

Knowledge of caregivers of febrile children about fever, paracetamol use and paracetamol induced hepatic toxicity in Lagos Nigeria.

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ABSTRACT

Background: Fever is as a result of immune response to many pathogens. Paracetamol is widely and irrationally used at home for treatment of fever in children before presentation at the health facility but it is not clear whether caregivers are aware of the toxicity that can result from non-rational use of paracetamol.

Objectives: The aim of this study was to evaluate the knowledge of fever, the use of paracetamol, and paracetamol induced hepatic toxicity amongst caregivers of febrile children.

Methods: This was a prospective descriptive study in which we interviewed two hundred and ten caregivers who brought febrile children to Onwusikawa Children's Medical Center Okota Lagos over a period of one year (Jan 2013- Dec 2013). A pretested closed ended questionnaire was used to collect data on the use of paracetamol, knowledge about fever, and toxicity of paracetamol during routine clerking.

Result: Paracetamol in both syrup and tablet formulations was administered by the study population to febrile children before presentation in hospital. Majority of the respondents (61%) knew fever as an increase in body temperature. About 8% of those interviewed gave paracetamol to their children including neonates almost on a daily basis to prevent fever or because they felt the baby especially the head was hot. Ninety five percent of all respondents were not aware that paracetamol could cause adverse effects while 98% did not know that paracetamol could cause hepatic toxicity.

Conclusion: The knowledge regarding toxicity of paracetamol was poor. It is proposed that education of caregivers by health workers on dangers of paracetamol misuse should be routine. Pharmaceutical companies that manufacture paracetamol for children must provide a risk management plan.

Key words: Paracetamol, caregiver, febrile children, liver toxicity.

Connaissances des personnes s'occupant des enfants fébriles à propos de la fièvre, l'usage de paracétamol et la toxicité hépatique provoquée par le paracétamol à Lagos au Nigeria.

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RESUME

Contexte : La fièvre provient de la réaction immunitaire contre plusieurs pathogènes. Le Paracétamol est largement et irrationnellement utilisé à domicile pour le traitement de la fièvre chez les enfants avant qu'ils soient présentés à un centre de soins mais ce n'est pas clair si les personnes qui pourvoient les aides à domicile sont conscientes de la toxicité qui peut résulter de l'usage non-rationnel du paracétamol.

Objectifs : Le but de cette étude est d'évaluer la connaissance de la fièvre, l'usage du paracétamol, et la toxicité hépatique provoquée par le paracétamol parmi les personnes qui s'occupent à domicile des enfants fébriles.

Méthodes: Ceci était une étude prospective descriptive dans laquelle nous avons interviewé deux cent dix aides à domiciles qui ont amené des enfants fébriles à Onwusikawa Childrens Medical Center Okota Lagos sur une période d'un an (Jan 2013- Déc 2013). Un questionnaire pré-testé fermé fut utilisé pour recueillir to des données sur l'usage du paracétamol, de la connaissance sur la fièvre, et de la toxicité du paracétamol au cours de l'assessorat de routine.

Résultat: Le paracétamol dans les deux formulations de sirop et de comprimé était administré par la population étudiée à des enfants fébriles avant l'arrivée à l'hôpital. La majorité des personnes interrogées (61%) connaissaient la fièvre comme une montée de la température du corps. Près de 8% des interviewés ont donné le paracétamol à leurs enfants, y compris les nouveau-nés presque de façon quotidienne pour prévenir la fièvre ou parce qu'ils sentaient que le bébé, en particulier la tête était chaude. Quatre-vingt-quinze pourcent de toutes les personnes interviewées ne savaient pas que le paracétamol pouvait causer des effets adverses, alors que 98% ne savaient pas que le paracétamol pouvait causer une toxicité hépatique.

Conclusion: La connaissance en ce qui concerne la toxicité du paracétamol était faible. On propose que l'éducation des personnes s'occupant des maladies à domicile par les agents de santé sur les dangers de l'abus du paracétamol soit une routine. Les compagnies pharmaceutiques qui fabriquent le paracétamol pour les enfants doivent fournir un plan de gestion de risque.

Mots-clés: Paracétamol, aides à domicile, enfants fébriles, toxicité du foie.

