Sickle Cell Today

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Sickle Cell Vaso-occlusive Pain Crisis: Role of Fluids in Management

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Fluid therapy in the management of sickle cell vaso-occlusive pain crisis (1) has historically been considered of paramount importance. A common term in the literature used to describe this therapy is "vigorous hydration," which in children the recommendation is to administer fluids between one and 1 ½ the maintenance requirements (2) and in adults fluid replacement should be administered at 250cc/hr for eight hours and then reduced to 125 cc/hr in the absence of renal insufficiency or congestive heart failure (1). While the role of hydration in management of sickle cell vaso-occlusive pain crisis is not validated in prospective, randomized controlled trials, there is indirect scientific data that supports use of fluid administration in its management. What is known is that in sickle cell disease there is an inability of the kidney to concentrate the urine normally (hyposthenuria) which can lead to the excretion of large volumes of urine and intravascular dehydration (3, 4, 5). In this setting, water is lost in excess of sodium resulting in an increased serum osmolality which favors the movement of fluid from the sickle red blood cell (SRBC) and increased concentration of hemoglobin S in the SRBC (intraerythrocytic dehydration). A second compounding factor to intraerythrocytic dehydration is potassium and water being pumped out of SRBCs by potassium channels (i.e., Gardos channel and K-Cl co-transporter) resulting in potentially a further increase in the concentration of hemoglobin S which favors sickling (6, 7, 8, 9). While intravascular dehydration resulting from the excretion of large volumes of urine should always be clinically addressed, objective findings supporting this diagnosis (i.e., postural changes in BP and pulse, increased BUN:Cr, increased serum sodium, etc.) are usually not present probably because of a normal thirst response being intact.

When fluids are administered, what is the appropriate fluid and what is the best route of administration? To date, randomized control trials have not been executed that address the safety and efficacy of the type of fluid, quantity of fluid or best route of administration. What is known is that inability of the kidney to concentrate the urine normally can contribute to an increase in serum osmolality, intravascular dehydration, and SRBC dehydration all of which favor sickling when hemoglobin S is deoxygenated. The induction of severe dilutional hyponatremia using a vasopressin analogue and 5% dextrose in water or half normal saline failed in clinical trial due to inconsistent demonstration of a decrease in red blood cell hemoglobin S concentration and severe adverse effects (10, 11, 12). Furthermore, the administration of hypotonic fluids (D5W or half normal saline) alone is relatively ineffective in decreasing the serum osmolality (with normal renal function), reducing SRBC

hemoglobin S concentration, or treating pain episodes (11). This being said, in the absence of intravascular dehydration, the replacement of fluids by the fluid being loss is a reasonable approach, i.e., half normal saline or D5W. If dietary intake is poor, D5 half normal saline administered at maintenance (see above) will provide enough glucose to keep the patient out of a catabolic state. If the patient is clinically volume contracted, normal saline should be administered until hemodynamically stable then converted to a hypotonic fluid at maintenance. When administering fluids in the sickle cell patient, basic tenets of fluid management after the initial period of fluid administration should be adhered to. The volume of fluid administered, urine out, vital signs and O2 saturation should be monitored. The practicing clinicians must remember, "Primum non nocere" – first do no harm, until well designed studies addressing the safety and efficacy of the types of fluids, appropriate volume of fluids and routes of administration can be determined.

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Save the Date – Sickle Cell Disease Practical Issues XVIII: What's in Your Genes? The Promise of a Cure

On May 30, 2020 the USA Comprehensive Sickle Cell Center will host its 18th Annual Regional Sickle Cell Conference in Mobile AL. The conference will feature national, regional, and local experts addressing the recent FDA approval of Adakveo and Oxbryta in the treatment of sickle cell disease and advances in gene therapy. A highlight of the conference will be to engage a sickle cell client who has actually undergone gene therapy. This conference promises to be one of the most exciting and informative educational experiences in the conference's 18 year history. For more information on the conference visit www.southalabama.edu/colleges/com/research/sicklecell.html, email acsmith@health.southalabama.edu or call 251-470-5893. Register online at: usa-cme.com.

Alabama State Medicaid on Board with New Therapies for Sickle Cell Disease

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November 2019 proved to be of historic significance for sickle cell disease (SCD). The U.S. Food and Drug Administration approved two drugs for the treatment of SCD, Adakveo (crizanlizumab-tmca) and Oxbryta (voxelotor). Both drugs are approved for use in adults and pediatric patients beginning at age 16 years for Adakveo and age 12 years for Oxbryta.

