

Impact of the American Heart Association Scientific Statement on Screening Electrocardiograms and Stimulant Medications

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Objective: To evaluate the impact of the American Heart Association (AHA) scientific statement regarding electrocardiograms (ECGs) and stimulant medications on the practice of community pediatricians.

Design: Retrospective evaluation and survey analysis.

Setting: Academic tertiary care center.

Participants: Patients with ECGs referred to our institution by pediatricians with an indication of stimulant medication screening in the year after the AHA statement.

Intervention: We compared the ECG ordering practices of community pediatricians and the outcomes of further evaluation and estimated the associated cost before and after the AHA scientific statement.

Main Outcome Measures: Abnormal ECG findings, further workup, and change in clinical practice.

Results: In the year after publication of the 2008 AHA scientific statement, 372 ECGs were ordered with an in-

dication of stimulant medication screening. Before publication of this statement, a mean (SD) of 6.9 (3.2) ECGs per month were referred for this indication. Despite continuing controversy, this number increased 4-fold to 31.2 (9.5) ECGs per month in the subsequent year. Twenty-four ECGs (6.4%) had abnormal findings. Eighteen patients were referred for further evaluation, and, at last follow-up, none had been found to have definitive disease. Six of 24 patients with abnormal ECG findings (25.0%) had a perceived significant delay in therapy because of the process. In responding pediatricians, 34.6% reported that the scientific statement had clearly affected their practice.

Conclusions: The clinical practice of community pediatricians in regard to screening ECGs and stimulant medications has been affected by the recent AHA scientific statement. The yield of performing ECGs with an indication of stimulant medication screening is very low.

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ATENTION-DEFICIT/HYPERactivity disorder (ADHD) is the most common neurobehavioral disorder among school-aged children, with a reported prevalence ranging from 5% to 20%.¹⁻⁵ Stimulants are widely used to treat children diagnosed as having ADHD. At a US Food and Drug Administration (FDA) advisory committee meeting, testimony indicated that 2.5 million children are currently receiving stimulant medications for ADHD.⁶

In recent years, there has been significant concern about the safety of stimulant treatment in children diagnosed as having ADHD. From January 1, 1992, through February 28, 2005, there were 28 reports of sudden death in children treated with methylphenidate hydrochloride or

amphetamine.^{7,8} Of these, 12 cases were in children with underlying structural cardiovascular abnormalities or other potential risk factors for sudden cardiac death.⁷ In 2004, the labeling for a combination of amphetamine and dextroamphetamine (Adderall XR) was changed to include a warning that patients with underlying heart disease might be at increased risk for sudden death while taking the drug,^{7,9} and subsequently an FDA advisory committee assigned a "black box" warning to the medication.¹⁰ At a follow-up meeting of the FDA Psychopharmacology Pediatric Advisory Board, however, the committee concluded that stimulant medications do not pose undue cardiovascular risk in healthy children and adolescents.²

As concern over the safety of stimulant medications has grown, controversy

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over the best method to screen for underlying cardiac defects has risen. Consensus is that a thorough personal history, family history, and physical examination should be included.^{2,11,12} This recommendation is supported by the American Heart Association (AHA), American Academy of Pediatrics (AAP), and American Academy of Child and Adolescent Psychiatry, among others. However, the AHA published a scientific statement in April 2008 suggesting universal electrocardiographic (ECG) screening for patients prescribed stimulant medications for the treatment of ADHD,¹¹ and this has resulted in significant debate. The purpose of our study was to evaluate the impact of the AHA scientific statement on the practice of community pediatricians and to assess the utility of ECG screening in this patient cohort.

