

# Accuracy of acetaminophen dosing in children by caregivers in Saudi Arabia

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**BACKGROUND AND OBJECTIVES:** Fever contributes to a significant number of visits by children to the emergency department (ED), where it is often treated with acetaminophen. The objective of this study was to determine if caregivers give children with fever an accurate dose of acetaminophen and determine factors associated with dosing inaccuracy.

**DESIGN AND SETTING:** Cross-sectional study at the ED of a tertiary referral center over a 6-month period (March-August 2008)

**METHODS:** We interviewed 200 caregivers who gave acetaminophen to children with fever in the preceding 24 hours.

**RESULTS:** Of 200 caregivers, 178 (89%) were included in the study. Seventy-six caregivers (43%) gave an accurate dose of acetaminophen, 54 (30%) gave a subtherapeutic dose, and 48 (27%) gave suprathreshold doses. Caregivers who gave accurate doses were more likely to give an acetaminophen dose in less than a 4-hour frequency (risk ratio [RR] 0.63.  $P < .04$ , 95% CI, 0.37-1.07). Patients receiving acetaminophen per rectum had a significantly greater rate of suprathreshold doses than those receiving the drug by mouth (9/28 [32%] versus 39/149 [26%]), respectively (95% CI=0.14 to 0.48). Sixteen caregivers (9%) gave more than five doses per 24 hours (RR, 1.11; 95% CI, 0.74-1.67). Physicians, pharmacists, and parents (the latter with intermediate and secondary levels education) more often gave inaccurate doses, but the differences were not statistically significant suggesting that they may be the source of inaccurate dosing. (RR, 1.29; 95% CI, 0.95-1.75), (RR, 1.27 95% CI, 0.75-2.18), (RR, 1.28; 95% CI, 0.91-1.79), and (RR, 1.20, 95% CI, 0.92-1.57), respectively.

**CONCLUSION:** More than half of caregivers gave an inaccurate dose of acetaminophen to children suggesting that education may be valuable in ameliorating this common problem.

Fever in children is a common and usually benign symptom.<sup>1,2</sup> It is one of the most recognized symptoms of childhood illness, and it is the single vital sign that most parents know. Fever is one of the most common presenting complaints in emergency departments (EDs) and ambulatory clinics, and it is estimated that up to one-third of the pediatric ED visits are attributable to a primary complaint of fever.<sup>3-6</sup>

Acetaminophen is the most widely used antipyretic in both the pediatric and adult populations. It is available in most countries as an over-the-counter drug. It has a well-documented safety record when used in recommended doses. Accurate dosing of acetaminophen is important in alleviating the effects of fever in children. Children are given acetaminophen based on their weight or age as compared to an adult, which increases

the chance of acetaminophen misdosing.<sup>7-10</sup> Several previous studies have shown that caregivers commonly give an inaccurate dose of acetaminophen.<sup>11-16</sup> Underdosing may lead to inadequate management of fever and cause stress to the parents and the ill child. On the other hand, unintentional overdosing of acetaminophen can lead to hepatic damage.<sup>11-16</sup>

We have observed clinically that some children are not given an accurate dose of acetaminophen. We therefore conducted this study to find out whether caregivers in Saudi Arabia give children with fever an accurate dose of acetaminophen, and also to identify factors associated with inaccurate dosing. We were specifically interested in caregivers who were provided with information on acetaminophen dosing, to see whether the source of information related to the accuracy of acetaminophen

dosing. We were also interested in determining if the age and level of education of the caregiver were likely to be associated with accurate dosing of acetaminophen.

## METHODS

This prospective cross-sectional study was conducted over a 6-month period, from March 2008 to August 2008, in the setting of the ED at the King Faisal Specialist Hospital and Research Center (KFSHRC), the biggest tertiary care center in Saudi Arabia. All children younger than 14 years of age, who received a known quantity of acetaminophen for suspected or confirmed fever within the last 24 hours before the ED visit were eligible. Children who received fever medication other than acetaminophen or were given an unknown dose or received acetaminophen for a reason other than fever, and children who were not accompanied by a caregiver were excluded. Verbal consent was obtained from the caregivers before the interview. No caregiver refused to be interviewed. A standardized written questionnaire agreed upon by the research committee was completed first by the principal investigators during their randomized shifts.