INTRODUCTION

Paracetamol (Acetaminophen) is used worldwide for its analgesic and antipyretic properties and it can be obtained as prescription and non-prescription medications.^{1,2} Fever is an elevation of the body temperature above the normal range (36.5-37.5°C) due to an increase in the temperature regulating set point.^{3,4,5} Many pathogens cause fever in children⁶ and integrated management of childhood diseases (IMCI) recommend treatment of all fevers as part of the management of malaria, bacteraemia, meningitis, and pneumonia.^{7,8} In Nigeria and other malaria endemic countries, in Sub Saharan Africa febrile illnesses in children are treated at home prior to presentation at the clinic.⁹⁻¹⁵ The merits and demerits of drugs that reduce fever and dangers of fever are well documented.¹⁶⁻¹⁹ Other methods of reducing fever, such as tepid sponging, bath with luke warm water, use of fan and exposure to air are equally effective but temporary.²⁰ Paracetamol is one of the most available home remedy medicines at home in our environment.¹⁵ In recommended doses and for a limited course of treatment, the side effects of paracetamol are mild.²¹ Unlike aspirin, paracetamol is not associated with a risk of Reye's syndrome in children with viral illness thus, it is generally considered to be safe in children.²¹ Following chronic use, there may be a higher risk of developing blood cancer, skin reactions, such as Stevens-Johnson syndrome and toxic epidermal necrolysis.^{23, 22} Regular paracetamol use is associated with ototoxicity²⁴, however it does not cause gastric irritation and has fewer adverse gastrointestinal effects.²⁵ Paracetamol is generally believed to be safe for use in pregnancy as it does not affect the closure of the fetal ductus arteriosus.²⁶ Paracetamol overdose, poisoning or toxicity is a common cause of morbidity and mortality worldwide.²⁴ Repeated administration at supra-therapeutic doses which may be intentional or non-intentional, may result in hepatic toxicity.^{24,27} The mechanism of acetaminophen hepatic toxicity has been well studied²⁷ and depletion of hepatocellular glutathione reserves is central to the pathophysiology of hepatocellular injury and cell death.²⁷ Neonates and young children are said to be more dependent on sulphate than glucuronide conjugation of paracetamol at therapeutic doses and therefore may be less susceptible to acetaminophen hepatic toxicity.^{28, 29, 30} Children less than 10 years of age have been observed to be resistant to hepatotoxic effects of paracetamol.^{31, 32,33} Because of this developmentally associated increase in sulfation ability³⁰, few cases of hepatotoxicity from

paracetamol over dosage have been reported in young children.³¹⁻³⁶

As it occurs in adults sulphate conjugation could become saturated³²⁻³⁹ following overdose and therefore preventive measures must be instituted to prevent hepatic toxicity in our children in whom paracetamol use at present is inappropriate in some cases.¹⁵

The aim of this study was to evaluate the use of paracetamol in the management of fever at home before presentation in hospital and the knowledge of paracetamol toxicity among the caregivers of febrile children.

METHODS

The study was conducted at Onwusikawa Children's Medical Center, a private paediatric center located in Okota, a semi urban densely populated area in Oshodi Isolo Local Government Area of Lagos State, South West Nigeria. The center receives referrals from neighbouring Isolo, Ejigbo and Ikotun areas. Successive caregivers of all febrile children attending the clinic from January 2013 to December 2013 were prospectively interviewed during routine clerking in the clinic by the attending doctor. A pretested questionnaire with close ended questions was used to collect data on fever, prior use of paracetamol at home before presentation and knowledge about toxicity of paracetamol with emphasis on paracetamol induced hepatic toxicity. Informed Consent was obtained from caregivers after they were informed that the aspects of history on paracetamol use and knowledge about toxicity will be included in a study.

Data was analysed by calculating frequency and percentages and results are presented in a table and figures.

RESULTS

A total of 210 caregivers of febrile children were assessed on their use of paracetamol, knowledge about fever and of paracetamol toxicity. The children were aged between one week and fifteen years. The caregivers were adult males (5%) and females (95%). The demographic data of respondents are shown in table 1

Table 1: Demographic data of respondents

	Number of caregivers	Frequency %
Gender of care givers		
Male	11	5%
Female	199	95%
Gender of febrile children		
Male	88	42%
Female	122	58%
Age of febrile children		
0-28days	15	7%
>28days-12months	70	33%
>12months -59months	94	45%
>59months	31	13%
Educational level of caregivers		
No formal education	40	19%
Primary school education	30	14%
Secondary school education	98	47%
Tertiary education	42	20%

Majority of the caregivers (61%) knew that fever was an increase in body temperature. Twenty nine percent of them thought fever was a disease while the rest did not know the meaning of fever. (10%).

