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PEDIATRIC CARDIOLOGY TODAY

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SOTALOL: A BRIEF REVIEW AND POSSIBLE NEW INDICATION

By Sri O. Rao, MD and James C. Perry, MD

Overview

In the treatment of atrial reentry tachycardias, there are several choices for conversion to sinus rhythm. These include DC cardioversion, transesophageal overdrive pacing, overdrive pacing in those patients with internal pacemakers, or the use of intravenous antiarrhythmic agents. However, each of these modalities requires some considerations. Young patients may require sedation and that alone can entail some risk. In addition, there is the associated pain, discomfort, anxiety and possible skin burns. With transesophageal pacing, a physician must have access to specialized equipment and, again, there may be discomfort and anxiety associated with placing the transesophageal pacing catheter. In patients with temporary pacemakers, a physician must again have access to specialized equipment and must have some training beforehand to successfully overdrive pace patients in atrial arrhythmias. Finally, with intravenous medications, admission to an intensive care unit and availability of back-up pacing may be required. With intravenous medications, choices are few and may require frequent blood draws to check plasma levels of the few drugs that are available. Our experience with sotalol may provide an alternative modality in treating patients with stable atrial reentrant tachycardias. This report attempts to review some basics of sotalol for those unfamiliar with its use.

Mechanism of Action

Sotalol, as available in the United States, is a mixed isomer of *l*-sotalol and *d*-sotalol. The *l*-sotalol isomer acts primarily via class II mechanism, therefore as a non-selective beta blocker, it decreases heart rate, decreases AV node conduction and increases AV nodal refractoriness. The *d*-sotalol isomer acts as a class III antiarrhythmic blocking K+ channels in atrial, ventricular, and Purkinje fiber cells. As a result, *d*-sotalol prolongs the cardiac action potential and effective refractory period. It is because of the dual properties of sotalol that it may be effective for use in several types of arrhythmias. It is currently labeled for use in adults with chronic, life-threatening ventricular arrhythmias and in chronic atrial fibrillation/flutter. It is also used off-label in children with chronic supraventricular tachycardia, though not usually as first-line therapy. The adult literature is replete with studies involving sotalol in patients after myocardial infarction with associated ventricular dysrhythmias. Like much of pediatric cardiology, there are few studies showing efficacy in the pediatric population. Our experience in the pediatric cardiology practice setting has shown it be quite effective in the treatment of atrial tachycardias obviating the need for DC cardioversion, overdrive pacing or intravenous agents.

> ***"Our experience with sotalol may provide an alternative modality in treating patients with stable atrial reentrant tachycardias. This report attempts to review some basics of sotalol for those unfamiliar with its use."***

Dosing

Oral sotalol is almost entirely absorbed after administration. It is neither metabolized nor plasma protein bound and is excreted by the kidneys unchanged. The pharmacokinetics of sotalol in the pediatric population as reported by Shi and Saul,[1,3] demonstrated plasma concentra-

tions to directly correlate with body surface area. The increase in QTc and R-R intervals were also found to be linearly related to plasma concentration.[1] Smaller children (BSA < 0.33 m^2) display greater drug concentration, hence renal function should be considered. As reported by Saul et al,[2] significant beta-blocking effects may be seen at lower doses between 30mg/m^2 and 70mg/m^2 and class III electrophysiologic effects are seen at higher doses those in ranges of 70mg/m^2. The class III effects were also found to be linearly related to plasma concentration.

In our experience of 25 patients who presented in the out-patient clinic with hemodynamically stable atrial arrhythmias, 20 (80%) of 25 responded with a single oral loading dose of 2mg/kg on average 141 minutes after being given the oral load. When looking specifically at arrhythmia type, those with intra-atrial reentrant tachycardia (IART) converted to a sinus or paced rhythm in 13 (93%) of 14 patients on average 163 minutes after the initial oral loading dose. Those with atrial ectopic tachycardia (AET) converted to either a sinus or paced rhythm in 6 (60%) of 10 patients on average 89 minutes after the oral loading dose. The one remaining patient with atrial fib/flutter converted 160 minutes after receiving the oral loading dose. In a subset of Fontan patients, who numbered 8 of 25, we found all of these patients converted to a sinus or paced rhythm on average 150 minutes after the loading dose.

"It is currently labeled for use in adults with chronic, life-threatening ventricular arrhythmias and in chronic atrial fibrillation/ flutter. It is also used off-label in children with chronic supraventricular tachycardia though not usually as first-line therapy."

Adverse Reactions

As reported in the adult literature, the most common and severe adverse effects of sotalol include QT interval prolongation, torsade de pointes, bradycardia, asthma exacerbation, and heart block in patients with sinus node dysfunction. The majority of the life-threatening dysrhythmias reported in the adult population were in those with underlying cardiac dysfunction as a result of myocardial infarction. In the largest series (n=71) thus far in the pediatric population, Pfammatter[4] reported sotalol to be either completely or partially effective in 38 (93%) of 41 patients with supraventricular reentrant tachycardias. In patients with post-operative atrial flutter, there was complete or partial efficacy in 16 (84%) of 19 patients. And in patients with ventricular tachycardia 7 (64%) of 11 showed partial or complete control. However, in that study there was a 10% report of proarrhythmia which included symptomatic bradycardia from sinoatrial block and high grade AV block in 7 patients; asymptomatic high grade block in one patient; torsades de pointes in one; and relevant increased ventricular ectopy in three patients. As a matter of course, pre- and post- ECG monitoring to evaluate for QTc changes should be done when initiating sotalol.