The questionnaire gathered the following information: age, sex, weight, the presence of fever, the drug form (oral vs. rectal), brand, dose of oral preparation (tablets of 325 or 500 mg vs. liquids of 100 mg /mL or 160 mg/5 mL), dose of suppository (100, 125, 200, 250, 325 or 500 mg), and frequencies of acetaminophen doses given in the previous 24 hours. The caregivers either demonstrated dosing with their own bottle of the brand or informed the primary investigator how much of the medication was given in each dose.

The following information was asked for each patient:

- Who recommended the given doses?
- Who usually calculated and gave the child acetaminophen?
- What is the age of the caregiver?
- What was the level of education of the caregiver?

Correct dosages were defined as 10 to 15 mg/kg/ose, per mouth or rectum, of acetaminophen, based on previous studies.<sup>17</sup> An acetaminophen dose of >16 mg/kg/dose was defined as suprathereapeutic and <10 mg/kg/dose as subtherapeutic. Approximately 200 patients were needed to detect a 10% difference, with an expected incorrect dosing incidence of 15% and an alpha error of 0.05. The primary end point of the study was to determine the prevalence of an inaccurate dosing of acetaminophen. Data were collected in a Microsoft Excel spreadsheet (Microsoft Corporation, Redmond, WA, USA).

Children who received an accurate dose of medication were compared with children who received an

inaccurate dose of medication. Descriptive statistical analysis, including frequencies, percentages, means, standard deviations, and confidence intervals (CI), was performed using the software package SAS version 9.2 (Statistical Analysis System, SAS Institute Inc., Cary, NC, USA). Risk ratios (RR) were used for the comparison of nominal data. The *t* test was used to test the difference between accurate and inaccurate dose groups for continuous variables, and the chi-square was used for categorical variables. The level of significance was set at  $P < .05$ .

## RESULTS

Of 200 patients studied, 22 were excluded due to incomplete data. Males constituted 96 (48%) of the children with fever. The mean (standard deviation) age of all children was 44.8 (39.3) months and the median and

**Table 1.** Demographic characteristics of caregivers.

Caregiver	Number (%)
Father	14 (7.9)
Mother	151 (84.8)
Nanny	10 (5.6)
Relative	3 (1.7)
<b>Age of caregiver</b>	
<20 years	-
20-30 years	78 (43.8)
30-50 years	98 (55.1)
>50 years	2 (1.1)
<b>Source of information</b>	
Drug labeling	20 (11.2)
Physician	119 (66.9)
Pharmacist	10 (5.6)
Relative	9 (5.1)
Guessing	19 (10.7)
Other	1 (0.6)
<b>Education of caregiver</b>	
Postgraduate	7 (3.9)
University	85 (47.8)
Secondary	43 (24.2)
Intermediate	17 (9.6)
Primary	17 (9.6)
Illiterate	9 (5.1)

range were 28 (1-156) months. The mean weight was 15.9 (10.5) kg and the median and range for weight was 13.3 (3.3-91) kg. Demographic information on caregivers is shown in Table 1. The route of acetaminophen administration was oral in 150 (84%) and rectal in 28 (16%). Of the children who received oral acetaminophen, tablets were administered to five (2%).

Overall, 101 (57%) of the patients received an inaccurate dose of acetaminophen, 50 (30%) received subtherapeutic, and 48 (27%) received supratherapeutic doses of acetaminophen (Tables 2, 3). The mean (SD) age for those accurately and inaccurately dosed was 49.5 (40.0) years and 41.1 (35.6) years, respectively (difference statistically nonsignificant). The mean (SD) weight for those accurately and inaccurately dosed was 16.0 (8.2) kilograms and 15.8 (12.0) kilograms, respectively (difference statistically nonsignificant). Patients receiving acetaminophen per rectum had a significantly greater rate of supratherapeutic doses than those who received it via the oral route 9/28 (32%) versus 39/149 (26%), respectively (95% CI, 14 to 48%). Only one rectal dose was greater than 100 mg/kg (113.3 mg/kg) and no oral dose was greater than 50 mg/kg.

Most caregivers surveyed reported giving medications at appropriate intervals (Table 2); 9% gave more than five doses per 24 hours. Nearly 75% of the caregivers who gave acetaminophen stated that they gave the medication every 4 hours, 14% gave acetaminophen more frequently (at intervals of less than 4 hours), and 11% gave it less frequently (at intervals of more than 6 hours).

