T.J. is a seven-year-old boy who was diagnosed with asthma at three years of age. His asthma is of moderate severity and is well controlled with medications most of the time, although he has occasional (two or three times per year) exacerbations requiring a visit either to his physician or to the emergency room. Otherwise he is healthy, attends school regularly, and participates in age-appropriate sports. T.J.'s asthma medications include daily use of a corticosteroid inhaler and use of a bronchodilator inhaler as needed for worsening of his asthma symptoms or before physical exertion.

T.J. and his parents have been approached about his participation in a clinical study of a new medication for asthma to assess its safety and efficacy in treating children with asthma. This medication is taken as a flavored chewable tablet once daily by mouth and works by a totally different mechanism than the inhaled medications T.J. currently is taking. It has not yet been studied in children, but three studies have been completed in 550 adult patients with asthma. The preliminary evidence from the adult studies is that the new experimental drug does improve asthma in some patients and has very few side effects. The side effects so far in adults have been limited to occasional nausea, headache, and dizziness. However, these side effects occurred at about the same frequency in adults whether they were taking the experimental drug or a placebo.

If T.J. participates in this study, he will be on the study protocol for a total of fourteen weeks. During the first two weeks he will be stabilized on his standard therapy to assure he is well controlled at the time he enters the experimental phase. During weeks three through fourteen, he will be randomized to receive either his standard treatment, the experimental drug plus the bronchodilator inhaler as needed, or a placebo plus his bronchodilator inhaler as needed. Neither T.J., his parents, or his doctor will know which medication he is receiving during the study. In other words, the study is blinded. While he is on the study, he may not use any drugs for asthma other than those mentioned above. He will be seen at regular and frequent intervals during the study to assess his response to treatment and evaluate for any adverse events. This evaluation will require six additional visits to the physician's office. Along with other safety monitoring, he will be evaluated for linear growth, bone metabolism, and any eye lens abnormalities (some drugs are associated with formation of cataracts). During each office visit, breathing tests will be done and blood will be drawn for safety laboratory tests and to measure the amount of study drug in his blood.

T.J.'s family will not be responsible for the costs of the study-related office visits or testing. All medications will be provided free of charge. In addition, transportation costs for the required office visits will be covered. In addition, T.J. will receive $40 for each office visit — a total of $240 if he completes the entire protocol.

The details of the study have been explained to T.J. and his parents and they have been asked if they and T.J. will agree for him to enroll in this study

Case Study

Clinical Research Involving Children

Case and discussion questions by Ralph E. Kauffman, MD

Discussion

Questions

- What are the possible risks (if any) to T.J. if he were to enroll in this study?
- What are the possible benefits (if any)? To T.J.? To his parents? To other children with asthma?
- What are the risks of not including children in research?
- Since T.J. is only seven years old, he is not allowed by law to independently consent to medical care or agree to be in a study. What right do his parents have to volunteer him to be in a clinical trial? What are their responsibilities if they choose to do so? If they choose not to?
- What rights does T.J. have? Should he have the right to volunteer even if his parents refuse their permission? Should he have the right to refuse even if his parents agree for him to be in the study?
- Can it be ethically justified to withhold medications from a child for conducting a study?
- Can the use of placebos be ethically justified in research involving children? If so, under what circumstances?
- If T.J. were your child, would you give permission for him to be in this study?

Selected Reading

American Academy of Pediatrics Committee on Drugs. 1995. "Guidelines for the ethical conduct of studies to evaluate drugs in pediatric populations." *Pediatrics* 95:286-294.

Kauffman, R.E. 1994. "Drug Trials in children: Ethical, legal, and practical issues." *Journal of Clinical Pharmacology* 34:296-299.

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