METHODS

This study was an institutional review board–approved, single-center retrospective evaluation. The Muse ECG database at Texas Children’s Hospital was queried for ECGs performed with indications related to stimulant medication screening as ordered by community pediatricians. Ordering practice for the year before publication of the AHA scientific statement was compared with that for the year after publication. All ECGs performed subsequent to publication of the AHA statement were then reviewed by a pediatric electrophysiologist (J.J.K.), and the results were analyzed in regard to abnormal ECG findings, subsequent evaluations, and cost. Children with known pre-existing cardiac disease or arrhythmias were excluded. The ECG findings were classified as abnormal based on the definitions put forth in the AHA scientific statement, with only those abnormalities thought to have a “likelihood of correlating with the presence of cardiac disease” (categories II and III) being called positive.^{11(p2417)}

A single-question electronic survey was e-mailed to all community pediatricians in the Houston area who refer ECGs to our institution for interpretation. They were asked whether they had changed their clinical practice in response to the publication of the 2008 AHA scientific statement on screening ECGs and stimulant medications. They were also encouraged to elaborate on how they believed their practice was affected. Responses were reviewed and pediatrician demographic information was analyzed to determine factors associated with practice alteration.

RESULTS

In the year after publication of the AHA scientific statement recommending universal ECG screening for patients prescribed stimulant medications, 372 ECGs were ordered for this purpose. Before publication of the statement, a mean (SD) of 6.9 (3.2) ECGs per month were referred with this indication. Despite continued controversy, this number increased more than 4-fold to 31.2 (9.5) ECGs per month in the subsequent year. An AAP counterstatement published in August 2008 suggested using the history and physical examination as a primary screening modality with more prudent use of ECGs.¹² This had a transient effect on the ordering practice of pediatricians, with a brief decline in the number of screening ECGs ordered, but the numbers quickly rebounded without lasting effects (**Figure 1**).

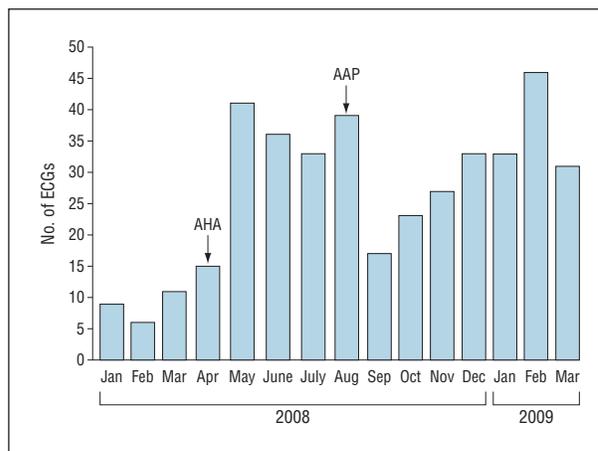


Figure 1. Number of electrocardiograms (ECGs) ordered per month with an indication of stimulant medication screening. The American Heart Association (AHA) statement was released in April 2008; the American Academy of Pediatrics (AAP) counterstatement, August 2008.

In total, 24 of 372 ECGs (6.4%) were found to have abnormalities. The most common abnormality found was ventricular hypertrophy in 13 (54.1%), followed by premature ventricular complexes in 3 (12.5%), premature atrial complexes in 2 (8.3%), left axis deviation in 2 (8.3%), mildly prolonged QT interval (QTc, 450–460 milliseconds) in 2 (8.3%), atrial enlargement in 1 (4.2%), and bizarre T-wave shape in 1 (4.2%). Thus far, 18 patients have been referred for further evaluation owing to the abnormal ECG findings on screening. Subsequent workup has ranged from an isolated second ECG to a referral to a cardiologist and outpatient evaluation, as given in the following tabulation:

Test	No. of Patients (n=18)
Echocardiography	13
Outpatient clinic	6
Second electrocardiogram	4
Holter monitoring	3
Treadmill	1
Chest radiography	1

Cost evaluation (based on average reimbursement from the 5 largest insurance contracts at our institution for hospital and professional fees) revealed the average (SD) reimbursed cost for workup of an abnormal ECG to be \$1870 (\$907), with a range of \$141 to \$3804. This excludes the cost of initial ECG screening, which was noted in our institution to increase from approximately \$970 per month before the statement to \$4400 per month after the statement.

