Effect of Recent Antipyretic Use on Measured Fever in the Pediatric Emergency Department

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Objectives: To determine the prevalence of recent antipyretic use among febrile infants at a pediatric emergency department (ED) and to test the hypothesis that recent antipyretic use is associated with lower measured temperatures in the ED.

Methods: We prospectively enrolled infants younger than 366 days at a pediatric ED. Eligible subjects had a history of fever prior to arrival at the ED or had a measured temperature of 38°C or higher at the ED. Research assistants collected detailed information about recent use of antipyretic drugs. Peak measured temperature prior to arrival at the ED (temperature maximum [Tmax]), measured temperature at the ED, defervescence from Tmax to measured ED temperature, and rates of diagnostic testing were compared between subjects who had or had not been treated with antipyretic medication within the past 6 hours.

Results: We enrolled 474 infants. Infants treated with an antipyretic medication (n=187) had a significantly higher Tmax and a significantly higher measured ED temperature than untreated subjects (n=287) (P<.001). Treated and untreated subjects did not differ in the amount of defervescence from Tmax to measured ED temperature (P=.41) unless treated subjects included only those who reportedly received therapeutic doses of antipyretic medication within 1 to 5 hours prior to arrival at the ED (P=.02).

Conclusions: Although many febrile infants seen in the pediatric ED have recently received antipyretics, only a few have received a therapeutic dose between 1 and 5 hours prior to arrival. Among febrile infants seen in the ED, recent antipyretic use is associated both with a higher reported Tmax and with higher measured temperatures at the ED. Patients treated with a therapeutic antipyretic dose 1 to 5 hours prior to arrival experience more defervescence from their Tmax than untreated subjects.


IN THE TREATMENT OF INFANTS with acute illness, the presence or absence of fever is a cornerstone of clinical diagnosis. The evaluation of many chief complaints (eg, seizure, petechial rash, irritability, or joint swelling) will proceed very differently depending on whether or not fever is present. Simply the presence of fever, in the absence of any other symptoms or signs, frequently leads to the pursuit of a diagnostic evaluation.1

Although physicians routinely inquire about a history of fever prior to the patient’s arrival, clinical guidelines for the treatment of febrile infants and the research data on which these guidelines are based emphasize the use of a precisely measured temperature at the time of arrival for diagnostic decision making.2-4

Antipyretic medications are often used with fevers, and ample data indicate that antipyretics are effective in reducing fever.5-14 If diagnostic decisions about infants with acute illness are based solely on the measured temperature at arrival without considering whether antipyretic drugs have recently been used, some cases of fever may be missed or the true level of the fever may not be appreciated. Some diagnoses of serious infections may be missed as a result. Only limited published data address the question of how recent antipyretic use affects measured temperature when the patient arrives for medical care.15

The goals of this study were (1) to describe the prevalence of recent antipyretic use in febrile infants who came to the emergency department (ED); (2) to assess the association between antipyretic use at home and likelihood of fever at arrival at the ED; and (3) to evaluate the degree of defervescence from the reported peak measured temperature (temperature maximum [Tmax]) to the measured ED temperature. Our primary hypothesis was that recent antipyretic use would be associated with lower temperatures in the ED.

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METHODS

PATIENT SELECTION AND INCLUSION/EXCLUSION CRITERIA

This was a prospective study. The study was approved by the Committee on Clinical Investigation at Children’s Hospital (Boston, Mass). Study participants were a convenience sample of infants who came to the ED at Children’s Hospital, a tertiary care pediatric facility. Subjects were eligible for inclusion if they were younger than 360 days and had either (1) a report by a guardian or physician of a tactile or measured fever prior to arrival at the ED; or (2) a temperature of 38°C or higher (rectal) at arrival at the ED. The parents of potential subjects were approached as they arrived at the triage area of the ED. Attempts were made to consecutively enroll all eligible subjects during designated shifts when research personnel were available. Infants were enrolled between August 24, 2000, and December 1, 2001.

Subjects with no reported or documented fever prior to arrival or while at the ED were excluded. Subjects were also excluded if they visited the ED within 7 days of a prior visit at which they were enrolled or if their medical records were unable to be obtained for the final stages of data analysis after enrollment was completed.

