Original Article

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Analysis of Acetaminophen Toxicity in Children in a Tertiary Care Setting

Lakshmi Muthukrishnan*, Radhika Raman**

Abstract

Background: Acetaminophen (paracetamol) is widely used in children as an antipyretic because its safety and efficacy are well established. Parental anxiety coupled with easy availability makes it one of the common poisonings seen in children. The symptoms of acetaminophen intoxication are non specific. The availability of acetaminophen in various concentrations and preparations, delays the diagnosis and treatment of acetaminophen intoxication in unintentional toxicity.

Objective: To analyse the toxic effects of acute and multiple dose acetaminophen ingestion in a tertiary care pediatric emergency setting.

Methods: Case records of 54 children diagnosed with acetaminophen toxicity between February 2009 and February 2013 were retrospectively analysed.

Result: Acetaminophen toxicity was common in infants, common diagnosis at presentation being viral fever with vomiting . Hepatomegaly and elevated liver enzymes were noted in the majority. Double strength preparation (250mg/5ml) in accidental and drops (100 to 125mg /ml) contributed to toxicity in multi dose ingestions. Parenteral N Acetyl cysteine was well tolerated.

Conclusion: Unintentional acetaminophen toxicity is as common as accidental ingestion. High index of suspicion is important. It mimics common childhood illness. Detailed prescription of acetaminophen and parental counseling are necessary.

Keywords: Acetaminophen; NAC; *N*-acetylcysteine; Paracetamol; Poisoning; Toxicity.

Introduction

Acetaminophen, also known as paracetamol or *N* -acetyl-p-aminophenol (APAP). the globally popular "over the counter" analgesic and antipyretic, is an important cause of poisoning in children. Acetaminophen poisoning, whether suicidal, accidental, or inadvertent, may cause hepatic injury presenting as isolated elevation of transaminases or acute liver failure (ALF).[1,2] It is available in various concentration and various preparations such as, suspension, tablet, drops, suppository, parenteral preparation and as combination with other analgesics. US Food and Drug Administration (FDA) is considering the removal of APAP from some popular analgesic combination products and possibly decreasing the recommended maximum daily dose.[3,4]

Materials and Methods

Case records of patients with a diagnosis of acetaminophen toxicity at our hospital between February 2009 and February 2013 were retrospectively analysed. All children with accidental ingestion of acetaminophen diagnosed as toxicity based on Rumack Mathew nomogram and diagnosed as toxicity due to multi dose ingestion based on history, acetaminophen dose, presenting symptoms and laboratory parameters were included.

Author Affilation: *Post doctoral fellow in Pediatric Emergency Medicine, Junior consultant in Pediatric Emergency Medicine, Kanchi Kamakoti CHILDS Trust Hospital, Chennai, **Senior consultant in Pediatric emergency, KKCTH.

Reprint request: Dr. Lakshmi Muthukrishnan , Kanchi Kamakoti Childs Trust Hospital, 12-A, Nageswara road, Nungambakkam, Chennai 600034

E-mail: **vcmlck@yahoo.co.in**

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Age, gender, single or multiple dose ingestion, strength and paracetamol preparation used, presenting complaints, mean time of presentation for single and multiple doses, diagnosis at presentation, laboratory markers, treatment given, complications and duration of hospital stay were analysed.

Demographic characteristics of study population

(N=54)

Patient characteristics	n(%)
Age	
< 1 yr	20(37)
1-5 yr	32(59)
>5 yr	2(3.7)
Acetaminophen Overdose	
Multi dose ingestion	30(56)
Accidental single dose ingestion	24(44)
Presenting symptoms	
Recurrent vomiting	32(59)
Fever	9(16)
Lethargy	7 (13)
Decreased urine output	6(11)
Loss of appetite	4(7)
Abdominal pain	1(2)
Asymptomatic	7(13)
Strength of acetaminophen used	
120 to 125mg /5ml syrup	7(13)
240 to 250mg /5ml syrup	21(39)
100 to 125mg /ml drops	22(41)
500mg tablets	4(7)
Suicidal and coingestion with other drugs	2(4)
Common formulation used	
Accidental single dose ingestion 240 to 250mg /5ml syrup	11/24(46)
Multiple dose ingestion 100 to 125mg /ml drops	19/30(63)
Diagnosis at admission	
Viral fever	11(20)
Acute gastro enteritis	4(7)
Dengue	3(5)
Febrile seizure	2(3)
Sepsis	2(3)
Acute CNS infection	1(2)
Hepatic failure	7/30(23)
Renal failure	3/30(10)
Treatment	
Intravenous NAC	43(80)
Oral NAC	5(9)
No NAC	6(11)
PICU management	6(11)
Mean time of presentation	
Accidental single dose ingestion	2.5 hours
Multiple dose ingestion	32 hours
Mean duration of hospital stay	
Accidental single dose ingestion	1.8 days
Multiple dose ingestions	4.8 days

