

American
Society of
Pediatric
Nephrology

2004 10-20-2004

NORTHWESTERN UNIVERSITY
FEINBERG SCHOOL OF MEDICINE
PEDIATRICS W140
303 E CHICAGO AVE
CHICAGO, IL 60611-3008
312-503-4000
FAX. 312-503-1181
ASPN@NORTHWESTERN.EDU
WWW.ASPNEPH.COM

August 18, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852.

OFFICERS:

PRESIDENT

SANDRA L. WATKINS, M.D.
SEATTLE, WA

PRESIDENT-ELECT

SHARON ANDREOLI, M.D.
INDIANAPOLIS, IN

SECRETARY-TREASURER

H. WILLIAM SCHNAPER, M.D.
CHICAGO, IL

PAST PRESIDENT

ELLIS D. AVNER, M.D.
MILWAUKEE, WI

COUNCILORS:

URI S. ALON, M.D.
KANSAS CITY, MO

JOSEPH T. FLYNN, M.D., M.S.
BRONX, NY

JOHN W. FOREMAN, M.D.
DURHAM, NC

BRUCE Z. MORGENSTERN, M.D.
PHOENIX, AZ

VICTORIA F. NORWOOD, M.D.
CHARLOTTESVILLE, VA

LISA M. SATLIN, M.D.
NEW YORK, NY

**WASHINGTON
REPRESENTATIVES:**

DOMENIC RUSCIO
JENNIFER SHEVCHUK
CRD ASSOCIATES, L.L.C.
316 PENNSYLVANIA AVE. S.E.
SUITE 403
WASHINGTON, DC 20003
202-546-4732
FAX 202-546-1257

RE: Docket #2004N-0254

To Whom It May Concern:

Pediatric nephrologists rely on a number of technologies and devices to provide care for our patients. These include hemodialysis, continuous renal replacement therapy (CRRT), peritoneal dialysis and automated blood pressure measurement. Each of these technologies requires that appropriate medical devices be available that not only fulfill the desired function, but are also appropriately designed for infants and children of various sizes.

For hemodialysis, a specialized central venous dialysis catheter is necessary to deliver adequate blood flow to the dialyzer. Sizes must be available that can be inserted in infants as small as 1.0 kg, up to small adolescents of 50-60 kg. Since the development of the long term indwelling central venous catheter by Robert Hickman and his colleagues, significant strides have been made in the types and sizes of these catheters, but the selection is still limited. Several manufacturers have made commitments to the pediatric nephrology community to develop new catheters and continue to provide them to our patients. However, the number of vendors is quite limited, especially for smaller children and infants. To date the smallest long-term cuffed catheter is 8 Fr, yet this may be too large for some infants with renal failure, in whom long-term hemodialysis is life-sustaining therapy, or for some critically ill newborns with inborn errors of metabolism in whom hemodialysis or CRRT may be life-saving.

Compared to the potential adult market, there is small financial reward for companies to develop such catheters and to continue to provide them. New catheters for children require the same rigorous and expensive testing as for adult catheters; yet only a fraction will be sold compared to new catheters designed for adults. Often most of the technological problems have already been worked out during adult studies. Similar problems exist for choice of the tubing carrying the blood to and from the dialyzer used on dialysis machines. Ideally less than 8-10% of a patient's blood volume should enter the dialysis circuit. For many of the currently available models of dialysis machines, the smallest volume tubing available is 40 ml, which may represent up to 15-20% of the blood volume of the average neonate. Smaller volume tubing is available by one vendor but is incompatible with a number of dialysis machine models. While no hemodialysis machine has been designed specifically for children, many models of machines have been adapted for use in infants and children. However, the lowest blood flow setting on some machines is only 50 ml/min, which is relatively high for use in small infants, making the dialysis procedure technically more difficult, and possibly less safe, than in larger children or adults.

Circuit volume is even more problematic in the newest form of renal replacement therapy, CRRT. In one of the popular machine models, only one circuit is currently available, and it has a blood volume of 90 ml. Because of this relatively large blood volume, the manufacturer does not recommend the use of this device in infants less than 15 kg, but

2004N.0254

C 8

without other options, pediatric nephrologists have to use this circuit, even in smaller infants. A smaller volume circuit has been available outside the USA for a number of years, but is not yet available in the USA, because it is just now undergoing FDA mandated testing to allow its sale in the USA.

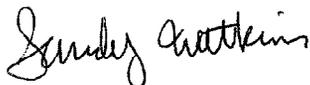
The automated blood pressure machine is another device that pediatric nephrologists use to deliver care to their patients with renal disease and with primary hypertension. These machines are the method of choice for evaluation of small children, because of the ease of measurement compared to manual devices and the need to avoid potentially toxic mercury manometers. There are a number of providers of automated BP machines. However, several studies have demonstrated significant variation in readings for a given measurement between different manufacturer's instruments. The values for systolic and diastolic blood pressure are the result of proprietary algorithms rather than direct measurements. Standardization of automated BP machines would improve the reliability of obtaining BP and facilitate more appropriate management of hypertensive children. Similarly, standardization of cuff dimensions would also be desirable, as cuff size can vary widely from manufacturer to manufacturer. Despite recommendations from consensus organizations such as the American Heart Association and the National High Blood Pressure Education Program, there is no standard size for infant, child, or small adult cuffs among different manufacturers.

While there have been significant strides over the years in the design and availability of medical devices for pediatric nephrology patients, challenges and barriers remain. The major barrier is the limited profitability of these devices compared to the adult market. Perhaps legislation similar to the Food and Drug Modernization Act of 1997 (FDAMA) mandating the development for and testing in children of new devices designed for use in adults would be helpful. The FDAMA and its successor legislation have been successful in increasing the information available on medication use in children.

In addition, advocacy by the FDA for NIH or other national support to develop multi-center pediatric renal consortiums designed to provide an infrastructure for investigating devices in more pediatric patients than can be found in a single center would be useful. An example of this is the Prospective Pediatric CRRT Registry, a consortium of centers that is doing the 510K work for the infant M10 CRRT filter. With regard to the automated blood pressure machines, the FDA could develop standards for such machines so that comparable, accurate blood pressures would be obtained with any machine with the same size cuff, and could endorse the recommendation for standardization of blood pressure cuff sizes that was recently issued by the National High Blood Pressure Education Project.

We appreciate the opportunity to comment about the special device needs for children with kidney disease and hypertension. If we can provide you with any more specific information to help in your assessment, please feel free to contact us. The American Society of Pediatric Nephrology is committed to working with the FDA on these issues to develop safer and more effective medical devices for pediatric nephrology patients.

Sincerely yours,



Sandra Watkins, MD
President, ASPN