Seventeen of the 18 patients referred for evaluation of abnormal ECG findings were found to have no underlying cardiac abnormalities. One of the 18 patients, who had left ventricular hypertrophy on the ECG, was noted to have slightly increased trabeculations of unclear significance in the left ventricle on echocardiography. The echocardiogram did not meet diagnostic criteria for noncompaction or cardiomyopathy, and the patient was asymptomatic with no arrhythmias and normal cardiac dimensions and function. He was examined by the cardiology department and cleared as having a probable normal variant. The patient was not restricted in any way. Of the 6 patients who were not referred for further evaluation, 3 had left ventricular hypertrophy, 1 had premature atrial contractions, 1 had premature ventricular

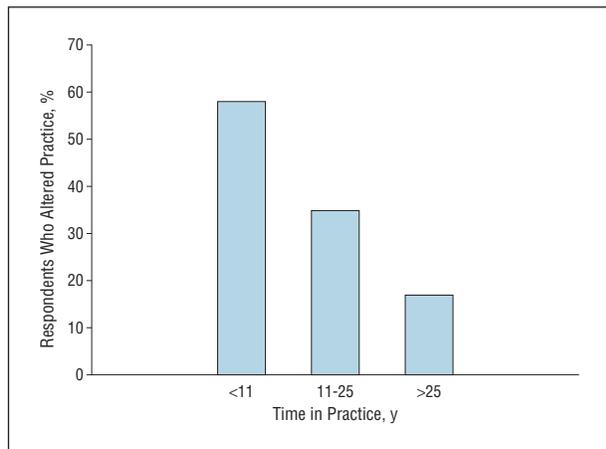


Figure 2. Graphic representation of the percentage of each group of physicians based on years in clinical practice who altered their practice in response to the American Heart Association statement.

contractions, and 1 had left axis deviation. Their pediatricians were contacted with the ECG interpretations, but further evaluation has not taken place to date. None of these patients has been restricted from taking stimulant medications based on the ECG findings. In summary, none of the patients with ECG abnormalities were found to have definitive cardiac disease, and none of the patients were restricted from taking stimulant medications. On review of medical records and discussion with ordering pediatricians, it was found that ECG screening for ADHD and subsequent workup delayed therapy in 6 of 24 patients with abnormal ECG findings (25.0%). In 1 patient, in whom subsequent evaluation ultimately revealed no cardiac disease and to whom clearance was given to start stimulant therapy, the parents elected to refuse medications because of “anxiety triggered by the screening process.”

In total, 201 community pediatricians from the Houston area were invited to participate in an electronic survey regarding the impact of the AHA scientific statement on their clinical practice, and 104 (51.7%) responded. Of all respondents, 65.3% reported that they did not ultimately alter their clinical practice because of the AHA scientific statement. Thirty-five percent of respondents stated that their clinical practice was clearly altered, resulting in an increased number of screening ECGs performed, with most of those (23% of the total) stating that they now universally perform screening ECGs on all children before the initiation of stimulant medications.

The pediatricians’ demographic characteristics were analyzed regarding factors associated with clinical practice alteration because of the AHA scientific statement. Most of the demographic factors (sex, ethnicity, and practice size or type) were not associated with a difference in clinical practice alteration. However, there was a statistically significant difference in practice alteration based on years in clinical practice, with those closest to training being most likely to alter their approach ($P=.008$) (**Figure 2**).

COMMENT

Attention-deficit/hyperactivity disorder is the most common neurobehavioral disorder among children and ado-

lescents, with an estimated 6% of the current population treated with stimulant medications at some point in their life.³ Concern has continued to grow regarding the safety of these medications in children with potential cardiac abnormalities, and controversy regarding the most appropriate screening modality has arisen. The AHA scientific statement put forth in April 2008 suggested adding universal ECG screening to the already accepted standard of a detailed history and physical examination. The repercussions of this statement have yet to be elucidated.

Our study found that the clinical practice of Houston community pediatricians has clearly been altered in response to the AHA scientific statement. Although 65.3% of pediatricians stated that they have not significantly altered their clinical practice, there has been a more than 4-fold increase in the ordering practice of screening ECGs. This is consistent with a multitude of literature suggesting that clinical guidelines can result in profound change in the process of care in the direction proposed.^{13,14} The AAP counterstatement put forth 5 months later had only a transient effect on the ordering practice of pediatricians, with a temporary reduction in the number of ECGs ordered and a subsequent rapid rebound. The reason for this reduction and rebound is not entirely clear; however, survey responses suggest that parental anxiety created by media exposure may play a role.