Our protocol for starting patients on sotalol in the context of stable atrial tachycardia has been to admit to a monitored bed, place a heplock, and obtain an ECG 1hr after the oral load and every morning thereafter for 48-72 hrs. All ECG's were evaluated to document significant QTc prolongation. If our patients had been on digoxin as an outpatient, then they were continued on the same dose. In our group, 11 of 20 that responded to sotalol and 4 of 5 that did not were all on maintenance digoxin. Those patients that converted to sinus rhythm were discharged home on maintenance sotalol of 1mg/kg/dose twice daily. In our series of 25 patients, we have yet to see the adverse effects reported in the adult population or in the Pfammatter study. However, one patient with Holter documented long-standing sinus node dysfunction required pacemaker implantation for sustained bradycardia after sotalol therapy. Intermediate and long-term results of home sotalol therapy have yet to be analyzed in our patient population.

Summary

Sotalol, a drug that has shown much potential in the adult population, may have some utility in the pediatric population. The risk of prolonging the QTc and possible torsades has been seen in the former group, but has yet to be clearly demonstrated in the pediatric population. This may reflect the difference in the underlying substrate for arrhythmias in the two populations. In our experience, albeit limited thus far, sotalol has become a useful modality in the treatment of hemodynamically stable atrial arrhythmias in most patients.

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MAY CONFERENCE FOCUS

The Society for Cardiovascular Angiography and Interventions' (SCAI) 28th Annual Scientific Sessions and Melvin P. Judkins Cardiac Imaging Symposium
May 4-7 2005; Ponte Vedra, FL
www.scai.org

The pediatric cardiology component of SCAI's Annual Scientific Sessions will be exciting and appealing. A group of nationally and internationally renown experts will present the latest developments in pediatric cardiac intervention. Topics include:

- percutanoeus closure of ventricular septal defects,
- stenting of the ductus as an alternative to a surgical shunt
- first stage palliation in the cath lab for HLHS.

There will also be a combined adult/ pediatric session where transcatheter management of atrial communications, percutaneous mitral valve repair and percutaneous aortic valve replacement will be reviewed. The highly popular "I blew it" session should be as entertaining and informative as ever. This meeting should be informative and of interest to all health care providers that take care of children and adults with congenital heart disease.

For more information or to register for the meeting, visit **www.scai.org**.

PREPARING CHILDREN AND ADOLESCENTS FOR INVASIVE CARDIAC PROCEDURES

By E. Marsha Elixson, RNc

Although congenital heart disease (CHD) remains constant, evidenced-based medicine shows staged surgical and medical interventions in children and adolescents to have improved outcomes. Advancing technologies requires many CHD patients to have multiple invasive cardiac procedures at various developmental stages thus, encouraging researchers to investigate ways to minimize disease related morbidity and psychosocial adjustment.[1] In an effort to facilitate systematic implementation of pre-procedure preparation for pediatric patients and their parents, groups such as the AHA CVN Writing Task Force have utilized a developmental approach, delineating subgroups of children with CHD to target effective pre-procedural preparation.[1,2]

Figure 1. Grant getting ready for the hospital tour.

The severity of cardiac disease may affect patient / family perceptions of the risks and benefits of invasive cardiac procedures, the dynamic effects of acute and chronic illness as well as having a longstanding vs. newly developed relationship with a healthcare provider. Anticipated outcomes for pre-procedural preparation include reduction in anxiety for patient / family, and improved cooperation and adjustment during and between procedures. Enhanced post-procedural recovery, increase sense of mastery and self-control for patient / family and healthcare providers, and improve long-term emotional and behavioral adjustments in patients and families.[2,3]

"Pre-procedural planning, individualized for each patient, acknowledges language, cultural considerations and other special needs of the patient / family."

While working with children and adolescents with CHD, the healthcare provider assesses the child, looks at the cognitive development, temperament, coping styles, previous healthcare experiences, as well as family composition, support network, stressors and coping styles.[3] Pre-procedural planning, individualized for each patient, acknowledges language, cultural considerations and other special needs of the patient / family:

- Implementing individualized pre-procedural preparation begins with utilization of multiple age appropriate venues.
- Information Giving: verbal, written, AV/Video/CD, pre-op classes, hospital tours, medical play and Internet resources.
- Coping Skills Training: guided imagery, positive self-talk, muscle relaxation, conscious breathing, refocusing and biofeedback.
- Play Therapy
- Peer Modeling / Counseling

Information Giving. *Verbal information giving* provides a description of the rationale for the procedure and what to expect, enhances anticipated sensory experiences, and involves health team members but requires an understanding of developmental level and knowledge of age appropriate language. Individualization of information and enhanced efficacy of self-directed teaching materials is supported but relies on family's memory or perceptions and may increase anxiety in children with prior experiences.

Written information giving promotes anticipatory guidance regarding child / family responses, may promote positive coping (ability to later reference), availability of appropriate materials, but relies on ability to read and may be difficult to individualize.

Figure 2. Zoe after her staged palliations for HLHS.

Standard AV / CD educational materials are not individualized to each patient circumstance.

Hospital tours and pre-op classes information giving presents sensory information, play experiences with 'props' but may be inaccessible to families due to inability to travel from home to hospital because of location.[2,4]

Coping Skills Training. *Relaxation* includes cognitive training skills aimed at relaxation, with the ability to focus attention away from the procedure, and replaces fearful thoughts with peaceful, nurturing scenes. Imagery, breathing regulation and self-talk can be enhanced and reinforced by a 'coach' but can be limited during prolonged procedures. This requires practice (time), a coach and the ability of the child to engage in self-regulatory behavior. Biofeedback can promote conscious relaxation by feedback, has a high acceptance by older children but requires sophisticated equipment and a lengthy training period.[4]

Distraction utilizes methods to refocus away from stressful stimuli and can be assumed by healthcare professionals or family members to engage the child's attention away from the procedure.[4,5]

Play Therapy incorporates the child's usual means of processing information and life experiences by use of self-directed play activities under the direction of a trained child life therapist or health care team member. Utilizing age appropriate toys and medical 'props' provides information and assists with processing.[1,3]

Peer Modeling utilizes direct interaction with peers who have successfully managed similar stressful circumstances but requires health team members to link with an appropriate patient / family. Adolescents highly accept this method (congruent with peer focus and developing independence from families).

