Myth or Reality?

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ABSTRACT

Objective: To assess the spectrum of accidental paracetamol-induced liver disease (PILD) in children and to study the pediatrician's perspective on the possible reasons and remedial measures.

Materials and Methods: A questionnaire-based online survey among pediatricians all over India was sent to members of the Indian Academy of Pediatrics (IAP), the Indian Society of Pediatric Gastroenterology, Hepatology and Nutrition (ISPGHAN), and institutions.

Results: 86% considered PILD in their diagnosis and 42% had encountered one or more cases in the previous 6 months. 54% reported acute hepatitis as the most common presentation. Half the respondents attributed it to an error by the mother while 30% held the pharmacists responsible. As remedial measures, a majority suggested color coding of different strengths and mentioning the dose in bold letters on preparations containing drops.

Conclusion: Accidental PILD among children is not uncommon but is preventable and treatable. It should be considered in the differential diagnosis of acute hepatitis. Steps to prevent errors by the mother and pharmacist are easy to enforce.

Keywords: Acute hepatitis, Children, Liver disease, Paracetamol.

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What This Study Adds?

- Paracetamol-induced liver disease among children is common in India and acute hepatitis is perceived to be the most common presentation.
- Medication errors are most commonly by the mother, followed by pharmacists.
- Color coding of different strengths and labeling the dose in bold letters on bottles containing drops are suggested remedial measures.

INTRODUCTION

Paracetamol is among the most common over-the-counter drug used for the treatment of pain and fever. Worldwide, it is one of the leading causes of drug-induced liver disease, acute liver failure (ALF) as well as liver transplantation in the west.¹ While in older children it is usually intentional and suicidal, in younger children it is accidental.² In India, paracetamol is available in various strengths and preparations such as suspension, drops, tablets, injections, and suppositories as well as in combination with other analgesics. There is very little data on accidental PILD in India and so we conducted this study among pediatricians to evaluate their experience.

MATERIALS AND METHODS

A questionnaire-based online survey was conducted using the SurveyMonkey tool from 15th February 2020 to 15th March 2020. The survey link was sent to all pediatricians through the IAP and ISPGHAN. Participation was voluntary and no personal contact or incentives were offered.

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RESULTS

A total of 317 doctors participated in the study. About 45% of them were practicing pediatricians, 29% were faculty from teaching institutions, 12% were from nonteaching hospitals, 11% were from corporate hospitals, and 2% were working in tertiary pediatric gastroenterology centers. Around 60% were general pediatricians, 30% practiced both general pediatrics and gastroenterology while 10% confined themselves only to pediatric gastroenterology. While 28% were in practice for less than 5 years after postgraduation, 23% had over 20 years of experience. Nearly 86% of respondents considered PILD when dealing with liver disease. About 42% had encountered one or more children in the previous 6 months, while the remaining had not. Among them, 76% had treated one to two

cases, 17% saw three to five cases, and 7% saw more than five cases in 6 months. Around 54% reported acute hepatitis as the most common presentation, of which nearly 2/3rd had ALF. Worsening of acute hepatitis of other etiology (viral, dengue, etc.) was noted by around 30% while 3% noticed it to present as acute on chronic liver disease.

About 50% of the respondents reported that the reason for overdose was an error on the part of the mother giving a higher dose using drops in place of syrups or more than the recommended number of doses, while in around 30% it was an error on the part of pharmacist dispensing a higher strength. Regarding suggestions for prevention, 81% supported paracetamol usage only on an "as necessary" basis. 58% wanted color coding of different strengths of preparation and 50% suggested that drops should carry the dosage in bold letters on the bottle. About 38% suggested banning strengths in excess of 250 mg/5 mL, while 22% wanted a total ban on paracetamol as drops.

DISCUSSION

Parental anxiety about high fever and febrile seizures leads them to use paracetamol even when not indicated. Availability as an over-the-counter medication allows indiscriminate use in practice. PILD is a treatable medical emergency and this makes early diagnosis very crucial.

About 86% of pediatricians considered it in their diagnosis. In an Indian study, 13% of all poisonings in children were attributed to paracetamol.³ Around 42% of our survey participants had managed at least one or two children with paracetamol toxicity in 6 months. The 7% who have encountered more than five cases probably represent tertiary care centers. Nearly 54% reported acute hepatitis as the most common presentation with two-thirds of them having ALF. Paracetamol overdose is the second most common cause of ALF in children in the west.⁴

About 50% of our respondents reported an error on the part of the mothers either giving higher strengths or more doses as the reason, while 30% attributed it to an error in dispensing by the pharmacist. Lakshmi and Radhika have reported that paracetamol liquid preparation of 250 mg/5 mL (46% of accidental ingestion) and drops of 100 to 125 mg/mL (63% of multiple-dose ingestion) resulted in toxicity.³ In our country where many mothers are only partially literate and pharmacies are manned by untrained or inadequately trained personnel, the availability of paracetamol as an over-the-counter drug is fraught with danger.

Medication errors are a serious problem in children, both in the hospital setting and in ambulatory practice.⁵ A report by the American Academy of Pediatrics states that 11% of children under the age of 6 years who are exposed to drugs experience a medication error. Of the 238 instances in that study, 162 occurred at home. The most common single agent responsible for a serious life-threatening medication error was paracetamol and of the 24 deaths reported, one-third were due to it.⁶ It is pertinent to note that in the US, only two liquid formulations of paracetamol are available. Lemer et al. have reported that higher error rates occurred below 5 years of age and in children taking two or more medications.⁷ There is greater awareness about medication safety today and in 2009, Canada enforced labeling standards for all products containing paracetamol with warnings on the packaging about the risk of overdose. It also mandates the inclusion of weight-based dosing charts on the product.⁸

As remedial measures for prevention, over 80% of respondents advocated paracetamol use only "as necessary" rather than round

the clock. This needs parental education that fever in a child is not a cause for panic and that febrile seizures are not as common as they think. Color coding of different strengths and labeling the dose in bold letters on bottles containing drops are suggestions endorsed by over half of the respondents. Others advocate a ban on paracetamol drops and strengths above 250 mg/5 mL.

Dart et al. in a review of deaths caused by cough and cold medications in the US, identified accidentally administered high doses as the cause in most cases. One factor that was identified was the lack of an appropriate device to administer drugs.⁹ Spoons and droppers that are most often used by parents are inaccurate. The acetaminophen hepatotoxicity working group of the Food and Drug Administration has recommended improved packaging to facilitate delivery of an appropriate dose as a practical intervention.¹⁰ It has also been suggested that paracetamol preparations for children be removed as an over-the-counter medication.

The strength of our survey is the heterogeneity of the respondents both in experience and in area of work. The weakness is that it is an online survey with its own limitations. However, the results indicate a need to address an issue of great importance, both preventable by simple measures as well as treatable if diagnosed early. Prospective studies are required to assess the exact extent and severity of PILD among children in India.

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