RESEARCH DESIGN AND METHODS

At the time of enrollment, after oral informed consent was obtained, parents of the study subjects were asked to report any antipyretic use within the preceding 6 hours. The medication name, dose, route of administration, and time of administration were recorded by research personnel. The subject’s weight and rectal temperature were measured by an ED triage nurse according to the usual clinical protocol. Rectal temperature was measured using a digital thermometer (Datex Welch Allyn Inc, Skaneateles Falls, NY). In addition, the infant’s medical record from the ED visit was queried for the following data points: (1) presence or absence of tactile or measured fever prior to arrival at the ED; (2) highest temperature measured prior to arrival (if known); (3) tests performed at the ED as part of the evaluation for a febrile illness (including a complete blood cell count and/or blood culture, urinalysis and/or urine culture, cerebrospinal fluid analysis, or chest radiograph); and (4) discharge diagnosis. Medical record abstraction was performed by the first author (S.Y.H.), a board-certified pediatrician, who was not blinded to the study hypotheses. Data were obtained using a standardized data collection form and entered into a database software program.

INTERPRETATION OF DATA

The primary outcome measures were the measured temperature at triage, the presence or absence of fever (temperature ≥ 38°C), and the presence or absence of high fever (temperature ≥ 39°C) at the ED. Comparisons were made for these outcome measures between the group of subjects who had received antipyretics within the past 6 hours and the group of subjects who had not. Continuous variables, such as measured temperature at triage, were compared using an unpaired 2-sample t test. Dichotomous variables (such as the presence or absence of fever) were compared using χ² analysis. The results of t test analyses are reported as mean differences with 95% confidence intervals. The results of χ² analysis are reported as odds ratios with 95% confidence intervals.

As a secondary analysis, for the subgroup of infants for whom we knew the highest measured temperature (Tmax) prior to ED arrival, we evaluated the effect of antipyretic use on those who reportedly had a previous high fever (Tmax ≥ 39°C). The motivation for this subgroup analysis was the supposition that the effect of antipyretic medication might be most evident in the group of patients with high fevers prior to therapy.

As an additional secondary analysis for the subgroup with available Tmax data, we evaluated the effect of antipyretics on the measured defervescence by the time of arrival at the ED. The measured defervescence was defined as the Tmax minus the measured temperature at triage. The mean defervescence in the group that received antipyretic medication was compared with the mean defervescence in the group that did not receive antipyretics using the unpaired t test.

As another secondary analysis, the measured temperature at triage and the magnitude of defervescence were compared for the subgroup of infants who had been given an appropriate dose of an antipyretic between 1 and 5 hours prior to arrival and the group who received either no antipyretic medication or a subtherapeutic dose. For this analysis, we determined a priori that doses of acetaminophen less than 10 mg/kg or doses of ibuprofen less than 7 mg/kg should be considered subtherapeutic. The selection of patients who had received an antipyretic drug between 1 and 3 hours previously was based on the expectation that the antipyretic drugs would have their maximum effect within this interval. Finally, we analyzed the relationship between recent antipyretic use and the performance of diagnostic testing in the ED. Because recommendations for diagnostic evaluation (and usual practice in our ED) differ for children younger than 90 days and those 90 days or older,1–4,7 the evaluation of rates of diagnostic testing was performed separately for these 2 different age groups. Data were analyzed using SPSS version 11.0 for Windows (SPSS Inc, Chicago, Ill).

RESULTS

Study investigators initially approached the parents of 544 infants who had a history of fever at home or a measured fever at arrival at the ED. Of these 544 patients, the parents of 474 (87%) consented to enrollment and had complete ED physician notes available for review. These 474 subjects constitute our study population. The mean age was 186 days with a range of 3 to 365 days; 446 subjects (94%) had a reported fever prior to ED arrival, and 28 (6%) had no reported fever prior to arrival but had a temperature of 38°C or higher at arrival at the ED.

Of our study population, 338 (71%) had a measured temperature of 38°C or higher at the ED, and 147 (31%) had a measured temperature of 39°C or higher at the ED. A review of the infants’ medical records revealed that 312 (66%) had a measured Tmax of 38°C or higher prior to ED arrival, and 120 (25%) had a measured Tmax of 39°C or higher prior to arrival.