Families can best support their child if they have adequate, appropriate pre-procedural preparation.[2] Health care team members, working to provide pre-procedural information to children and adolescents, need to be cognizant of the developmental age and all stressors associated with the medical / surgical procedure to gear their individualized intervention plan to enhance preparation, promote coping skills, and present a supportive role for patient / family as the child or adolescent enters the hospital on their journey.

Special acknowledgement to the AHA Ped CVN authors S LeRoy, P O'Brien, E Tong, S Turpin and K Uzark and the AHA CVN and CVDY.

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HIGHLIGHTS OF THE FIFTH INTERNATIONAL SYMPOSIUM ON PEDIATRIC CARDIAC INTENSIVE CARE - DECEMBER 1-4, 2004 FOUR SEASONS HOTEL, MIAMI, FLORIDA

By Anthony C. Chang, MD

The meeting was attended by close to 650 attendees from about 40 countries with representation from 10 subspecialties, with many of the attendees in leadership positions from many pediatric heart centers.

The symposium was preceded by a special half-day cardiac anesthesia conference, the first meeting of its kind. There were well over 200 attendees who were present. Special topics that were covered included cardiac anesthesia issues with transplantation and adults with congenital heart disease, as well as all the pertinent problems in the care of the single ventricle patient. The highlight of the session was the update on cardiopulmonary bypass, particularly the controversy that surrounds selective cerebral perfusion and neurological monitoring. As the survival of neonatal cardiac palliative and corrective surgeries continue to improve, the long term neurological outcome of these patients is of paramount importance. The second half-day program was the pediatric cardiac intensive care workshop, attended by over 350 attendees that focused on areas such as complex dysrhythmias, mechanical support, single ventricle pathophysiology, cardiac anatomy, and transesophageal echocardiography.

The opening session of the symposium focused on the importance of the multidisciplinary integration in cardiac intensive care to include pediatric cardiology, cardiac surgery, intensive care, cardiac anesthesia, and nursing, as well as other important subspecialists such as neonatologists, pulmonologists, and others. The session on management of low cardiac output syndrome focused on recent encouraging data on the use of arginine vasopressin and steroids, as well as the future of mechanical assist devices in the intensive care setting (such as the DeBakey implantable VAD). A concomitant session on new cardiac pharmacological agents addressed the use of human recombinant natriuretic peptide in the intensive care setting as well as the future availability of the calcium sensitizer levosimendan, already in use in Europe. In addition, a panel discussion on the best surgical strategy for hypoplastic left heart syndrome with varying opinions by five preeminent cardiac surgeons highlighted the advantages and disadvantages of the traditional Norwood vs. the recent Sano modification. There was also a group discussion on the best pulmonary vasodilator in intensive care with preferences for agents other than inhaled nitric oxide (such as inhaled prostacyclin and intravenous sildenafil). The first half day concluded with an open forum on our interaction with parents as well as physicians and nurses on the panel. There were enlightening comments made especially by parents on the importance of parental involvement in varying situations, particularly around the time of death of children. The afternoon sessions were focused on catecholamine resistant hypotension and acute respiratory distress syndrome, as well as interesting case discussions that were brought by both the attendees and the faculty. The selected scientific abstracts (of which there were 50 total) were presented in poster format at the end of the afternoon, with faculty leading the discussions.

The first session of the second day of the symposium was dedicated to the accomplishments of the past two decades as well as the future of pediatric cardiac intensive care. Morning sessions were then devoted to the use and investigations of nitric oxide in cardiac intensive care and a concurrent session on neurological monitoring using near-infrared spectroscopy.

"The opening session of the symposium focused on the importance of the multidisciplinary integration in cardiac intensive care...."

Discussion sessions that followed delineated the faculty responses to the questions: what is the ideal inotropic agent and what is the preferred mode of ventilation for cardiac patients? While there was no clear consensus during either of these sessions, it was essential for the attendees to appreciate the range of opinions from many clinical perspectives. The afternoon sessions focused on specific issues such as manipulation

"Additional sessions on this final day highlighted recent innovations of cardiopulmonary resuscitation and neurologic recovery as well as long term follow up data in children after cardiac surgery...."

of single ventricle physiology, both during the neonatal period, as well as after the bidirectional cavopulmonary anastomosis, the latter session highlighting the importance of cerebral blood flow on pulmonary blood flow. A concurrent nursing session focused on a myriad of topics chosen by the nursing members of the organizing committee. These topics included the low birth weight neonate with congenital heart disease and mechanical support principles.

The symposium concluded on the third day with presentation of three outstanding abstracts on various aspects of cardiac intensive care, ranging from inflammatory mediators after cardiopulmonary bypass to safety and prevention of cardiac arrest during cardiac anesthesia. Additional sessions on this final day highlighted recent innovations of cardiopulmonary resuscitation and neurologic recovery as well as long term follow-up data in children after cardiac surgery, particularly after the Norwood operation for hypoplastic left heart syndrome. Discussion sessions then focused on quality and safety issues in cardiac intensive care as well as the importance of drug trials in clinical research. The symposium concluded with comments from the leadership in pediatric cardiac intensive care, and a musical tribute to the children and caretakers in pediatric cardiac intensive care.

The Pediatric Cardiac Intensive Care Society (PCICS) meeting that immediately followed the symposium was attended by the leadership in pediatric cardiac intensive care. Various issues were discussed, such as future academic meetings, and the clinical and educational role of the society at the international level.

The next meeting will take place in Miami, FL on December 6-11, 2005. It will focus on two increasing, but complex patient populations in pediatric cardiac intensive care: the low birth weight neonates, as well as adults with congenital heart disease.

