Palatability of Oral Antibiotics Among Children in an Urban Primary Care Center

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Objective: To evaluate the palatability of antimicrobial agents effective against β-lactamase–producing bacteria in American children.

Design: In a taste test of 4 antimicrobial agents, azithromycin (cherry flavored), cefprozil (bubble gum flavored), cefixime (strawberry flavored), and amoxicillin–clavulanic acid (banana flavored) were compared.

Setting: An urban inner-city primary care clinic.

Subjects: A volunteer sample of 30 healthy children (aged 5-8 years).

Intervention: Palatability was determined using a single-blind taste test of 4 flavored antimicrobial agents. The 4 antimicrobial agents used were azithromycin, cefprozil, cefixime, and amoxicillin–clavulanic acid.

Main Outcome Measures: After each antimicrobial test dose, subjects rated the taste on a 10-cm visual analog scale incorporating a facial hedonic scale. Preference assessments for the best-tasting and worst-tasting agent were also conducted.

Results: Of the 20 children who expressed a preference, significantly more children (9 [45%], P<.05) selected the cefixime preparation as the best-tasting formulation compared with the other preparations. The cefixime preparation was also significantly the least likely to be selected as the worst-tasting preparation (2 [10%], P<.05). There were no significant differences between the other 3 preparations with respect to being selected as either the best or worst tasting. The mean (±SD) visual analog scale score for cefixime was highest (8.53 [2.49]) compared with the scores for azithromycin (6.78 [3.45]), cefprozil (6.26 [4.04]), and amoxicillin–clavulanic acid (6.24 [4.01]).

Conclusion: The cefixime preparation was most commonly rated as best tasting by children.


Editor’s Note: Isn’t it lucky for the grant-supporting company that the study resulted as it did? I guess they had great confidence in their product.

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In the past decade there has been an explosion in the number and variety of antimicrobial agents available for the treatment of infants and children. In some cases, antimicrobial selection is relatively simple, as there are clear guidelines for agents of first choice. In other circumstances, in which there are numerous agents with no clear therapeutic advantage, the situation is more complex.

When there are several alternative agents of comparable efficacy, other factors may come into play to determine which agent would be optimal in a given setting. Some of these factors include safety, cost, ease of administration, and palatability of the preparation. Both ease of administration, in terms of number of daily doses required, and palatability are believed to be important determinants of compliance.

There have been few studies examining the issue of palatability of antimicrobial agents designed for infants and children. This lack of studies may be partially owing to the difficulty in developing methods to determine differences as rated by children. We have demonstrated that it is possible to compare palatability of antimicrobial agents with different flavors among children by using a visual analog scale, which is a standard tool for quantification, modified by including a facial hedonic scale.
SUBJECTS, MATERIALS, AND METHODS

SETTING

The study was conducted in the General Pediatrics Clinic of the Department of Pediatrics, Children's Hospital of Michigan, Detroit. This is a group practice serving an area adjacent to the urban core of Detroit. Subjects were recruited by a research nurse from patients coming for routine clinic visits (n = 14) and from healthy children of employees (n = 16). A $20 gift certificate to Barnes & Noble Bookstore was awarded to each participant. The sample size of 30 is appropriate for this type of study.

DETERMINATION OF PALATABILITY

Palatability was determined by administering a single-blind taste test of 4 flavored antimicrobial agents to 30 healthy volunteer children. Exclusion criteria for the study included known hypersensitivity to any of the antimicrobial agents being studied, being treated with antimicrobial medication, clinical suspicion of infection, or the presence of a medical condition that would contraindicate the administration of 1 of the 4 antimicrobial agents.

The 4 antimicrobial agents used were azithromycin (cherry-flavored Zithromax, 200 mg/5 mL; Pfizer Pharmaceuticals, New York, NY), cefprozil (bubble-gum–flavored Cefzil, 125 mg/5 mL; Bristol-Myers Squibb, Wallingford, Conn), cefixime (strawberry-flavored Suprax, 100 mg/5 mL; Wyeth-Ayerst, Philadelphia, Pa), and amoxicillin–clavulanic acid (banana-flavored Augmentin, 125 mg/5 mL; SmithKline Beecham Pharmaceuticals, Philadelphia). Only 4 different antimicrobial agents were used because it was anticipated that testing of a larger number of agents would result in taste fatigue.

Each child was given 2.5 mL of each antimicrobial agent in a plastic medication cup by the research nurse or the principal investigator. The antimicrobial agent was identified to the child by letter only. The antimicrobial agents were presented in a balanced, randomized order as determined by arrangement in a Latin square.

No food or drink was allowed for 1 hour before the study and no attempt was made to disguise the appearance of the different preparations. Between tastings of the various formulations, the children were given a cracker to eat and were asked to rinse their mouths with water and swallow to remove any residual taste from the previous antibiotic.