A review of discharge diagnoses for the 474 study subjects revealed that 270 (57%) were diagnosed as having either febrile illness or viral syndrome, 37 (8%) otitis media, 30 (6%) upper respiratory tract infection, 27 (6%) gastroenteritis, 24 (5%) bronchiolitis, 18 (4%) urinary tract infection, 15 (3%) meningitis, and 53 (11%) as having other illnesses (including pneumonia, croup, and stomatitis). In total, 195 subjects (41%) reportedly received either acetaminophen or ibuprofen within 6 hours prior to ED arrival, and 150 subjects (32%) were reportedly given acetaminophen at home within 6 hours prior to coming to the ED. Of these 150 subjects, the parents of 111 (74%)


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were able to report the dose of acetaminophen given; those of 59 (39%) reported therapeutic doses of acetaminophen (≥10 mg/kg). The mean ± SD dose of acetaminophen was 10.7 ± 4.2 mg/kg (range, 2.1-25 mg/kg). Of our study population, 45 (9.5%) of 474 reportedly received ibuprofen at home within 6 hours prior to coming to the ED. Of these 45 subjects, the parents of 27 (60%) were able to report the dose of ibuprofen given, and those of 14 (31%) reported therapeutic doses of ibuprofen (≥7 mg/kg). The mean ± SD dose of ibuprofen was 8.4±4.9 mg/kg (range, 1.3-20.4 mg/kg).

As indicated in Table 1, subjects who were treated with an antipyretic drug prior to arrival had a significantly higher mean temperature at arrival at the ED than those who were untreated (P<.001). Among subjects with a documented Tmax prior to ED arrival, those treated with an antipyretic drug also had a higher Tmax than subjects who were not treated (P<.001). For those with available Tmax data, the degree of defervescence from Tmax to ED temperature did not differ between subjects treated with any dose of antipyretic drug within the past 6 hours and untreated subjects (P=.41). However, when analysis was restricted to subjects treated with a therapeutic dose of antipyretic medication between 1 and 5 hours prior to ED arrival, treated subjects were found to have a significantly greater degree of defervescence than untreated subjects (P=.02).

Table 2 includes an analysis of only subjects with a high fever (Tmax=39°C) reported prior to ED arrival. Among this group, no difference in ED temperature was seen between subjects treated with antipyretic medication compared with untreated subjects (P=.64). However, subjects treated with an antipyretic drug prior to ED arrival had a significantly higher reported Tmax than subjects who were not treated (P=.005). Nevertheless, we did not detect a significant difference between treated and untreated subjects in the degree of defervescence from Tmax to ED temperature (P=.43).

To evaluate the effect of antipyretic use on rates of diagnostic testing, subjects were divided by age. As indicated in Table 3, subjects older than 90 days who were treated with antipyretics appear to be more likely than untreated subjects to undergo a urine culture or any form of diagnostic testing (P=.05). No form of testing was significantly less likely to be performed in the group treated with antipyretics. In a similar analysis for the group of younger subjects aged 0 to 90 days, prior antipyretic use was not associated with a difference in the likelihood of any form of diagnostic testing in the ED (P>.05 for all comparisons).

Table 1. Characteristics of Subjects Who Did or Did Not Receive Antipyretics Prior to Arrival

<table>
<thead>
<tr>
<th>Group</th>
<th>Untreated Group (n=287)</th>
<th>Group Treated With Any Dose of Antipyretic Medication (n=187)</th>
<th>Group Treated With a Therapeutic Dose of Antipyretic Medication Within 1 to 5 h Prior to ED Arrival (n=48)</th>
<th>Difference Between Group Treated Therapeutically Within 1 to 5 h and Remaining Patients*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean temperature at triage (95% CI)</td>
<td>38.3°C (38.2 to 38.4)</td>
<td>38.7°C (38.6 to 38.9)</td>
<td>0.4°C (0.3 to 0.6)</td>
<td>38.6°C (38.3 to 39.0)</td>
</tr>
<tr>
<td>Subjects with temperature ≥38°C at triage†</td>
<td>188 (66)</td>
<td>150 (80)</td>
<td>P = .001</td>
<td>35 (73)</td>
</tr>
<tr>
<td>Subjects with temperature ≥39°C at triage†</td>
<td>68 (24)</td>
<td>79 (42)</td>
<td>P&lt;.001</td>
<td>20 (42)</td>
</tr>
<tr>
<td>Subjects with reported Tmax data available from home†</td>
<td>183 (64)</td>
<td>129 (69)</td>
<td>NA</td>
<td>31 (65)</td>
</tr>
<tr>
<td>Mean reported Tmax at home (95% CI)</td>
<td>38.7°C (38.6 to 38.8)</td>
<td>39.2°C (39.1 to 39.3)</td>
<td>0.6°C (0.4 to 0.7)</td>
<td>39.3°C (39.1 to 39.6)</td>
</tr>
<tr>
<td>Mean defervescence (Tmax−triage temperature) (95% CI)</td>
<td>0.05°C (0.39 to 0.71)</td>
<td>0.64°C (0.47 to 0.82)</td>
<td>0.10°C (−0.14 to 0.34)</td>
<td>0.91°C (0.55 to 1.28)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NA, not applicable; Tmax, temperature maximum.
*Data are presented as mean difference (95% confidence interval) or P-value from χ² analysis.
†Data are presented as number (percentage) or P-value from χ² analysis.