For comments to this article, send email to: FEBACC@PediatricCardiologyToday.com

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The complete symposium binder and accompanying CD-ROM is available through Dr. Anthony C. Chang

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MEDICAL CONFERENCES

4th Annual Charleston Mini-Symposium on Pediatric Cardiology
February 25-27, 2005; Charleston, SC
www.pediatrics.musc.edu/pedscard

ACC 54th Annual Scientific Session 2005
March 6-9, 2005; Orlando, FL
www.acc.org

10th Vail Symposium on Pediatric Cardiac Disease
March 13-16, 2005; Veil, CO
www.thechildrenshospital.org

International Workshop on Interventional Pediatric Cardiology
March 31-April 2, 2005; Milan, Italy
www.workshopIPC.com

2005 SIR 30th Annual Scientific Meeting
March 31-April 5, 2005; New Orleans, LA
www.sirweb.org

AATS 85th Annual Meeting
April 10-13, 2005; San Francisco, CA
www.aats.org/annualmeeting/

3rd Charleston Symposium on Interventional Pediatric Electrophysiology
May 1-3, 2005; Kiawah Island, SC
www.pediatrics.musc.edu/pedscard/

SCAI's 28th Annual Scientific Sessions
May 4-7, 2005; Ponte Vedra Beach, FL
www.scai.org

2005 PAS Annual Meeting
May 14-17, 2005; Washington, DC
www.pas-meeting.org

ASE 16th Annual Scientific Sessions
June 15-18, 2005; Boston, MA
www.asecho.org

8th International Workshop Catheter Interventions in Congenital Heart Disease
June 16-18, 2005; Frankfurt, Germany
www.chd-workshop.org

5th International Pediatric Cardiovascular Symposium: Management of Complex Congenital Heart Disease from Infancy to Adulthood
June 23-26, 2005; Amelia Island, FL
www.choa.org

12th World Congress on Heart Disease
July 16-19, 2005; Vancouver, Canada
www.cardiologyonline.com

SURVEY: EXPRESS YOUR OPINION ON THE AMERICAN COLLEGE OF CARDIOLOGY MEMBERSHIP DUES INCREASE

Please Answer the Following Questions and FAX this Sheet to: (240) 465-0692

1. Who pays for your various medical association membership dues? (✔ Check one)

❒ Paid by Self ❒ Paid or reimbursed by Hospital ❒ Paid or reimbursed by Practice (as employee) ❒ Paid or reimbursed by Practice (owner/partner)

❒ Paid out of a limited annual "CME Fund" which frequently competes with monies needed to attend CME meetings

2. How would you rate the value of your membership as a pediatric cardiologist in the ACC? (✔ Check one)

❒ Not Valuable ❒ Somewhat Valuable ❒ Valuable ❒ Very Valuable ❒ Extremely Valuable

3. Does the almost 80% jump in the ACC membership dues have an adverse impact on you financially? (✔ Check one)

❒ Yes ❒ No

4. Do you feel that the ACC membership dues should be discounted for pediatric cardiologists? (✔ Check one)

❒ Yes ❒ No

5. If you answered "Yes" to Question #4, what do you feel would be a fair discount? (✔ Check one)

❒ 10% ❒ 25% ❒ 50% ❒ 75% ❒ 90%

6. Please check the medical associations of which you are currently a member. (✔ Check all that apply)

Medical Association	Rank
❒ American College of Cardiology (ACC)	
❒ American Academy of Pediatrics (AAP)	
❒ American Heart Association (AHA)	
❒ Society of Cardiac Angiography and Intervention (SCAI)	
❒ American Society of Echocardiography (ASE)	
❒ Pediatric Electrophysiology Society (PES)	
❒ Pediatric Cardiac Intensive Care Society (PCICS)	
❒ Regional Pediatric Societies (e.g. Western Society of Pediatric Cardiology)	
❒ American Medical Association (AMA)	
❒ Other (name) _____	

7. Go back to Question #6, and Rank the three most valuable associations to you by placing the numbers 1, 2, and 3 in the "Rank" Column next the appropriate association. (1=Most important, 2 = Second most important; 3=Third most important)

8. Comments:_____

_____

PEDIATRIC DIGITAL ECHOCARDIOGRAPHY

By Nader H. Atallah, MD and Frank C. Smith, MD

In 1988, Dr. Harvey Feigenbaum first described digital recording, display and storage of echocardiograms in adult patients. Since then, advances in digital technology and the demand for increased efficiency in busy laboratories, have led to the establishment of many digital pediatric echocardiography laboratories. The advantages of a digital laboratory are many (Table 1).

Successful conversion to a digital echocardiography laboratory, however, requires time, thought, and commitment of the entire laboratory staff and cardiology division. For many centers, the cost of a digital system will represent one of the lab's largest expenditures. Like any major system change, the conversion from analog to digital format may generate anxiety not only among echocardiographers and sonographers within the lab, but other cardiologists within the division, as well as department and hospital chiefs who must justify the substantial allocation of money and time for the conversion. We present here the experience of our lab during this transition and hope that it may assist other laboratories that are considering taking the plunge into the digital world.

"Successful conversion to a digital echocardiography laboratory...requires time, thought, and commitment of the entire laboratory staff and cardiology division."

Advantages of Digital Echocardiography
Improved image and report management • Preserved image quality with no degradation with time • Easy access to images and reports throughout the network • Serial image comparison
Improved Efficiency • Increased patient throughput • Faster turnaround of reports • No filing of reports or videotapes required • Easy database management
Improved Cost Management • No transcription required • No on- or offsite videotape storage needed • Less time/personnel required
Improved Database Management • Easy and quick database query • Database tracking allows lab quality assurance and ICAEL accreditation

Table 1. Advantages of Digital Echocardiography

Background

The Division of Pediatric Cardiology at Upstate Medical University in Syracuse, New York serves pediatric patients in the 18-county region of central and northern New York. We provide inpatient coverage in two adjoining Syracuse hospitals. Our echo laboratory and clinics are located in a separate building that is connected to the two hospitals through underground tunnels. There are telemedicine links with seven community hospitals and five satellite clinics within the referral region. We perform and interpret 4500 transthoracic, fetal, transesophageal, stress, and intracardiac echo studies annually.