Most caregivers (67%) used information from their doctor in deciding how much medication to give, followed by package labeling (11%), guessing (11%), pharmacist's advice (6%), and basing the dose on the advice of a relative (5%). The source of information was not significantly different between patients who received an accurate dose of acetaminophen and those who received an inaccurate dose. When characteristics of caregivers who gave inaccurate doses of acetaminophen were compared with those who gave an accurate doses, those who gave the accurate doses were more likely to space acetaminophen doses at less than a 4-hour frequency and those who gave inaccurate doses were more likely to space the doses at intervals of four-to-six hours. Physicians, pharmacists, and parents (the latter with intermediate and secondary levels education) more often gave inaccurate doses but the differences were not statistically significant suggesting that they may be the source for inaccurate dosing (RR, 1.29%; 95% CI, 0.95-1.75), (RR, 1.27; 95% CI, 0.75-2.18), (RR, 1.28%; 95% CI, 0.91-1.79), and (RR, 1.20. 95% CI, 0.92-1.57), respectively.

**Table 2.** Comparison of factors in patients who received accurate and inaccurate dosing of acetaminophen (n=178).

	Accurate dosing (n=77)	Inaccurate dosing (n=101)			Risk ratio (95% CI)	P
		Supratherapeutic (n=48)	Subtherapeutic (n=53)	Total for inaccurate dosing		
<b>No. of doses in 24 hours</b>						
≤5	71 (40)	46 (50.1)	45 (49.9)	91 (51)	0.89 (0.60 to 1.35)	NS
≥5	6 (3)	2 (20)	8 (80)	10 (6)	1.11 (0.74 to 1.67)	NS
<b>Spacing of doses</b>						
<4 hours	15 (8)	3 (30)	6 (70)	9 (5)	0.63 (0.37 to 1.07)	.04
4-6 hours	51 (29)	42 (51)	41 (49)	83 (47)	1.51 (1.04 to 2.21)	.02
>6 hours	11 (6)	3 (33)	6 (67)	9 (5)	0.77 (0.47 to 1.28)	NS
<b>Caregiver</b>						
Father	5 (3)	3 (33)	6 (67)	9 (5)	1.15 (0.76 to 1.73)	NS
Mother	68 (38)	42 (51)	41 (49)	83 (47)	0.82 (0.61 to 1.12)	NS
Nanny	4 (2)	2 (33)	4 (67)	6 (3)	1.06 (0.63 to 1.79)	NS
Relative	0 (0)	1 (33)	2 (67)	3 (2)	-	
<b>Caregiver age</b>						
<20 years	0 (0)	0 (0)	0 (0)	0 (0)		
20-30 years	33 (16)	23 (51)	22 (49)	45 (25)	1.03 (0.79 to 1.33)	NS
30-50 years	42 (24)	25 (45)	31 (55)	56 (31)	1.02 (0.78 to 1.32)	NS
>50 years	2 (1)	0 (0)	0 (0)	0 (0)	-	NS

## DISCUSSION

This study demonstrated that caregivers frequently gave an inaccurate dose of acetaminophen. Fifty-seven percent of the caregivers in our study gave inaccurate doses of acetaminophen, which is in agreement with the Linder study.<sup>18</sup> Simon and Weinkle found a similar rate of inaccurate doses,<sup>7</sup> although others found both higher<sup>9-20</sup> (68, 47, and 55%) and lower<sup>21</sup> (27%) rates. Clearly, a significant portion of our population gives inaccurate doses of acetaminophen, reflecting lack of knowledge or misuse of the drug on the part of caregivers treat-

**Table 2 (continued).** Comparison of factors in patients who received accurate and inaccurate dosing of acetaminophen (n=178).

