Anti-clotting pill may spare kids from frequent injections, blood tests, dietary changes

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For children with rare heart conditions such as Kawasaki disease, heart failure or congenital heart defects that increase the risk of blood clots, a daily anti-clotting pill may safely allow them to avoid the frequent injections, blood tests and changes in diet and medication dosage required with currently approved treatments, according to preliminary research to be presented at the American Heart Association's Scientific Sessions 2022.

The meeting, held in person in Chicago and virtually, Nov. 5-7, 2022, is a premier global exchange of the latest scientific advancements, research and evidence-based clinical practice updates in cardiovascular science.

Some heart conditions that are rare in children increase their risk for forming blood clots, sometimes resulting in stroke, heart attack or pulmonary embolism. To prevent this, children may need long-term or life-long treatment with medications to prevent clotting, such as heparin or warfarin. hile these medications work well at preventing clots, they present other challenges – particularly for children. Heparin requires twice-daily injections. Warfarin, an oral tablet that blocks vitamin K from making proteins needed for blood clotting, requires frequent blood tests, dosage changes and dietary adjustments to avoid food interactions.

In contrast, the medication edoxaban – an anticoagulant and a direct factor Xa inhibitor – acts directly on the clotting system, is an oral pill taken once a day and does not require frequent blood tests. Edoxaban is already approved by the U.S. Food and Drug Administration (FDA) to prevent stroke in adults with irregular heartbeats known as atrial fibrillation, to prevent pulmonary embolisms and to prevent blood clots in deep veins after leg surgery. Some side effects of edoxaban may include bleeding that takes longer to stop, bruising more easily, skin rash, reduced liver function and low red blood cell count (anemia).

"Our findings point to edoxaban as a new and, perhaps, better alternative to the current medications and may improve quality of life for these children," said lead author of the study, Michael A. Portman, M.D., FAHA, director of research in the division of cardiology at Seattle Children's Hospital and professor in the department of pediatrics at the University of Washington

School of Medicine. “A once-a-day, oral anticoagulant would be a distinct advantage for children and families, and eliminate injections and reduce the need for frequent blood tests.”

Studies in several countries

The current study to explore the safety of edoxaban in children was conducted at centers in the U.S. and in several other countries, including Canada, Austria, Germany, Egypt, India, Israel, France, Poland, Hungary, Ukraine, Great Britain, Lebanon, Russia and Italy. Researchers evaluated 168 children younger than 18 years of age (average 8 years of age, 65% male, 71% white) between May 2018 and September 2021.

Each child had heart disease and was receiving the current standard of care to help prevent blood clotting (either heparins or warfarin). Among the children in the study, the heart conditions included Kawasaki disease, which creates inflammation in blood vessels in the heart and sometimes bulging, weakened artery walls, raising the risks of blood clots in the arteries that feed oxygen-rich blood to heart tissue; having only one side of the heart working properly since birth and having open heart surgery (the Fontan procedure) to enable one side of the heart to do the work of two; and heart failure, commonly because they were born with an abnormality in their heart muscle or heart structure that interfered with proper heart function.

Two-thirds (112) of the children were randomly assigned to receive edoxaban, with the dosage based on their age and weight. The remaining one-third (56) of the participants continued on the standard treatment of either heparin or warfarin. In the main study, the children were followed closely for three months, which included monthly clinical visits, symptom history and echocardiograms. After 3 months, all study participants were offered the opportunity to take edoxaban for an additional 9 months, with continued clinic visits and observation.

To assess the safety of edoxaban vs. standard treatment, all children were monitored for the occurrence of clinically significant bleeding that required treatment, which would mean something more severe than a minor nosebleed or an extra-heavy menstrual period. The researchers also tracked the occurrence of blood-clot formation leading to stroke, pulmonary embolism, heart attack or clots in heart arteries visible on the echocardiogram screening, which was performed monthly on all participants in the study.

The study’s major findings include:

One child in each of the two groups (standard treatment vs. edoxaban) experienced bleeding that required treatment, however, it was not considered major bleeding.

The rate of adverse events was similar in both groups, including things such as a common cold or sniffles and stomach upset.

One child in the standard medication group developed clotting in the legs and lungs.

Of the 152 children who participated in the extended 9-month period of observation taking edoxaban, one had bleeding that required treatment after a trauma; two had strokes; and two developed clots in their coronary arteries.

“Cases of bleeding and clotting were very rare in both the edoxaban and standard care groups with only one clinical bleeding even in each group. The data indicate edoxaban did just as well at keeping bleeding and clotting instances rare, which is important in considering it as a viable alternative to current treatments,” Portman said.

Exactly how effectively edoxaban prevents clots could not be quantified in this study since there were similar reductions in clots in both groups. Due to the rarity of these diseases in children there were a relatively small number of participants involved compared to larger, adult trials. However, the rate of clot formation seen in this study was comparable to what has been previously observed in a few retrospective studies of children receiving standard treatment, according to Portman. In addition to the small size of the study, it is limited by the absence of a control group that continued to receive standard treatment during the extended observation period of 9 additional months.

“If a child is having difficulty with anticoagulant treatment – for instance becoming tired of the twice-daily injections – it would be reasonable to discuss with the child’s physician or health care team about whether edoxaban is an option,” Portman said.

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“This study is an important first step of studying the safety of using the oral anticoagulation medication, edoxaban, in young children. Oral anticoagulant medicines like edoxaban have potential to be real “game-changers” by improving the quality of life for young patients with heart disease who are at risk for developing blood clots,” said John S. Kim, M.D., a member of the American Heart Association’s Council on Lifelong Congenital Heart Disease and Heart Health in the Young and director of the Cardiac Thrombosis Management Program at the Heart Institute of the Children’s Hospital Colorado in Aurora. “We look forward to additional research to further demonstrate the effectiveness of these types of medications compared to standard treatment options.”

Edoxaban is not currently approved by the FDA for use in children.

Co-authors are Jeffrey P. Jacobs, M.D.; Jane W. Newburger, M.D., M.P.H., FAHA; Felix Berger, M.D.; Michael A. Grosso, M.D.; Anil Chander Duggal, M.D.; and Neil A. Goldenberg, M.D., Ph.D. Authors’ disclosures are listed in the abstract.

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The findings are considered preliminary until published as a full manuscript in a peer-reviewed scientific journal**. -eurekalert.org/news-releases/969072, October 31, 2022**