Choosing the right system

We began to explore digital echocardiography in 2001 and spent over one year acquainting ourselves with several available systems before we decided upon the solution for our laboratory. Each large ultrasound company offered a digital system to complement its ultrasound imaging units. In addition, several stand-alone software companies offered digital systems with capability of incorporating ultrasound systems from different vendors within their network. We became familiar with the various options after brief demonstrations in our laboratory by different companies and by visits to booths at national meetings. We also made several site visits to other centers that had already completely converted to specific digital systems. Seeing staff and patient interaction with the systems "in real time" particularly helped to clarify strengths and potential weaknesses of each system and which system would be optimal for our lab. Intuitive workflow and superior vendor support were key factors in our evaluation. We eventually narrowed our choice to two systems and asked their respective companies to install temporary

2-D Calculations	Doppler Calculations	Doppler Calculations
Chamber Dimensions Thickness, Thickening % Area Perimeter E.F. from Single and Biplane Volumes using Simpson's rule E.F. from Diameters (Quinones method) and Bullet Volume Cardiac Output and Index Fractional Area Change Fractional Shortening LV Mass using Area/Length & Truncated Ellipsoid methods Regional Wall Motion Analysis using the Centerline Method	***Hemodynamic Assessment*** Stroke Volume Shunt Qp/Qs Cardiac Output Flow Regurgitant Fraction Regurgitant Area Ratio *Mitral Valve Assessment* TVI Peak Velocity Mean Velocity Peak Gradient Mean Gradient Pressure Half Time Area from Pressure Half Time ***Valvular Assessment*** TVI Peak Velocity Mean Velocity Peak Gradient Mean Gradient Acceleration Time/Eject Time Peak Acceleration Rate ***Valve Area from Continuity Equation*** TVI method Peak velocity method ***Ventricular Filling Dynamics*** A velocity E/A ratio Acceleration Time Deceleration Time Peak Filling Rate Normalized Peak Filling Rate 1st 1/2 Filling Fraction 1st 1/3 Filling Fraction Atrial Filling Fraction Mitral Annulus M-R IVRT, LVEDP	***Atrial Filling Dynamics*** Systolic & Diastolic TVI Total Forward TVI Systolic TVI / Diastolic TVI Atrial TVI Peak Sys & Diast Velocity Peak Velocity Peak Atrial Velocity Peak Systolic / Diastolic Vel ***Systolic Time Intervals*** Pre-Eject Period (PEP) E velocity Acceleration Time (AT) Ejection Time (ET) PEP/ET, PEP/AT, AT/ET ***Estimated PA Systolic Pressure*** Tricuspid Regurgitant Velocity method, Pulmonary Flow Indicies method and RV Relaxation Time method ***Regurgitation (PISA method)*** Regurgitant Flow & TVI Peak Regurgitant Velocity ERO Regurgitant Volume ***Diastology*** ***Tissue Doppler*** Am, Sm, Em, E/Em ***Pulmonary Veins*** Velocities Systolic, Diastolic A wave times Duration, Reversal ***Color M-Mode*** Propagation Velocity
M-mode Calculations Dimensions Shortening Fraction Thickness Thickening Fraction Volumes by Teicholtz method Ejections Fraction Cardiac Output/Index LV Mass End-Systolic Wall Stress VCF and VCFc (corrected for heart rate PEP & LV Ejection Time Q to Value Closure EF Slope Cusp Separation Excursion & EPSS		

Table 2. Digiview Echo Quantitation Menu

workstations in our laboratory for several days of use. By mid-2002, we had made our decision to acquire the DigiView Image Management and Reporting System from Digisonics, Inc.

DigiView salient features

Images are digitally acquired and saved in DICOM format, and are thus interchangeable with other DICOM systems. Images from different studies can be displayed for side-by-side comparison. Studies can be reviewed in the reading room of the echocardiography laboratory, as well as workstations strategically located in each hospital, in the outpatient clinic area, in conference rooms and in the offices of the echocardiographers. Review, offline measurement and reporting of videotaped studies are still possible and reports of these studies can be incorporated within the system. In addition, videotaped images can be easily digitized and saved on the system for future comparison to digital studies. A remote mode option allows a user to access the database securely via a VPN connection using the Internet for study review, measurement and report generation. Images can be saved to CD in AVI format with an embedded viewer that opens automatically on any Windows-based PC. Images from other modalities including angiography can be imported and archived, as well, allowing for a complete digital cardiac image archiving system.

"Conversion to a digital echocardiography laboratory constitutes a major change for most laboratories, but it is a change well worth taking."

Measurements performed by the sonographer are automatically transferred with the images into the report. In addition, there is an extensive offline measurement package (Table 2), which can further be customized to comply with a laboratory's specific protocol. Normal values and z-scores for age or body surface area are displayed in the report and abnormal measurements values are highlighted. In addition, measurements from different stud-

ies can be compared using trend plots to show change over time (Figure 1).