Very few (19%) patients had a digital thermometer at home and used it while about 24% of the respondents had a thermometer but did not use it. Majority of the caregivers did not have a thermometer. Figure 2 shows data on possession of digital thermometers.

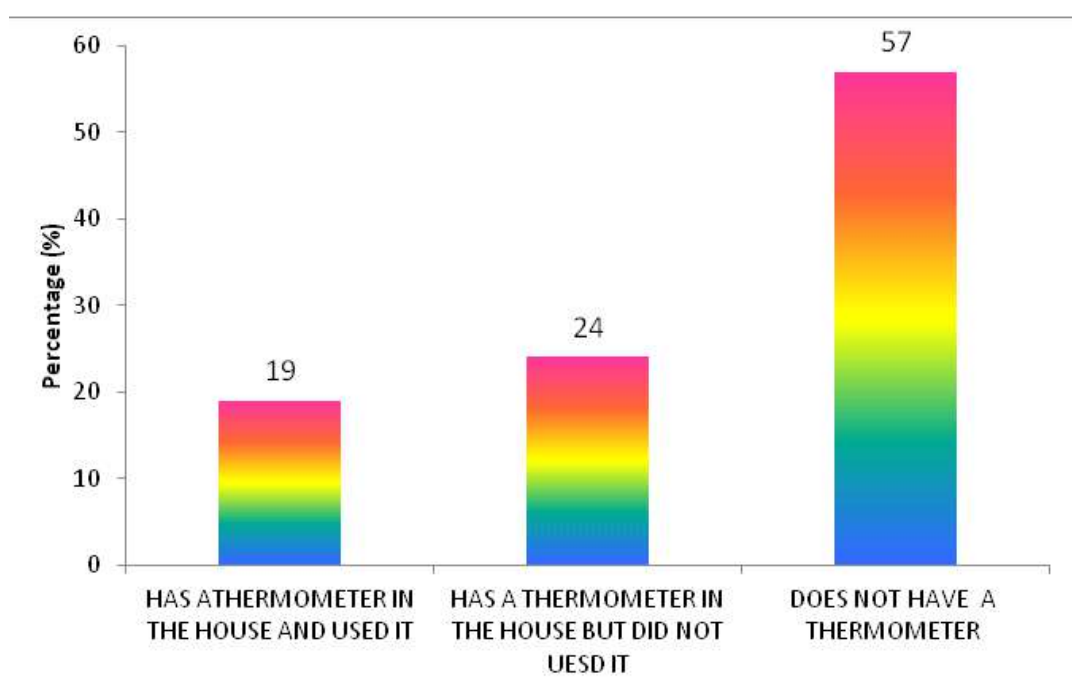


Figure 1: Possession of Digital Electronic Thermometer

Forty eight percent of the respondents sourced their paracetamol from nearby pharmacy shops with very few (2%) obtaining paracetamol from hospital. Thirty six percent of the caregivers had a new unopened bottle at home while fourteen percent had a remnant of paracetamol used previously at home.

Syrups were the predominant formulation used (53%). Twenty-nine percent used syrups initially and switched to tablets when the fever persisted. Eighteen percent of the caregivers used tablets because they felt syrups were not effective. This data is shown in figure 2.