Results

Acetaminophen toxicity formed 13% of all poisonings diagnosed during the study period Out of 54 children, 37% were <1 year age, 3.7% were >5 year age and the remaining were in the 1-5 year age group. Majority were males (57%) and multiple dose ingestion was common (30/54 = 56%). The presenting symptoms were vomiting (59%), fever (16%), lethargy (13%), decreased urine output(11%), loss of appetite (7%), abdominal pain (2%) and asymptomatic (13%). 41% of children had hepatomegaly at admission. The strength of acetaminophen used were 120 to 125 mg /5 ml syrup (7/54), 240 to 250 mg /5 ml syrup(21/54), 100 to 125mg /ml drops(22/54) and 500mg tablets(4/54). Two children had history of co- ingestion with other drugs and two of them were suicidal. Double strength acetaminophen (250 mg/5 ml) was commonly used in accidental single dose ingestion (11/24=46%) and acetaminophen drops was the common formulation causing toxicity due to multiple dose ingestion (19/30 = 63%). All children with single dose accidental ingestion presented within 10 hours and the mean time of presentation was 2 ½ hours. The duration of presentation for multiple dose toxicity was between 1 to 5 days and mean was 32 hours. The diagnosis at presentation were viral fever (20%), acute gastro enteritis(7%), dengue(5%), febrile seizure / sepsis (3% each), acute CNS infection (2%) and acetaminophen toxicity (57%). The most common laboratory parameter to get deranged was elevation of liver enzyme(37/54 = 69%). Hepatic failure(7/30 = 23%) and renal failure(3/30 = 10%) were observed only in children with multiple dose ingestion. Four children presented with hypoglycemia. N-acetyl cysteine through intravenous and oral routes were administered to 43 and 5 children respectively and none of them had adverse reactions. Six of them were given only symptomatic treatment. Eight children required PICU management. The

duration of hospital stay was 1.8 days in single dose and 4.8 days in multiple dose ingestion.

Discussion

Acetaminophen toxicity due to multiple dose ingestion is as common as accidental ingestion, as evident from our study. Recent reviews identified several factors associated with acetaminophen hepatotoxicity in children, including: age less than 10 years, inappropriate dosing, delay in onset of symptoms after a potentially toxic ingestion, unintentional multiple overdosing, ingestion of acetaminophen along with another hepatotoxic drug, delay in initiation of NAC treatment.[5] A case series of 231 children aged six weeks to 16 years has been reported from Nigeria.[6] The commonest reason for using paracetamol tablet instead of the syrup was that it was more effective. Parental anxiety about the ill effects of high grade fever especially seizures was a common factor for multiple dose toxicity in our group of children. From our study it was evident that double strength paracetamol syrup (250 mg/5 ml) and paracetamol drops can cause inadverdent overdosage. Hence caregivers need to be educated about using age-appropriate formulations. Potential medication dosing errors can occur especially in outpatient pediatrics and 4 children in our study developed toxicity due to dosing error. Proper and adequate pharmaco vigilance is lacking in children's drug therapy, especially in developing countries , therefore children are at risk of developing adverse reactions to drugs as a result of medication errors.[7] Unintentional overdose of paracetamol causing toxicity is sparsely reported from India and may even be considered as nonexistent. Recently a series of 6 children with this type of paracetamol overdose has been reported.[8] Therapeutic misadventure is a unique problem where the existing nomogram used for acute poisoning is not applicable. A high index of suspicion is required to recognize toxicity due to multiple dose ingestion which presents with non specific signs and symptoms and can mimic common childhood illness. As seen in our study vomiting, lethargy and reduced urine output were the most common nonspecific presenting symptoms which could explain the delay in diagnosing paracetamol toxicity in multiple dose ingestion. Hepatomegaly in a child with nonspecific symptoms could be a pointer to paracetamol toxicity as it was observed in a significant number (41%) of children in our study. Intravenous N-acetylcysteine (NAC) is probably relatively safe in children and ensures adequate drug levels as emesis is a presenting symptom of paracetamol toxicity. Oral administration is associated with vomiting which may limit NAC effectiveness.[9] Caregivers should be counseled about the potential for toxicity of this medication and the need to follow appropriate dose based on age and weight which should be reviewed by the paediatrician at every visit. Medical prescriptions should mention appropriate dose, strength, formulation and dosing interval. Tamper proof containers for pediatric formulations will help prevent fatalities.

Limitation

This was a retrospective analysis hence details regarding social and other factors which led to repeated or accidental ingestion could not be ascertained. We included only children who were admitted. Hence there is the possibility of not including children with mild forms of multidose acetaminophen toxicity.

Conclusion

1. Unintentional acetaminophen toxicity is as common as accidental ingestion.
2. Double strength and drops are commonly associated with acetaminophen toxicity.
3. Acetaminophen drops is the common cause of unintentional toxicity.
4. Acetaminophen toxicity mimics common childhood illness hence leading to a delay

in recognition.

5. Intravenous N- Acetyl Cysteine can be safely administered in children.

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