therapy for food allergy are ongoing in the United States and Europe.

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Specific Oral Tolerance Induction in Children With Very Severe Cow’s Milk-Induced Reactions

PURPOSE OF THE STUDY. To evaluate the safety and efficacy of specific oral tolerance induction for children with severe cow’s milk protein (CMP) allergy.

STUDY POPULATION. The study included 97 children (aged 5 to 17 years) with a history of severe allergic reactions and CMP-specific immunoglobulin E (IgE) levels of >85 kU/L.

METHODS. All subjects underwent a double-blind, placebo-controlled food challenge (DBPCFC) starting with very low amounts of diluted milk. Children were considered eligible for random assignment only if they had symptoms during the DBPCFC to the lowest doses (0.8 mL of whole milk). Sixty had positive test results and were randomly assigned to 1 of 2 groups: group A started the specific-oral-tolerance-induction protocol immediately after the DBPCFC; and group B maintained a milk-free diet for 1 year and then underwent another DBPCFC. CMP-specific IgE levels were obtained at enrollment and at 6 and 12 months. Subjects in group A were monitored as inpatients for 10 days during rapid, daily increases in milk dosage and then discharged from the hospital with instructions for increasing milk ingestion to a final goal of 150 mL per day. Once on 150 mL, subjects were instructed to add dairy products to their diet.

RESULTS. After 1 year, 11 (36%) of 30 children in group A were tolerant to the highest dose of 150 mL of cow’s milk per day with some ingesting additional dairy products, thus allowing them an unrestricted diet. Sixteen (54%) could take limited amounts of milk (5–150 mL), and 3 (10%) were not able to complete the protocol because of persistent respiratory and abdominal complaints. CMP-specific IgE levels measured in group A at 6 and 12 months showed a significant decrease in 15 of 30 subjects. In subjects in group B, DBPCFC results were positive with only minimal amounts of milk in all 30 cases, and only 2 subjects showed a decrease in specific IgE levels. Clinical differences between the groups were significant (P < .001). Adverse reactions were common among the subjects in group A, with multiple subjects requiring treatment throughout the protocol. It is interesting to note that 20% of the subjects in group B had adverse reactions after accidental exposure to CMP.

CONCLUSIONS. Specific oral tolerance induction is effective in a significant number of patients with severe cow’s milk allergy.

REVIEWER COMMENTS. Oral desensitization is a novel form of immunotherapy that is under investigation for food allergy, with benefits noted in several clinical studies. Unlike previous studies, this study addressed oral desensitization in children with very severe cow’s milk allergy. The authors noted their success among the subjects studied but were also quick to point out the number of adverse events that occurred when using their protocol. These results are encouraging for patients who suffer from food allergy but highlight the need for additional studies before implementation in clinical practice and the need for close monitoring in highly controlled settings.

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ANAPHYLAXIS

Platelet-Activating Factor, PAF Acethylhydrolase, and Severe Anaphylaxis

PURPOSE OF THE STUDY. To characterize the roles of platelet-activating factor (PAF) and PAF acetylhydrolase, the enzyme that inactivates PAF, in humans.

STUDY POPULATION. The population was a variety of pediatric and adult patients with different levels of allergic disease along with nonallergic controls.

METHODS. Serum PAF levels and activity of PAF acetylhydrolase were measured in 41 patients with anaphylaxis and in 23 control patients. Serum PAF acetylhydrolase activity was also measured in 9 patients with fatal anaphylaxis who had peanut allergy and compared with that in 26 nonallergic pediatric control patients, 49 nonallergic adult control patients, 63 children with mild peanut allergy, 24 patients with nonfatal anaphylaxis, 10 children who died of nonanaphylactic causes, 15 children with life-threatening asthma, and 19 children with non–life-threatening asthma.

RESULTS. Mean serum PAF levels were significantly higher in patients with anaphylaxis than in patients in the control groups and were correlated with the severity of anaphylaxis. The proportion of subjects with elevated
PAF levels increased from 4% in the control groups to 20% in the group with grade 1 anaphylaxis, 71% in the group with grade 2 anaphylaxis, and 100% in the group with grade 3 anaphylaxis. There was an inverse correlation between PAF levels and serum PAF acetylhydrolase activity. The proportion of patients with low PAF acetylhydrolase activity increased with the severity of anaphylaxis. Serum PAF acetylhydrolase activity was significantly lower in patients with fatal peanut anaphylaxis than in control patients.