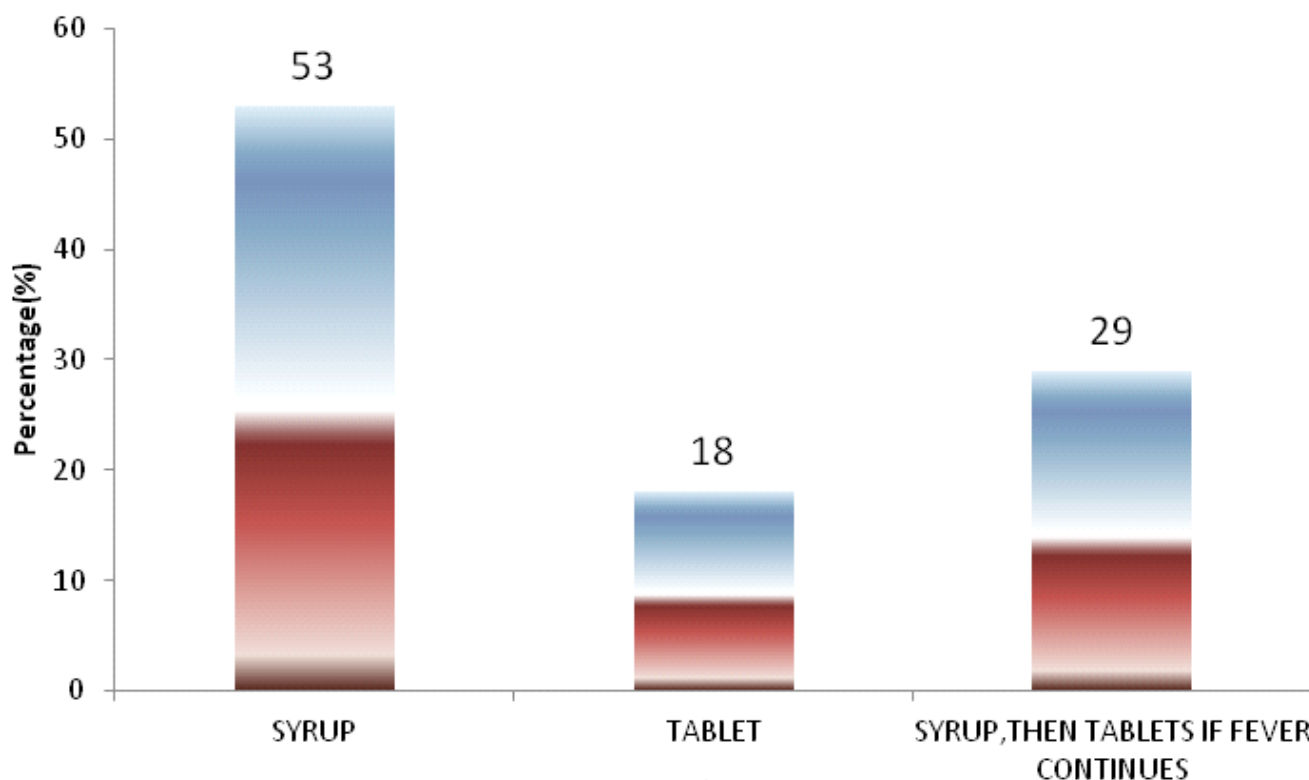


Figure 2: Formulation of paracetamol used

Majority of the respondents 38% did not know the dose of paracetamol while 33% of them knew the dose. Twenty nine percent of the caregivers use the doses recommended on the package insert. Forty percent of the caregivers give paracetamol to the febrile child once or twice in a day before presenting at the hospital, while 32% gave paracetamol for two to three days before going to hospital. Twenty percent continued paracetamol until fever

disappeared and eight percent give paracetamol everyday as prophylaxis for fever.

7. With regards to knowledge about toxicity ninety five percent of the caregivers considered paracetamol to be very safe and did not know paracetamol had any side effects. Furthermore ninety eight percent of the caregivers did not know paracetamol could cause liver toxicity (Figures 3 and 4)