COMMENT

We have found recent antipyretic use to be common among infants who come to the ED with a febrile illness, with 40% of our study patients reportedly receiving an antipyretic drug within the past 6 hours. Interestingly, however, only about 10% of our study patients had been treated with therapeutic doses of an antipyretic drug between 1 and 5 hours prior to arrival, an interval that would allow the drugs to have their maximal effect.8,14

In general, we found that febrile infants who had received antipyretics prior to evaluation in the ED had higher fevers at arrival than the group that did not receive antipyretics. This unexpected finding is probably because these same patients had higher fevers at home prior to administration of the antipyretic drug. Furthermore, because approximately three fourths of the patients who had been given an antipyretic drug had either been given a subtherapeutic dose or had been treated less than 1 hour or more than 5 hours earlier, few of the study patients were likely experiencing a substantial effect of the antipyretic drug at the time of arrival. However, even among patients who had been treated with a therapeutic dose of an antipyretic drug between 1 and 5 hours prior to arrival, the ED temperatures were no lower than in untreated subjects.
Our finding that recent antipyretic use is not associated with lower temperatures in the ED is in keeping with the 1 previously published study showing that reported antipyretic use at home did not predict the presence of fever at arrival at the ED. As in our study, this previous publication found that only 47% of patients had actually been treated with a therapeutic dose of the drug. The finding that patients who were recently treated with an antipyretic drug had higher fevers at ED arrival likely explains why these patients appear to be more likely to undergo certain forms of diagnostic testing than subjects not given an antipyretic. Although we were limited by small sample sizes, we found no evidence that patients who were recently treated with antipyretics were less likely to have data regarding the route by which temperatures were measured at home. Furthermore, in the cases in which temperature was previously measured, the temperature measurement was not necessarily within several hours of arrival at the ED. In addition, data for antipyretic dose were based on parental report, which has been shown not to accurately reflect the amount of medication taken. Although we generally found that recent antipyretic drug use was not associated with lower temperatures in the ED, our data support the idea that an infant recently treated with a therapeutic dose of an antipyretic medication may have experienced substantial defervescence prior to arrival. Specifically, our data show that for the small fraction of in-

Table 2. Characteristics of Subjects With Reported Tmax $\geq 39^\circ$C Who Did or Did Not Receive Antipyretics Prior to ED Arrival*