Immediately after each test dose, the child was asked to rate the taste on a previously described, modified 10-cm visual analog scale incorporating a facial hedonic scale (Figure). In addition, at the end of the session the children were asked which antimicrobial formulation they thought tasted the best and which tasted the worst. Overall taste was assessed, as it was thought that children of this age would be too young to record aftertaste and texture.

Data were recorded by the research nurse or the principal investigator, whoever had administered the drugs. Any adverse events occurring during the study were recorded.

ETHICS

The study was approved by the Human Investigation Committee, Wayne State University, Detroit. Informed consent was obtained from parents or guardians and assent was obtained from all children.

RESULTS

The children enrolled in the study were aged 6 years on average, with an age range from 5 to 8 years (Table 1). Approximately equal numbers of boys and girls were recruited. The children were predominantly African American, reflecting the population served by the General Pediatrics Clinic.

The results of the taste testing with respect to the agents selected as best and worst tasting are presented in Table 2. When asked which antimicrobial preparation they preferred, 20 of the 30 subjects expressed a preference. The agent most commonly selected was cefixime (P < .05); 9 (45%) of the children selected this agent as best tasting, while roughly equivalent numbers of children selected 1 of the other 3 agents as best tasting (Table 2). Significantly more children selected cefixime, while there was no difference between the other 3 agents. The converse applied with respect to the worst-tasting agent: While roughly one third of the children selected each of the other 3 antimicrobials as worst tasting, only 2 (10%) selected cefixime as the worst-tasting agent (P < .05, F3 = 2.58). This was confirmed by the visual analog scale score assigned to each of the antimicrobials (Table 3).

The visual analog scale score assigned to cefixime was higher than the average visual analog scale score assigned to the other 3 agents (8.53 vs 6.43). The order of presentation did not have an effect on the selection of an agent as best or worst tasting. The remaining 10 children stated that “all” were best tasting and “none” were worst tasting. There were no sex differences. No adverse effects were noted during the study.

COMMENT

The problem of nonadherence to therapy has recently been identified as a major cost to the health care system and is a major source of morbidity and, for some common and important problems, mortality. The problem is compounded by several factors, including the fact that parents typically administer medication to children, the formulations are often by necessity liquid, and many activities that children are involved in (such as school or day care) do not allow for ease of medication administration. As
part of the complex equation determining compliance among infants and children, the issue of palatability of the medication preparation becomes of much greater importance than is the case among adults.

We have previously demonstrated that there are considerable differences in the palatability of different antimicrobial agents used for staphylococcal infections. In that study, we demonstrated the following: First, children as young as 5 years can reliably evaluate palatability when a visual analog scale is combined with a facial hedonic scale. Second, there was a clear preference for noncloxacillin preparations among the children in that study. Third, there were differences between the taste preferences of children and adults. Although this last finding is of intuitive sense to pediatricians, there have been very few data on this with respect to the issue of palatability of preparations for children. This strongly supports the role of testing of palatability for products intended for use among infants and children, using children as the subjects studied.

Among the limited studies of palatability of antimicrobial agents performed on children to date, there are certain key issues that limit the generalizability of these findings to urban American children. Most studies have been performed on non-American white children. Ethnocultural variations in taste preferences are well known. Therefore, products being evaluated for use among American children should be evaluated, as much as possible, among American children with an appropriate representation of diverse ethnic groups.

The current study was designed to address this issue by using a group of antimicrobial agents for which controversy exists as to which might be most effective against infections involving β-lactamase–producing bacteria. An urban primary care center serving a representative population in a large American city was chosen as the study site, while all the formulations selected were those now being marketed in the United States.

This study has demonstrated that a single agent (cefixime) was significantly more likely to be selected as best tasting by the children, while the other 3 agents (azithromycin, cefprozil, or amoxicillin–clavulanic acid) were equally likely to be selected as best tasting by the remainder of the children. Given the fact that many antimicrobial agents have been shown to be effective in the treatment of infectious problems among infants and children, factors other than efficacy clearly must be important in the selection of the agent of choice for a particular child. These factors include ease of administration, timing of doses, cost, and palatability. Cefixime was the antimicrobial agent most highly rated by children in this study. The current study, which was conducted in an urban primary care clinic with American children, may be useful in the selection of antimicrobial agents in conjunction with the other factors described earlier.

Our study has demonstrated the utility of palatability assessment using the modified visual analog scale combined with a facial hedonic scale. The children studied were primarily African American, a group that historically has been understudied in new drug development. This suggests that the evaluation of palatability using techniques such as those employed here would not only be feasible, but also should be part of the routine strategy in the development of formulations intended for use among infants and children.

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REFERENCES