"Adakveo is the first targeted therapy approved for SCD, specifically inhibiting selectin, a substance that contributes to cells sticking together and leads to vaso-occlusive crisis," said Richard Pazdur, M.D., director of the FDA's Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA's Center of Drug Evaluation and Research. Adakveo is the first non-opioid drug developed and FDA-approved shown to reduce the number of pain crisis in SCD. Pazdur goes on to say, "Oxbryta is an inhibitor of deoxygenated sickle hemoglobin polymerization, which is the central abnormality in SCD. With Oxbryta, sickle cells are less likely to bind together and form the sickle shape, which can cause low hemoglobin levels due to red blood cell destruction." Clinical effectiveness of this drug was based on findings from a clinical trial demonstrating an increase in hemoglobin of 1 gm/dL or more (affected individuals when treated are less anemic). Accelerated FDA approval of Oxbryta is based on its action of increasing hemoglobin. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

The New York Times (https://www.nytimes.com/2019/12/07/health/sickle-cell-adakveo-oxbryta.html) published an article December 7, 2019, Two New Drugs Help Relieve Sickle Cell Disease. But Who Will Pay? Both drugs are projected to cost an estimated $100,000 a year. The estimated cost to treat a child with SCD is $10,000/year and $30,000 for an adult. Everyone agrees that these cost likely under-estimates the true economic burden encountered caring for those with SCD. The issue of cost and who will pay is valid. Having good treatments whose cost precludes access to those treatment is like having no treatment at all. Needless to say, this discussion is ongoing particularly when an existing therapy, Hydroxyurea, is under-utilized and has been demonstrated to have clinical benefit at an estimated cost of $1000/year. While it is too soon to tell, the two new drugs may actually decrease overall cost of care for individuals with SCD by decreasing the overall associated morbidity (end organ damage, ie., stroke, pulmonary hypertension) and mortality.

The good news, Alabama Medicaid has moved extraordinarily quickly to approve coverage for Adakveo and Oxybryta. Please contact your provider if you have questions and are interested in being evaluated for these drugs as potential therapeutic options.

Gabapentin: Prescription Drug Update

Jessica King, CRNP

Effective November 18, 2019, Gabapentin was reclassified as a Schedule V Controlled Substance in the state of Alabama. Gabapentin is currently FDA approved to treat seizures, post-herpetic neuralgia, fibromyalgia, and neuropathic pain. The drug reclassification of Gabapentin will require providers prescribing this medication to allow no more than 5 refills on a prescription and the prescription will expire in 6 months. If you are prescribed Gabapentin and have additional questions or concerns you will need to contact your healthcare provider's office.

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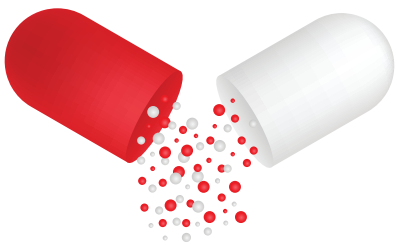

Giving the Gift of Life: Good Things Happen when a Community Works Together

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September 14, 2019 marked the 21st year of a partnership between Alpha Phi Alpha Fraternity Inc., the University of South Alabama Comprehensive Sickle Cell Center, Franklin Primary Health Center and the American Red Cross in sponsoring the annual blood drive. This event is sponsored every year in September, which is National Sickle Cell Awareness Month. Perennial supporters of the blood drive were the: Classic Corvette Club, Student National Medical Association, Alpha Elites, and the Mobile community. The goal set for the drive was 40 units of blood and 39 units were collected. 105 individuals will potentially benefit from this effort.

A special thanks goes out to the Classic Corvette Club from the USA Comprehensive Sickle Cell Center. They not only adorned the blood drive with their beautiful Corvettes and donated blood, 2019 marked their 12th year of making a financial contribution to the Center. The sponsors express their sincere gratitude to all who gave the gift of life through blood donation and volunteered their time to make this blood drive a success.

The 2020 blood drive is tentatively scheduled for Saturday, September 12, 2020 at Franklin Primary Health Center Medical Mall located at 1303 Martin Luther King Avenue, Mobile Alabama.