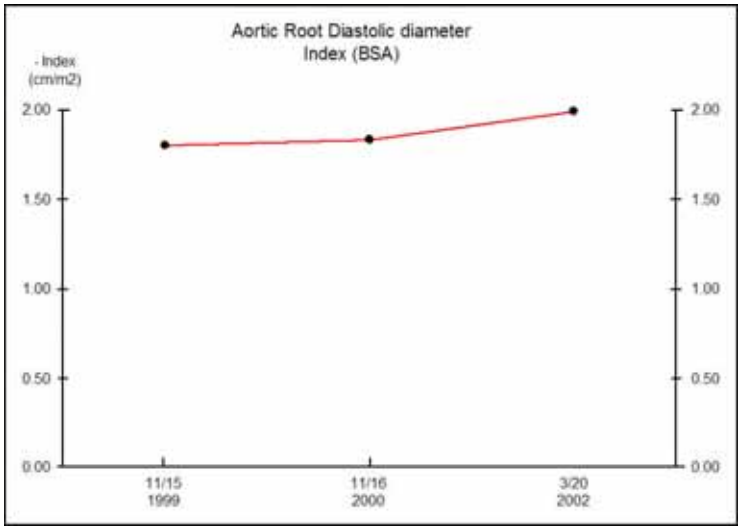

Figure 1. Trend plot of aortic root measurements indexed to BSA over time in a patient with Marfan syndrome

The DigiView reporting package is particularly pediatric user friendly and can be customized according to the preferences of different centers. Congenital abnormality diagrams can be edited and annotated. Customizable Macros are available for different lesions and procedures. An extensive customizable pick list of findings is integrated within the report package. There is a Microsoft Word type interface with free text entry and medical grade spell checker. A current study report can be built from the Word report of any previous study and quickly forwarded into the new report. This may be particularly helpful for complex cases. The report can be electronically signed and transmitted electronically to the referring physician or hospital information system.

The Transition

Despite anxiety associated with conversion to a new, unfamiliar format, our transition into digital acquisition and storage was surprisingly smooth. We planned to follow the same imaging protocols for videotape studies except that acquisition of each view would be limited to two cardiac cycles per clip. The acquisition time would be increased to allow for longer sweeps of pertinent anatomy. We initially planned to videotape all studies that were acquired digitally as a "safety net" for the first two months during the transition. After two weeks, however, it was clear that videotaping was interfering with workflow within our laboratory and all physicians had quickly become comfortable with digital images alone and rarely reviewed the videotape. Within a month, fetal and TEE studies were fully acquired digitally as well, with no videotape backup.

Each laboratory may require a "videotape back-up period" and it is important to have a digital system that can easily incorporate video. The duration of the transition period will depend upon technical difficulties with every component of the digital system, as well as the comfort and experience of the sonographers and physicians who access the system. We should note that our staff was relatively experienced. The two senior sonographers each had over 17 years of pediatric and/or adult echo experience, and four of the six cardiologists had over 17 years of clinical experience in the field at the time of the transition.

The Results

We were initially concerned that digital acquisition of only a few cardiac cycles per view along with relatively short sweeps could lead to loss of important data. Every digital lab that we contacted or visited reassured us that this was highly unlikely. Our laboratory results were compared with catheterization data and operating room observations in bi-weekly confer-

Figure 2. Dr. Atallah reviewing pre- and post-operative TEE images with the PICU team

ences. In over two years, we have not identified one case in which the echocardiographic diagnosis was in error because of inadequate quality or quantity of digital images. Physician review and report time has been significantly shortened and reports are usually generated within 24 hours. Sonographers have more time for scanning, rather than searching for videotapes and queuing them to a specific study. The robust query and search package of the system quickly affords information necessary for lab quality assurance and ICAEL accreditation. The potential for collecting and analyzing data for research studies is endless. Finally, the systems based within our two hospitals and conference rooms have served as excellent teaching stations for students, nurses, and house staff. For example, pre- and post-operative TEE can be reviewed with the ICU staff at the ICU station in order to discuss anatomy, physiology, and management of each diagnosis even before the child has left the operating room (Figure 2).

"Each laboratory may require a "videotape back-up period" and it is important to have a digital system that can easily incorporate video."

Conclusion

Conversion to a digital echocardiography laboratory constitutes a major change for most laboratories, but it is a change well worth taking. Since it involves a significant investment of time and money, labs should obtain opinions from physicians and sonographer staff, and request reimbursement to make site visits. Financial cost of the system may be offset by the increased efficiency in performing and interpreting studies, the potential for increased and efficient research time, and the potential for innovative teaching.

For comments to this article, send email to: FEBNHA@PediatricCardiologyToday.com

~PCT~

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JUNE CONFERENCE FOCUS

5th International Pediatric Cardiovascular Symposium: Management of Complex Heart Disease from Infancy to Adulthood

June 23-26, 2005; Amelia Island, FL
www.choa.org

Course Co-Director: Kathy Murphy, 404-785-6480
Coordinator: Jane Darrish, 404-785-7842

This four day symposium will address advances in medical and surgical management of patients with single ventricular heart disease.

Who should attend: This conference is planned for cardiac nurses and respiratory therapists, cardiologists, cardiothoracic surgeons, anesthesiologists, perfusionists and other health care professionals involved in caring for children/adults with complex congenital heart disease.

Some of the topics presented:
- Pre-op Stabilization and Monitoring of the Single Ventricle Patient
- Periventricular Leukomalacia and Genetic Markers of Neurological Insults
- Monitoring the Brain During Cardiopulmonary Bypass
- Perioperative Monitoring of the Single Ventricle Circulation: SVO2, NIRS and Lactate
- Neurological Outcomes of Newborns with CHD Undergoing Neonatal Repair
- Molecular Etiologies of Single Ventricle
- Norwood Modifications
- Hypoplastic Left Heart Syndrome: Path Specimens
- Surgical Options to Achieve Extracardiac and Lateral Tunnel Fontan
- Functional Outcome Post Fontan
- Neonatal Repairs in Light of New Neurological Insult Data

MEDICAL NEWS

Scientists Align Billion-Year-Old Protein with Embryonic Heart Defects

University of Rochester scientists studying a vital protein called Serum Response Factor (SRF) in mice learned new and unexpected facts about SRF's role in early cardiovascular development, and how a defect in this gene may be an underlying cause in human miscarriages.

The research was reported in the December 7, 2005 issue of Proceedings of the National Academy of Sciences (PNAS) - www.pnas.org. At this point it is unclear whether subtle defects in SRF might also be linked to adult cardiovascular disease. However, the research provides a foundation for understanding how gene mutations may disrupt heart function, perhaps making some adults more susceptible to heart failure or irregular reactions to drugs.