It was also noted in our study that the pediatricians closest to training were most likely to change their clinical practice in response to the AHA scientific statement. This is consistent with previous studies suggesting that less experienced clinicians are more likely to have favorable opinions of clinical guidelines, whereas more experienced clinicians tend to be concerned with effects on clinical autonomy and are more likely to rely on personal experience.¹⁵ Other factors analyzed, including sex and practice size or type, had no effect on clinical practice change.

Our data suggest that the yield of ECGs as a screening tool for patients undergoing initiation of stimulant medication treatment is relatively low. Approximately 6% of ECGs performed had any abnormal findings thought to have a “likelihood of correlating with the presence of cardiac disease” as defined by the AHA scientific statement. Furthermore, none of the patients with abnormal ECG findings had definitive cardiac disease on subsequent evaluation, and no one was ultimately restricted from initiating therapy. This is consistent with other recent studies suggesting that the positive predictive value of ECG screening in this population would likely be low and that the false-positive rate would be high.¹⁶

Although our study lacks the statistical power to perform a complete cost-effectiveness evaluation, potential implications to the health care system in terms of money and manpower are relevant. Based on average reimbursement at our institution, the mean (SD) cost for workup of an abnormal ECG finding was \$1870 (\$907). With 2.5 million children currently taking stimulant medications and a 6.4% rate of abnormal findings on ECG, 160 000 children would potentially need further workup, resulting in an additional total national cost of approximately \$300 million. This would be added to the cost of already agreed on screening algorithms and does not take into account the

actual cost of the initial screening ECG. It is yet to be determined whether this cost is warranted.

The risk of not treating or delaying treatment for ADHD must also be considered because more than one-third of children diagnosed as having ADHD are reported to exhibit emotional and behavioral difficulties and nearly 40% have impairments in daily living, including poor academic performance, conduct problems, substance abuse, and antisocial activities.¹⁷⁻²² In our study, false-positive ECG findings led to a "significant delay" in initiating appropriate treatment for ADHD in 25.0% of cases. It is probable that this would continue to be a repercussion of the screening process. Also, parental anxiety regarding the use of stimulant medications can be triggered by the screening process itself and, in some cases, can result in unwarranted voluntary withholding of therapy.

It is well known that clinical guidelines and scientific statements can improve the quality and consistency of care in patients over time.^{13,14} In 1 meta analysis,¹⁴ 55 of 59 studies detected significant change in the process of care in the direction proposed by the guidelines, demonstrating that their impact on clinical practice can be profound. This proved to be true even when the guideline in question was found to lack substantial scientific merit. For this reason, care must be taken when developing clinical guidelines and putting forth scientific statements owing to the broad-reaching effects they may have. In regard to the topic of ECG screening in children being considered for stimulant drug therapy, we believe that further evidence is necessary to provide appropriate clinical guidance.

This study had several limitations. First, it was a single-center regional study, and the results may not be universally applicable. Second, owing to the relatively small number of abnormal ECG findings, the power remains limited and statistical determination of sensitivity, specificity, and predictive value was not possible. Third, because 6 patients have yet to undergo follow-up, there is a lack of information in 25.0% of the children who had abnormal findings noted on screening ECG, making definitive determination of predictive value even more difficult. Last, the pediatrician survey was self-selective and therefore could predispose to a response bias.

CONCLUSIONS

Based on this study, we conclude that the clinical practice of community pediatricians has been affected by the recent AHA scientific statement, with a significant increase in the number of ECGs ordered for this purpose. In our cohort, the yield of performing ECGs with an indication of stimulant medication screening was low and was unlikely to alter the ultimate treatment algorithm. However, false-positive ECGs led to a delay in the initiation of appropriate therapy for ADHD on many occasions. We agree with the authors of the AHA scientific statement that future studies are necessary to assess the true risk of sudden cardiac death in association with the use of stimulant drugs in children. Furthermore, additional data are needed to determine the efficacy of universal ECG screening in this group. Until further evi-

dence is available, we recommend following the AAP screening guidelines for stimulant medications with a thorough history (including cardiac symptoms and family history) and physical examination. Electrocardiography should be included as part of this process only when clinically indicated.

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