Stimulant-Drug Therapy for Attention-Deficit Disorder (With or Without Hyperactivity) and Sudden Cardiac Death
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Stimulant-Drug Therapy for Attention-Deficit Disorder (With or Without Hyperactivity) and Sudden Cardiac Death

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Things just get “curiouser and curiouser.”

Alice in Wonderland, Lewis Carroll

Alice’s Remark as she visited wonderland is quite applicable to the rapidly changing medical knowledge base. The more we know, the more questions that occur, and this “quest for truth” is daunting. This is a daily element of clinical decision-making in a busy practice, face to face with patients and parents. This is particularly true when addressing the area of drug therapy for attention-deficit disorder with or without hyperactivity [ADD(H)].

Over the past 2 years, there has been a lot of information on this topic. Parents are aware of the emotionally charged aspects of ADD(H) therapy through the rapid access of information from all forms of media. They are raising important questions regarding the safety of use of the stimulant class of drugs for treating ADD(H). The recent concern of sudden cardiac death in patients who are taking these drugs is certainly worth evaluation. What follows is a brief synopsis of the clinically relevant, best evidence-based aspects of this issue.

Sudden cardiac death occurs at an estimated rate of 1.3 per 100,000 patient-years in the pediatric population.1 It is often assumed under conditions of an unexplained, unexpected death in an otherwise presumed healthy person. Although an autopsy can help with the diagnosis, the diagnosis is still sometimes presumed in the absence of direct evidence of heart disease. Until better pathologic markers are available, the diagnosis of sudden cardiac death carries with it some uncertainty.

Within the last 5 years, the risk for sudden cardiac death in patients on methylphenidate therapy for ADD(H) has been estimated to be 0.22 deaths per 1 million prescriptions and, for amphetamines, 0.56 deaths per 1 million prescriptions (the total number of deaths was 25).2 It is not possible to compare this directly to the estimate for sudden cardiac death shown above.

It is clear that there is a benefit from drug treatment for ADD(H). Results of a large study comparing closely monitored drug therapy alone, intensive standardized behavior therapy alone, drugs and intensive behavioral therapy, nonstandardized behavioral therapy alone, and nothing clearly showed that for ADD(H) symptoms, combined intensive standardized behavioral therapy and drug treatment was no better than drug therapy alone.3 Both of these categories of therapy were better than all others, with standardized behavioral therapy following next, and nonstandardized behavioral therapy being only slightly better than nothing.3

In deciding on therapy for ADD(H), the long-term negative outcomes associated with untreated ADD(H) are important to recognize. In addition to struggling with school performance, social-interaction problems leading to low self-esteem and even depression (potentially with suicide), impulsive behavior leading to increased risk-taking behavior resulting in morbidity and mortality.

Abbreviation: ADD(H), attention-deficit disorder with or without hyperactivity

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and substance abuse and its associated adverse health effects are all associated with untreated ADD(H). It is also clear that patients who are treated medically for ADD(H) have not only improvement in school performance but also improvement in the above-mentioned social and behavioral areas including a reduction in substance abuse risk.

Recent meetings occurred in spring 2006 in Washington, DC, with members of the US Food and Drug Administration’s Pediatric Advisory Committee to evaluate the risk of treatment of ADD(H) with stimulant drugs. The outcome of these meetings was that there would not be a black-box warning on stimulant drugs for ADD(H) therapy but an increased awareness of the concern by labeling and a recommendation to refrain from prescribing these drugs to children with known structural heart disease.

Where does all of this leave the practicing pediatrician? Like many clinical issues, as good as the clinical evidence is, it will not answer every question facing the clinician. We derive clinical therapeutic information from the best evidence available, usually a well-designed clinical trial or, in the case of adverse outcomes, epidemiologic information. The physician must assess as best as possible how these population-derived data are to be used to make decisions about individual patients. No therapy is risk free, and how risk is assessed can be quantitated, but the value of the risk/benefit of therapy is determined by thoughtful consideration by the physician and parents or patient, as the case may be. Jellinek wrote a very good article in the May 2006 issue of Pediatric News to address this point.

What is central in decision-making is having the best available scientifically derived evidence, understanding its limits and strengths, and then applying that to a given clinical situation as best as possible. This approach should be tempered within the context of individual patient circumstances. This is what “clinical judgment” really means.

In the specific case of stimulant drugs for ADD(H), it would seem that the risk for sudden cardiac death is very low and the benefits of therapy, after an appropriate, thoughtful evaluation, outweigh the risks in otherwise healthy patients. The long-term benefits of treating ADD(H) seem to outweigh the risks. Members of the American Academy of Pediatrics who are experts in the field have critically developed a set of practice guidelines for the evaluation and treatment of ADD(H). These guidelines represent the best evidence available to guide the clinician.

As with any clinical decision, any new relevant information should be evaluated critically. Clinicians must be aware of new evidence and its validity. This process should be the basis for clinical decision-making. There are many economic, political, celebrity, and other not-evidence-based voices that are attempting to influence clinical decision-making. Whatever the intention, they ultimately do not aid in effective therapeutics.

As pediatricians we must remain advocates for our patients in this regard. We need to be aware of other therapies and their validity or lack thereof. We need to support the development of drug therapy for children through valid, well-designed pediatric clinical trials. We must be able to effectively communicate with our patients and families regarding any therapy regardless of its source of development. We must likewise remain open and let the critical review of clinical evidence be the foundation of the knowledge base on which we act.

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