"One reason for studying the biology of our genetic blueprint is so that we can understand how mutations in the genes encoding for proteins such as SRF may relate to human disease," says Joseph M. Miano, Ph.D., associate professor of Medicine in the Center for Cardiovascular Research, at the UR's Aab Institute of Biomedical Sciences. "Defining the full spectrum of genetic mutations is key to genetic screening and gene-based therapies."

SRF is one of nature's oldest proteins and is essential for life because it supports the basic internal structure of all living cells. Its function is to carefully turn on 300 of our 30,000 genes. But until now, scientists did not know much about its role in the heart region.

Miano's laboratory led a collaborative study of SRF with investigators from the Medical College of Wisconsin and Johns Hopkins University School of Medicine. They studied mouse embryos, using genetic trickery to nullify SRF in heart cells and key blood vessel cells called smooth muscle cells. They compared the mutant mice to those with a normal amount of SRF in the heart and blood vessels. The heart and related vessels did not develop properly in the mice without SRF, the team discovered.

Dr. Joseph M. Miano, Ph.D.

In fact, while analyzing the heart cells under a high-powered electron microscope, the lab discovered that normal heart cells (with SRF) contained the expected bundles of healthy fibers. Shaped like rubber bands, the bundles work like bands of muscle to keep the heart contracting normally. But in the absence of SRF, the neat bundles were gone. Instead, they were scattered about the heart region, as if the rubber band had been "shredded," Miano says.

Scientists concluded that cells lacking SRF could not sustain life because they lacked the necessary shape, structure and function to stay vital.

"SRF serves a very critical function in directing genes to develop an internal structure that acts sort of like the skeleton in the human body," Miano explains. "You can imagine that without a skeleton, our bodies would flop to the floor. Cells need the same structure and form in order to migrate, contract, and work properly."

Thus, although other scientists have defined hundreds of genes that may cause miscarriages due to cardiovascular defects, the latest research also links SRF for the first time to embryonic heart development. The National Heart Lung and Blood Institute of the National Institutes of Health funded the research.

The long-tem goal of the research is to provide a foundation for genetic screening for all types of cardiovascular disorders, and perhaps a way to replace the faulty genes through targeted therapy. For more information: www.urmc.rochester.edu

Animal Studies Show Stem Cells Might Make Biological Pacemaker

In experiments in the lab and with guinea pigs, researchers from Johns Hopkins have found the first evidence that genetically engineered heart cells derived from human embryonic stem (ES) cells might one day be a promising biological alternative to the electronic pacemakers used by hundreds of thousands of people worldwide.

Electronic pacemakers are used in children and adults with certain heart conditions that interfere with a normal heartbeat. However, these life-saving devices can't react the way the heart's own pacemaker normally does -- for example, raising the heart rate to help us climb stairs or react to a scary movie.

In the researchers' experiments, described in the December 20, 2005 online edition of Circulation (http://circ.ahajournals.org/), human ES cells were genetically engineered to make a green protein, grown in the lab and then encouraged to become heart cells. The researchers then selected clusters of the cells that beat on their own accord, indicating the presence of pacemaking cells. These clusters triggered the unified beating of heart muscle cells taken from rats, and, when implanted into the hearts of guinea pigs, triggered regular beating of the heart itself.

"These implanted cells also responded appropriately to drugs used

to slow or speed the heart rate, which electronic pacemakers can't do," says study leader Ronald Li, PhD, assistant professor of medicine. "But many challenges remain before this technique could be used for patients. We want to bring this to the clinic as fast as possible, but we need to be extremely careful. If this process isn't done properly, it could jeopardize a very promising field."

The genetic engineering of the ES cells, accomplished by Tian Xue, Ph.D., a postdoctoral fellow at the School of Medicine, inserted a gene (for green fluorescence protein) so that the human cells would be easily distinguished from animal cells in the experiments. Since the engineered cells survived and worked properly, other more clinically important genetic engineering of the cells also will probably not interfere with the cells' fate, say the researchers.

"To our knowledge, these are the first genetically engineered heart cells derived from human ES cells," notes Xue. "We're now using genetic engineering to customize the pacing rate of these cells, for example. For any future clinical applications, you want to make sure that the beating rate is what you want it to be."

First isolated at the University of Wisconsin, the human ES cells used by the researchers have the natural ability to become any type of cell found in the human body, and therefore they hold the potential to replace damaged cells. But such applications await proof that the desired type of cells can be obtained, isolated and controlled, because expected risks include primitive cells developing into tumors or implanted cells being rejected.

In the researchers' experiments, clusters of beating human heart cells derived from ES cells were injected into the heart muscle of six guinea pigs. A few days later, the researchers destroyed each animal's own pacemaking cells, located near the point of injection, by freezing them. Careful electrical measurements on the hearts revealed a new beat, coordinated by the implanted human cells and slower than the animals' normal heart rate -- likely reflecting humans' lower heart rate.

To prove that the human heart cells were controlling the beat of the guinea pigs' hearts, colleagues Fadi Akar, Ph.D., and Gordon Tomaselli, MD, conducted careful experiments that showed exactly where the electrical signal originated and followed the signal's conduction across the heart's surface. Sure enough, the signal started from the transplanted human cells, easy to locate because of their fluorescence.

"We've answered three very important questions," says Xue. "We've shown that these human cells survived when we put them into the animals, they were able to combine functionally with the animal's heart muscle, and they didn't create tumors for as long as we have watched."

But new questions have come up because of these promising results, notes Li. For instance, the researchers don't know why the animal's immune system didn't attack and kill the human cellular "invaders " -- that was a surprise. One possibility is that the cluster of cells didn't connect enough with the animal's circulatory system to trigger an immune response, but more experiments will be necessary to see whether that's the case and, if so, how that might affect the implanted cells' long-term survival.