ASH Publishes New Clinical Practice Guideline on Cardiopulmonary and Kidney Disease in Sickle Cell Disease

The American Society of Hematology (ASH) recently published the first chapter of the SCD guidelines: cardiopulmonary and kidney disease. In total, five chapters will be published with the remaining chapters scheduled for publication in the first quarter of 2020. The guidelines will address both the pediatric and adult populations. Sixty-one clinical experts of which Johnson Haynes, Jr., MD, Director, USA Comprehensive Sickle Cell Center, was a participant, 10 patient representatives, and five methodologist reviewed published evidence used to form all recommendations. For more information visit hematology.org/SCDguidelines
Reference: blood advances. 2019; 3(23):3867-3897

Impact of the Pediatric to Adult Care Transition Program (PACT) from a Participant's Perspective

T'Shemika Perryman, RN-PACT, Coordinator
Cimone Smith, Transition Coordinator, ST3P-UP Study Facilitator

The Pediatric to Adult Care Transition program (PACT) was started in 2012 to bridge the gap between the pediatric and adult healthcare systems for sickle cell disease clients between 13-21 years of age. The goal of the PACT program is to not only educate clients about their condition, but also help them acquire skills they need to live full, successful, and productive lives. We instill in our clients that they are more than just a condition. We share with them that they can be and do anything they put their hearts and minds to accomplish. We encourage them to enroll in college, find a trade, and secure employment doing something they enjoy. We recently caught up with one of our former participants, Briana Kennedy, who recently earned a Bachelor of Science degree in Early Childhood Studies from the University of South Alabama. We wanted to get her point of view on how the PACT program helped her successfully transition into adulthood.

Do you remember when you first entered the PACT program? Do you recall your first thoughts about the program?

"Yes, I remember when I first entered PACT. I was really nervous because I thought I would be meeting new doctors, but once I started I realized that it was most of the doctors that I already knew. "

In addition to the doctors, who else worked with you in the PACT program? What role did they play?

"In the PACT program, I worked closely with Dr. Ardie Pack-Mabien and Ms. T'Shemika Perryman. I also worked with all the other doctors and nurses on my health care team. They were the ones to guide me and they provided me with ample information about how I can control my pain management at home.

In the PACT Program, I started out working closely with Dr. Ardie and Ms. T'Shemika. When I was going to the pediatric clinic I would have my regular visit with Dr. Wilson, Dr. Imran, or Dr. Ardie then Ms. T'Shemika would come in for the PACT part of the visit. We would go over my type of sickle cell, medications, school, and life goals. Dr. Ardie and Ms. T'Shemika are also on the adult side. But on the adult side, I also see Dr. Haynes and the nurse

practitioner, Ms. Jessica King."

Do you feel being a part of the PACT program was beneficial to you? Why?

"Yes, I feel it was beneficial to me because it taught me how to control my health with the help of my health care team. This program taught me to be more responsible which helped me to focus on my health and education."

In your own words can you explain what PACT is and what it means to you?

"PACT is a program that helped shaped me into who I am today. It guided me into adulthood. Because of PACT, I'm extremely comfortable, educated, and well aware of my health and health care needs. For example, the PACT program held various programs and classes. There was a money management class that taught us about money management, budgeting, and credit. There was also a class on sex education and an open house event for us to meet the adult doctor before we switched over."

What are you doing now?

"I am currently a Preschool Teacher."

Do you feel PACT helped you to achieve these milestones? How so?

"Yes. Because of this program, I was able to focus more of my time in the classroom rather than in a hospital. I was given many tips that I can try at home to help manage my pain."

Now that you have completed PACT what are your thoughts on the program?

"I am extremely grateful that I took part in this program. It made a huge impact in my life and my future. I can have a more open relationship with my doctors and nurse practitioners if there is even the slightest of problems. I can always count on them. They are always there for me regardless of the time or circumstances. I also feel that I am more educated on my disease because of the program."

What advice would you give any teen who was hesitant about actively participating in PACT?

"Don't be afraid! They are here to help and guide you. If you allow them to, the type of advice they can give can last a lifetime."

Do you have any words for parents who are hesitant about encouraging their teens to actively participate in PACT?

"Be open minded, you have people here to help you and your child. Bringing them to events now will help them be prepared when it is their turn to care for themselves as adults. They are in excellent hands and it's worth it in the long run. These health care professionals will work with you and your teen every step of the way, like they did and continue to do with me."

Visit the Comprehensive Sickle Cell Center website at:
http://www.usahealthsystem.com/sicklecellcenter

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