CONCLUSIONS. Serum PAF levels were directly correlated and serum PAF acetylhydrolase activity was inversely correlated with the severity of anaphylaxis. PAF acetylhydrolase activity was significantly lower in patients with fatal anaphylactic reactions to peanuts than in patients in any of the control groups. Failure of PAF acetylhydrolase to inactivate PAF may contribute to the severity of anaphylaxis.

REVIEWER COMMENTS. PAF is 1 of the proinflammatory mediators that are released systemically by the degranulation of mast cells and basophils. Although PAF is not the only mediator that plays a role in anaphylaxis, these results suggest that PAF is very important. Therefore, it may be useful to develop new pharmaceutical agents that block its actions. Additional research is also needed to determine if PAF and PAF acetylhydrolase measurements may be used as a screening tool to select patients at highest risk for fatal anaphylaxis.

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DRUG HYPERSENSITIVITY

Drug Allergy Claims in Children: From Self-reporting to Confirmed Diagnosis

PURPOSE OF THE STUDY. To assess the prevalence of self-reported adverse drug reactions and drug allergy in a pediatric population and confirm the diagnosis in children with suspected drug allergy.

STUDY POPULATION. Patients (n = 1426) responded to an initial cross-sectional survey. A total of 60 of 67 patients with reported drug allergy were evaluated at an allergy clinic.

METHODS. The first phase included a cross-sectional survey that assessed the life occurrence of adverse drug reactions and self-reported drug allergy in the outpatient clinic of a pediatric hospital. The second phase involved a diagnostic workup in children with parent-reported drug allergy, including detailed clinical history and in vitro and in vivo investigations. Specific immunoglobulin E (IgE) level determination for β-lactams, prick and intradermal skin testing for β-lactams, local anesthetics and sulfonamides, and patch tests (if a delayed reaction was reported) were performed. If all other investigations were inconclusive and a provocation test was not contraindicated, this test was performed.

RESULTS. The prevalence of self-reported adverse drug reactions and drug allergy were 10.2% and 6.0%, respectively. The frequency of a medical diagnosis of drug allergy was 3.9%. The majority of the suspected allergic reactions were nonimmediate cutaneous events attributed to β-lactam antibiotics in younger children. Of 60 patients evaluated in the allergy clinic, 39 patients had a plausible clinical history, and additional investigation including a skin test, IgE-level measurement, and possible provocation tests were conducted. Drug allergy was diagnosed in 3 children on the basis of positive responses in skin (n = 1) and oral provocation (n = 2) tests.

CONCLUSIONS. Although adverse drug reactions and suspected drug allergy are frequently reported in children, after a complete evaluation, only a few of these reactions can be attributed to immediate and nonimmediate drug allergy. Overall, 94% of the patients could tolerate the initially suspected drug.

REVIEWER COMMENTS. This study underscores a serious problem: patients who experience or perceive a drug reaction are often classified as being truly allergic when this may not be the case. Such overdiagnosis and misdiagnosis may result in suboptimal medication choices. These results show that only 6% of the patients with initially suspected drug allergy were truly allergic. This study demonstrates the importance of a complete and detailed history, with consideration of additional testing including skin-prick tests, specific IgE-level determination, and provocation tests. It should be noted that for nonimmediate drug allergy, an oral provocation test may require prolonged treatment to observe for symptoms. Such provocation tests would not be undertaken for severe previous reactions (eg, toxic epidermal necrolysis).

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HLA-B*5701 Screening for Hypersensitivity to Abacavir

PURPOSE OF THE STUDY. Abacavir is associated with severe and potentially life-threatening hypersensitivity reactions in up to 8% of the white population. In 2002, HLA-B*5701
Platelet-Activating Factor, PAF Acetylhydrolase, and Severe Anaphylaxis
Brian A. Smart

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