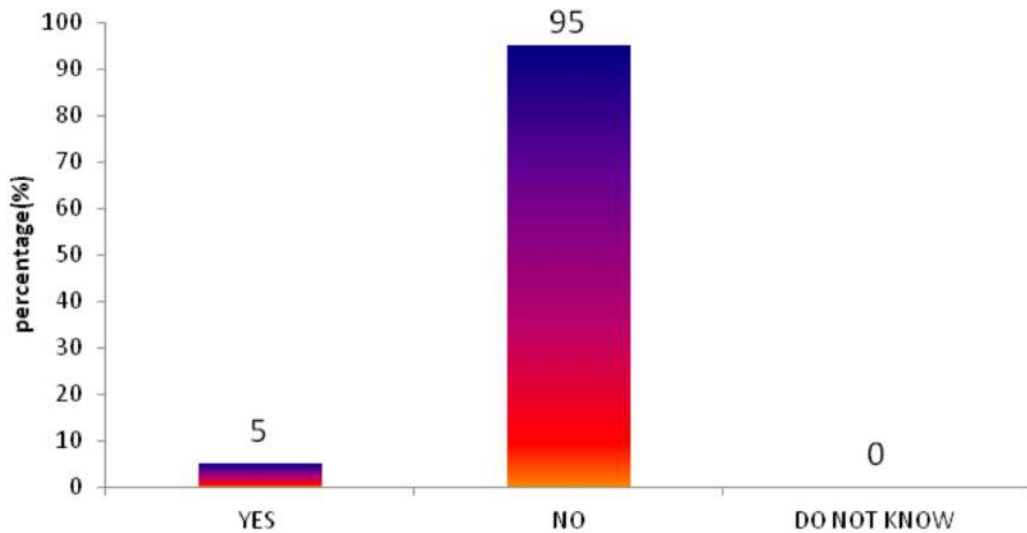


Figure 3; Knowledge of caregivers on adverse effects of paracetamol

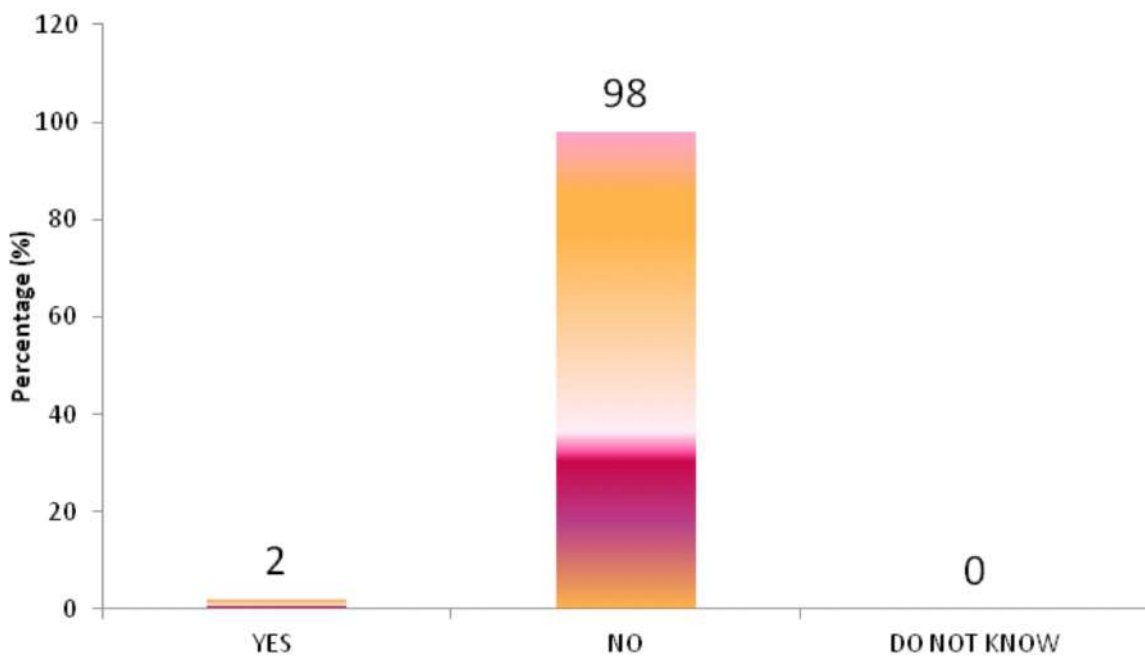


Figure 4: Knowledge of caregivers on paracetamol induced Liver Damage

DISCUSSION

This study evaluated the knowledge of paracetamol toxicity amongst caregivers of febrile children. The observations made on paracetamol use are similar to findings in previous Nigerian studies where poor knowledge of fever and inappropriate use of paracetamol has been documented.^{15,40,41,42} The use of paracetamol to effect relief of fever is very important to the caregivers who feel that their febrile children would be affected if fever is not reduced. The fear of fever, its

benefits and misconceptions are well documented.^{43,44}

Majority of the caregivers are mothers and they have different educational and socioeconomic backgrounds. A previous study had shown convincingly that parental educational and socioeconomic status impacted on the responses to fever in children.⁴⁰ this present study did not explore this relationship further.