<table>
<thead>
<tr>
<th></th>
<th>Untreated Group (n=56)</th>
<th>Group Treated With Any Dose of Antipyretic Medication (n=64)</th>
<th>Difference Between Treated Group and Untreated Group†</th>
<th>Group Treated With a Therapeutic Dose of Antipyretic Medication Within 1 to 5 h Prior to ED Arrival (n=17)</th>
<th>Difference Between Group Treated Therapeutically Within 1 to 5 h and Remaining Patients‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean temperature at triage (95% CI)</td>
<td>38.8°C (38.5, 39.1)</td>
<td>38.9°C (38.6 to 39.1)</td>
<td>0.1°C (−0.3 to 0.5)</td>
<td>38.8°C (38.1 to 39.4)</td>
<td>−0.1°C (−0.7 to 0.4)</td>
</tr>
<tr>
<td>Subjects with temperature $&gt;38^\circ$C at triage‡</td>
<td>44 (79)</td>
<td>56 (88)</td>
<td>P = .19</td>
<td>12 (71)</td>
<td>P = .13</td>
</tr>
<tr>
<td>Subjects with temperature $&gt;39^\circ$C at triage‡</td>
<td>29 (52)</td>
<td>32 (50)</td>
<td>P = .84</td>
<td>9 (53)</td>
<td>P = .97</td>
</tr>
<tr>
<td>Mean reported Tmax at home (95% CI)</td>
<td>39.6°C (39.5 to 39.7)</td>
<td>39.8°C (39.7 to 40.0)</td>
<td>0.2°C (0.1 to 0.4)</td>
<td>39.8°C (39.6 to 40.1)</td>
<td>0.2°C (−0.1 to 0.4)</td>
</tr>
<tr>
<td>Mean defervescence (Tmax-triage temperature) (95% CI)</td>
<td>0.78°C (0.47 to 1.10)</td>
<td>0.94°C (0.68 to 1.20)</td>
<td>0.16°C (−0.25 to 0.56)</td>
<td>1.04°C (0.44 to 1.64)</td>
<td>0.29°C (−0.26 to 0.85)</td>
</tr>
</tbody>
</table>

Abbreviations: Tmax, temperature maximum. *High temperature constituted a temperature of 39°C or higher. †Data are presented as mean difference (95% confidence interval) or P value from χ² analysis. ‡Data are presented as number (percentage) or P value from χ² analysis.

Table 3. Rate of Diagnostic Testing by Age Among Subjects Who Did or Did Not Receive Antipyretics Prior to Arrival*

<table>
<thead>
<tr>
<th>Diagnostic Test</th>
<th>Subjects Aged 0-90 d</th>
<th>Subjects Aged 91-365 d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Untreated Group (n = 100)</td>
<td>Treated With Any Antipyretic Medication (n = 21)</td>
</tr>
<tr>
<td>CBC count</td>
<td>89 (89)</td>
<td>18 (86)</td>
</tr>
<tr>
<td>Blood culture</td>
<td>77 (77)</td>
<td>15 (71)</td>
</tr>
<tr>
<td>Any blood test</td>
<td>89 (89)</td>
<td>18 (86)</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>81 (81)</td>
<td>17 (81)</td>
</tr>
<tr>
<td>Urine culture</td>
<td>76 (76)</td>
<td>15 (71)</td>
</tr>
<tr>
<td>Lumbar puncture</td>
<td>73 (73)</td>
<td>15 (71)</td>
</tr>
<tr>
<td>Chest radiograph</td>
<td>20 (20)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Any workup</td>
<td>92 (92)</td>
<td>19 (90)</td>
</tr>
</tbody>
</table>

Abbreviations: CBC, complete blood cell; CI, confidence interval; OR, odds ratio. *Data are presented as number (percentage) unless otherwise indicated.

In our study, we were limited by incomplete information about the level of fever and the use of antipyretics at home. Many parents were unable to report a measured temperature prior to arrival at the ED. Even for those who did report a measured temperature, the temperatures reported may not have been accurate. Previous data suggest that parents are not reliably able to use home thermometers accurately. We were also limited because we did not have data regarding the route by which temperatures were measured at home. Furthermore, in the cases in which temperature was previously measured, the temperature measurement was not necessarily within several hours of arrival at the ED.
There are limited published data regarding the effect of recent antipyretic use on measured temperature at the time of arrival for clinical care. Our study of infants with fever seen in the pediatric ED that patients recently treated with antipyretics have higher temperatures at arrival than untreated patients. This finding likely reflects the fact that antipyretic drugs are more commonly given to children with higher fevers. The small fraction of patients who have been treated with a therapeutic dose of an antipyretic drug between 1 and 5 hours prior to arrival have a greater degree of defervescence from the reported Tmax than untreated subjects.

Although many febrile infants seen in the pediatric ED have recently received antipyretics, only a few have received a therapeutic dose between 1 and 5 hours prior to arrival. Among febrile infants seen in the ED, recent antipyretic use is associated both with a higher reported Tmax and with higher measured temperatures at the ED. Patients treated with a therapeutic antipyretic dose 1 to 5 hours prior to arrival experience more defervescence from their reported Tmax than untreated subjects.

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