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 supratherapeutic 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 supratherapeutic 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.
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/dose, per mouth or rectum, of acetaminophen, based on previous studies. An acetaminophen dose of >16 mg/kg/dose was defined as supratherapeutic 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)    |

| Age of caregiver | Number (%) |
|------------------|------------|
| <20 years        | -          |
| 20-30 years      | 78 (43.8)  |
| 30-50 years      | 98 (55.1)  |
| >50 years        | 2 (1.1)    |

| Source of information | Number (%) |
|-----------------------|------------|
| 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)    |

| Education of caregiver | Number (%) |
|------------------------|------------|
| 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 dose, 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).

| No. of doses in 24 hours | Accurate dosing (n=77) | Inaccurate dosing (n=101) | Risk ratio (95% CI) | P |
|-------------------------|-----------------------|--------------------------|------------------|---|
| ≤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 |
| Spacing of doses        |                       |                          |                  |        |                |    |
| <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) | 1.15 (1.04 to 2.21) | .02 |
| >6 hours                | 11 (6)                | 3 (33)                   | 6 (67)           | 9 (5)   | 0.77 (0.47 to 1.28) | NS |
| Caregiver               |                       |                          |                  |        |                |    |
| 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)   | -                |    |
| Caregiver age           |                       |                          |                  |        |                |    |
| <20 years               | 0 (0)                 | 0 (0)                    | 0 (0)            | 0 (0)   | 1.03 (0.79 to 1.33) | NS |
| 20-30 years             | 33 (16)               | 23 (51)                  | 22 (49)          | 45 (25) | 1.02 (0.78 to 1.32) | 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. Simon and Weinkle found a similar rate of inaccurate doses, although others found both higher (68, 47, and 55%) and lower (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).

| Reference | Accurate dosing (n=77) | Inaccurate dosing (n=101) | Risk ratio (95% CI) P |
|-----------|------------------------|---------------------------|----------------------|
| **Total for inaccurate dosing** | | | |
| | | | NS |
| 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) | - | - |
| **Level of education of caregiver** | | | |
| 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 |

Table 3. Acetaminophen dose accuracy and route of administration.

| Dose Route | <10 mg/kg | 10-15 mg/kg | >15 mg/kg |
|------------|-----------|-------------|-----------|
| Oral (n=150, 84%) | | | |
| 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 |
| Rectal (n=28, 16%) | 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 |
| Total (n=178) | 54 | 76 | 48 |

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