PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

eLetters is an online forum for ongoing peer review. To submit an eLetter please go to the article you wish to respond to and click on the link that reads "eLetters: Submit a Response." Submission of eLetters are open to all health care professionals and experts in related fields.

eLetters to:

ARTICLES:
Florence T. Bourgeois, Kenneth D. Mandl, Clarissa Valim, and Michael W. Shannon
Pediatric Adverse Drug Events in the Outpatient Setting: An 11-Year National Analysis
Pediatrics 2009; 124: e744-e750
[Abstract] [Full text] [PDF]

eLetters: **Submit a response** to this article

eLetters published:

▼ **Adverse drug reactions to antibiotic use in young children**
Shih-Wen Huang, N/A (2 November 2009)

Adverse drug reactions to antibiotic use in young children

2 November 2009

Shih-Wen Huang, M.D.
University of Florida, Department of Pediatrics,
N/A
Send letter to journal:
Re: Adverse drug reactions to antibiotic use in young children
E-mail Shih-Wen Huang, et al.

Letter to the Editor:

We read with interest the article entitled "Pediatric Adverse Drug Events in the Outpatient Setting: An 11-Year National Analysis" by Bourgeois et al. (Pediatrics. 2009;124:e744–e750).1 The authors reported a spectacular number of clinical and emergency room visits related to adverse drug events (ADEs) in children. They stated in their discussion (and showed in Figure 1) that children 0 to 4 years old made up the majority of ADE patients, with 13.2 visits per 1000 persons. Of these, 56% presented with dermatologic symptoms, suggesting that a large number of the reactions were allergic in nature. Figure 1 in the paper showed that antimicrobial agents were most often responsible for the ADEs, and, although the authors did not state it implicitly, they seemed to strongly imply that ADEs in that age group, as evidenced by reports of skin rash, were largely due to sensitivity to antimicrobials. They concluded that age -specific approaches for monitoring and preventing ADEs may be most effective.

While we agree with their conclusion, we disagree that ADEs in children between 0 and 4 years of age are largely the result of sensitivity to antibiotics. The results of our earlier study of skin rashes related to antibiotic use in young children2 do not support this contention. In that study, we reported on 86 consecutive children presenting at our allergy clinic over a period of 5 years,2 80% of whom were under the age of 3. All of the patients had taken antibiotics in the form of a liquid suspension; the majority had taken either penicillin or cephalosporin. The onset of skin rash normally occurred within 3 to 5 days after ingesting the suspension. Twenty percent of the patients had never taken antibiotics in the past, but, interestingly, 33% of them had a history of reactions to the dyes contained in drugs or drinks.

In our study, the results of both skin test and RAST were negative for drugs. The patients were then given an oral challenge of a dye-free antibiotic suspension or

antibiotic suspensions.

Furthermore, the skin rashes of the patients upon presentation at our clinic were mostly bright erythema; a few had urticaria. We also observed that the majority of our children did not look ill in spite of the presence of extensive skin rashes.2 These clinical features are in sharp contrast to those typically seen with drug allergies, in which intolerable pruritus, irritability, and loss of quality of life (e.g., poor sleep or poor appetite) are the norms.

In considering other diagnoses, we initially speculated that the drug -related rashes were related to viral exanthem; however, we found that not all of the patients had viral illness. We then suspected that perhaps excipients such as dyes, flavorings, or preservatives in the suspension were the cause; however, patients later tolerated the dyes contained in the original drugs. We then wondered whether the skin reactions could have been due to a transient biochemical changes. Studies by Buhl et al.3 and Andre et al.4 had proposed this new hypothesis in trying to explain reports of rashes found in many HIV patients given sulfa drugs for the prevention or treatment of Pneumocystitis carinii. While they were unable to confirm that the rashes were due to sensitivity to the drugs, the authors also measured the blood level of glutathione (GSH), and found that patients with skin rashes had a significantly lower level of GSH. GSH is known to be a powerful antioxidant that serves as a scavenger of toxic, reactive metabolites created by drugs or excipients such as dyes, but its levels can fluctuate during periods of stress such as during an infection. The authors concluded that the rashes seen after sulfa drug use were likely due to a transient state GSH deficiency.

In our study, 17 of 28 (61%) patients had GSH levels below two standard deviations of the mean of the value for normal adults at the peak of infection. Since they later were able to tolerate dyes or food colorings after they fully recovered from infection, we believe that similar transient GSH deficiencies might have occurred in the children who developed rashes during treatment with antimicrobial suspensions.

It would be interesting to know if the cases presented by Bourgeois et al. had similar levels of GSH, especially those in the same age group. We agree that all patients who present with skin rashes related to drugs require a careful workup that includes oral challenge. If the reactions are found to be the result of sensitivity to excipients such as dyes, then a dye-free, compounded form of the drug should be substituted instead of abandoning the useful antimicrobials altogether. These efforts will not only result in better patient care, but will also help to reduce medical costs significantly.

References 1. Bourgeois FT, Mandl KD, Valim C et al. Pediatric drug events in the outpatient setting: An 11-year national analysis. Pediatrics 2009;124:e744–e750. 2. Huang SW, Borum PR. Study of skin rashes after antibiotic use in young children. Clin Pediatr. 1998;37:601–608. 3. Buhl R, Jaffe HA, Holroyd KJ, et al. Systemic glutathione deficiency in symptom- free HIV-seropositive individuals. Lancet. 1991;ii:431–433. 4. Andre JAM, Ven VD, Kooperman PP, et al. Adverse reactions to cotrimoxazole in HIV Infections. Lancet. 1991;ii:431–433.

Conflict of Interest:
None declared