The stem cell approach isn't the first Johns Hopkins research to create a biological pacemaker, but it is likely to be a better choice if the heart is very damaged. In 2002, Hopkins scientists reported that inserting a particular gene into existing heart muscle cells in a guinea pig allowed the cells to create a pacemaking signal. If heart damage is extensive, however, it might be preferable to introduce new pacemaking cells, rather than to convert existing cells into pacemakers, notes Li.

The research was funded by the National Heart, Lung and Blood Institute, the Blaustein Pain Research Center, the Croucher Foundation, and the Cardiac Arrhythmias Research and Education Foundation. Authors are Xue, Li, Akar, Tomaselli, Eduardo Marbán, Heecheol Cho, Suk-ying Tsang and Steven Jones, all of Johns Hopkins. For more information: www.hopkinsmedicine.org

Pediatrix Acquires Pediatric Cardiology Practice

FORT LAUDERDALE, Fla.--(BUSINESS WIRE)--Dec. 16, 2004--Pediatrix Medical Group, Inc. (NYSE:PDX), the nation's largest provider of newborn and maternal fetal physician services, has expanded its pediatric cardiology services with the acquisition of a physician group practice based in Austin, Texas.

Children's Cardiology Associates is a six-physician group practice that provides comprehensive pediatric cardiology services in Austin and surrounding communities throughout Central Texas including Temple, College Station, San Marcos and Killeen.

"We've been very fortunate in that our focus on clinical activities has allowed our practice to grow, and with that growth we're experiencing increasing demands from the business side of running our practice," said Patrick Finnigan, M.D., one of the founding physicians of Children's Cardiology Associates. "By joining with Pediatrix, we see an opportunity to benefit from advanced business and financial management while doing what we do best, which is to focus on our clinical activities."

Pediatrix began providing pediatric cardiology physician services in South Florida in 1991. During the past two years, Pediatrix has completed the acquisition of four pediatric cardiology physician groups that represent the foundation of a national group practice focused on constantly improving patient outcomes. A total of 28 pediatric cardiology physician subspecialists practicing as part of Pediatrix provide patient care in six metropolitan areas across the U.S.: Fort Lauderdale and West Palm Beach in Florida; Phoenix and Tucson in Arizona; Denver, Colorado; and Austin, Texas.

Pediatric cardiologists provide comprehensive physician services to fetal and pediatric patients with congenital heart disease, in-

cluding echocardiography and diagnostic, interventional cardiac catheterizations and pacemaker therapies.

Pediatrix paid cash for Children's Cardiology Associates and the transaction is expected to be immediately accretive to earnings. Specific terms were not disclosed.

During 2004, Pediatrix has used its cash and revolving credit facility to complete 12 physician group practice acquisitions in four physician subspecialties - neonatology, maternal-fetal medicine, pediatric intensive care and pediatric cardiology.

Pediatrix was founded in 1979. Combined, Pediatrix and its affiliated professional corporations employ more than 750 physicians in 31 states and Puerto Rico.

For more information: www.pediatrix.com

Jefferson Scientists Use Gene Therapy to Rescue Failing Hearts in Animals

Heart researchers at Jefferson Medical College have used gene therapy to bring failing rat hearts back to normal.

Scientists led by Walter Koch, Ph.D., Director of the Center for Translational Medicine in the Department of Medicine in Jefferson Medical College of Thomas Jefferson University in Philadelphia, used a virus to insert the gene for a protein called S100A1 into failing rat hearts.

"In contrast to other gene therapy strategies geared to overexpressing a gene," says Dr. Koch, who is W.W. Smith Professor of Medicine at Jefferson Medical College, "because this protein is reduced in heart failure, simply bringing the protein level back to normal restored heart function." Dr. Koch and his co-workers report their findings December 1, 2004 in the Journal of Clinical Investigation.

S100A1, which is part of a larger family of proteins called S100, binds to calcium and is primarily found at high levels in muscle, particularly the heart. Previous studies by other researchers showed that the protein was reduced by as much as 50% in patients with heart failure. A few years ago, Dr. Koch and his co-workers put the human gene that makes S100A1 into a mouse, and found a resulting increase in contractile function of the heart cell. The mice hearts worked better and had stronger beats.

Dr. Koch's Jefferson team now examined whether it could make failing hearts normal again. The researchers – 12 weeks after they simulated a heart attack in the rats – delivered the human S100A1 gene to the heart through the coronary arteries by injection of a genetically-modified common cold virus as a carrier. After about a week, they found the hearts began to work normally. In addition, the animals' heart muscle showed improved efficiency in using its energy supply, which was decreased in heart failure. According to Dr. Koch, the improvements were seen in both the whole animal as well as in individual heart cells.

"This is one of the first studies to do intracoronary gene delivery in a post-infarcted failing heart," he says. "This proves it could actually be a therapy since most of the previous studies of this type are aimed at prevention – giving a gene and showing that certain heart problems are prevented. In those cases, heart problems are not actually reversed. This is a remarkable rescue and reversal of cardiac dysfunction, with obvious clinical implications for future heart failure therapy."

Close to 5 million Americans have heart failure and more than 400,000 new cases are being diagnosed each year. While the overall death toll from heart disease has declined, the number of people dying from chronic heart failure continues to rise. For example, the death rate from coronary heart disease dropped 49% between 1970 and 1990, while deaths due to heart failure increased 64% over that period.

Dr. Walter Koch, Ph.D., of the Center for Translational Medicine .

"We have a unique molecule necessary for normal heart function," Dr. Koch says, noting that animals lacking the gene for S100A1 are seemingly healthy until they are subjected to cardiac stress, after which they usually die. The animals in the current study that received the gene transfer were fine.

Next, he and his colleagues hope to learn more about the mechanisms behind S100A1's actions, and eventually, develop gene therapy protocols in humans. S100A1 is also found in the cell's energy-producing mitochondria, he notes. He thinks the protein may be a link between energy production and calcium signaling in the heart cell – a crucial part of the process that makes the heart beat.

For more information: www.jefferson.edu

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