	Accurate dosing (n=77)	Inaccurate dosing (n=101)			Risk ratio (95% CI)	P
		Supratherapeutic (n=48)	Subtherapeutic (n=53)	Total for inaccurate dosing		
<b>Reference</b>						
Drug labeling	12 (7)	4 (50)	4 (50)	8 (5)	0.68 (0.39 to 1.18)	NS
Physician	46 (29)	37 (51)	36 (49)	73 (41)	1.29 (0.95 to 1.75)	NS
Pharmacist	4 (2)	1 (17)	5 (83)	6 (3)	1.27 (0.75 to 2.18)	NS
Relative	6 (3)	2 (67)	1 (33)	3 (2)	0.57 (0.23 to 1.46)	NS
Guessing	9 (5)	4 (40)	6 (60)	10 (6)	0.92 (0.59 to 1.44)	NS
Other	0 (0)	0 (0)	1 (100)	1 (1)	-	
<b>Level of education of caregiver</b>						
Postgraduate	6 (3)	0 (0)	1 (100)	1 (1)	0.24 (0.04 to 1.51)	NS
University	39 (22)	24 (52)	22 (48)	46 (26)	0.92 (0.71 to 1.19)	NS
Secondary	15 (9)	9 (32)	19 (68)	28 (16)	1.20 (0.92 to 1.57)	NS
Intermediate	5 (3)	5 (42)	7 (58)	12 (7)	1.28 (0.91 to 1.79)	NS
Primary	8 (5)	5 (56)	4 (44)	9 (6)	0.93 (0.58 to 1.48)	NS
Illiterate	4 (2)	5 (100)	0 (0)	5 (3)	0.96 (0.53 to 1.75)	NS

ing childhood fever.<sup>22</sup> Li et al and Goldman and Scolink found a lower rate of supratherapeutic doses (15 and 12%, respectively) compared to our rate 48%.<sup>7,19,21</sup>

Reasons reported for caregivers giving subtherapeutic doses are the use of inaccurate measurements of a 'teaspoon',<sup>23</sup> parental inability to determine, measure,<sup>24</sup> and administer the appropriate dose,<sup>7</sup> package labeling that gives the dose by age and not by weight, lack of understanding of different antipyretic preparations,<sup>9</sup> and having children who have outgrown a previously recommended dose. Mothers with an education of intermediate and secondary levels were a frequent source for inaccurate dosing, which is inconsistent with what had previously been reported,<sup>25</sup> the difference in accurate and inaccurate doses did not reach a statistical significance. Although Li et al<sup>19</sup> found that subtherapeutic doses were common in younger patients, McErlean et al<sup>20</sup> and our findings did not indicate an association between age and supra- or subtherapeutic dosing.

The findings of this study might be limited by recall bias, as physicians were the major source for inaccurate dosing information, as recalled verbally by the caregivers, without verification. The findings of this study might be limited by recall bias, without verification, physicians were more likely to be the source for inaccurate dosing information, vs. pharmacist or drug labelling.

The main limitation of our study was that a theoretical selection bias might have occurred, because, not all caregivers of febrile children were interviewed. Nevertheless, randomization of the shifts at different times of the day and night, when caregivers were interviewed, could have overcome this possible bias.

Although we used  $\geq 16$  mg/kg as a supratherapeutic dose of acetaminophen, in the pediatric population,

**Table 3.** Acetaminophen dose accuracy and route of administration.

Dose	<10 mg/kg				10-15 mg/kg				>15 mg/kg				
	Route	No. (%)	Mean	SD	Range	No. (%)	Mean	SD	Range	No. (%)	Mean	SD	Range
<b>Oral (n=150, 84%)</b>													
Tablets (n=5, 2%)	1	9.3	-	-	3	11.7	1.3	10.6-13.2	1	16.2	-	-	
Liquid (n=145, 82%)	46	7.1	2.2	3.0-9.8	61	12.6	1.41	10-15	38	21.4	7.2	15.1-45.7	
<b>Rectal (n=28, 16%)</b>	7	6.4	2.6	2.6-9.8	12	12.4	1.15	10.5-13.7	9	34.2	31.5	15.4-113.3	
<b>Total (n=178)</b>	<b>54</b>				<b>76</b>				<b>48</b>				

Mean (SD) and dose range in mg/kg.

doses of 20 mg/kg were very unlikely to cause harm. It took much higher doses of acetaminophen to produce toxicity in children than in adults, which explains why none of our patients suffered complications of overdosing. Inaccurate dosing of acetaminophen is an important issue that ED personnel, pediatricians, family physicians, pharmacists, and public educators should be aware of when educating caregivers about the medical

treatment of febrile children. We recommend intervention programs to educate the caregivers on the appropriate doses of acetaminophen and studying of the effectiveness of these programs.

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