The World Health Organization recommendations for management of fever in children includes the use of paracetamol when the body temperature is 39°C or

higher⁴⁵ With the availability and affordability of the electronic/digital (easy to use and read) thermometers, some caregivers have thermometers at home and could easily objectively determine if a child is febrile or not. However, despite the ease with which these thermometers could be used and read, some do not use these thermometers and still rely on feeling with their hands to decide if a child is febrile or not. In a previous study social class, maternal age and religion have been documented to influence the decision to use thermometers.⁴⁰ Non-use of thermometers could give unreliable conclusions on whether a child is febrile or not. In cool environments the hands and feet feel colder than the other body parts. A lot of heat escapes through the head while the rest of the body which constitutes a larger surface area is exposed to cooling breeze, so the body is cooler. The head is insensitive to cold but sensitive to warmth, feels warmer than the rest of the body in warm environments.⁴⁶

Paracetamol is available in Nigeria as syrups (125mg/5ml), tablets (500mg/tab), injections (300mg/2ml) and suppositories (125mg) and most of them have age based dosing guidelines on the package. Dosage and frequency of administration is important. Most of the mothers (38%) do not know the dosage of paracetamol and usually give some quantity. Quite a number know the dose appropriate for their child and others use the recommended dose on the package insert. Age-based dosing guidelines can lead to inappropriate dosing.⁴⁷ Due to wide variations in children's weight for a given age range, the paracetamol dose may be wrong for underweight or overweight children if the dosage is based purely on the age of the child rather than weight.⁴⁷

A variety of teething mixtures available as over the counter medications also contain paracetamol (120mg – 125mg/5ml) and there are unpublished reports of concomitant use with paracetamol use.

In this study some caregivers usually commence administration of paracetamol syrup but substitute the syrup with tablet form later because of perceived non response to syrup. Tablets contain higher doses and switches to a different formulation that contains a higher dose may predispose the child to toxicity if the tablet is not divided into proportions equivalent to the recommended dose. Absorption of paracetamol usually occurs at a greater rate in children if the syrup form is utilized.^{48,49}

Paracetamol which was readily available at home was given by a few of the women on a daily basis to prevent fever. In a paediatric population, chronic or repeated supra –therapeutic paracetamol ingestion has been

defined as the repetitive ingestion of greater than 90 mg/kg over a 24-hour period.^{48,49}

Paracetamol is generally perceived as a safe drug, and have been demonstrated to be effective at doses between 10-20 mg/kg administered every 4-6 hours.⁴⁹ Children may be relatively protected against hepatotoxicity arising from a single acute dose of paracetamol, however it has been demonstrated that substantial increases in paracetamol serum concentrations occurs following repeated therapeutic doses over 1-3 days. This may explain the apparently higher incidence of toxicity reported after multiple dosing.^{50,51}

Ninety five percent of all respondents were not aware that paracetamol could cause adverse effects while 98% did not know about hepatic toxicity. This finding is very significant in light of a background of inappropriate use of paracetamol in febrile children and there are reports of severe hepatotoxicity and even death resulting from prolonged repeated therapeutic and supra therapeutic dosing.^{48,52,53}

The risk of developing severe toxicity after a single, high dose of paracetamol ingestion however appears to be lower in children than in adults, which may be because of the age-related difference in metabolism.^{30,37} Several studies suggest that children, particularly young children, are more resistant to paracetamol toxicity and the threshold in children for toxicity resulting from a single acute ingestion may be likely 150 mg/kg – 200 mg/kg. There is, however, substantial individual variability and the level of toxicity following repeated doses or chronic administration is unclear.^{54,55}

The pharmacokinetics of paracetamol in children is generally similar to that in adults. The overall plasma elimination of acetaminophen is somewhat slow in the neonate, but is comparable to that of adults in both children and adolescents, as judged by half-life determinations.⁵⁶

This study had some limitations. The study was descriptive and non-interventional and therefore plasma levels of paracetamol and liver function tests were not determined especially in children whom their caregivers used paracetamol frequently and inappropriately.

CONCLUSION

Majority of parents and caregivers who use paracetamol regularly without prescription or guidance have poor knowledge about fever, paracetamol use and its potential dangers, including paracetamol induced liver toxicity. While febrile children enjoy some measure of protection against paracetamol hepatotoxicity, it is

important to educate caregivers of febrile children on appropriate use and potential dangers of inappropriate use of paracetamol. Pharmaceutical companies that manufacture paracetamol for children must put in place a clear and easy to understand risk management plan.

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