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Systematic Review: Barriers That Prevent Compliance With Hydroxyurea in Sickle Cell Disease

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This is to certify that the doctoral study by

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has been found to be complete and satisfactory in all respects,
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Abstract

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MS, Lehman College CUNY, 2012

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Project Submitted in Partial Fulfillment

Of the Requirements for the Degree of

Doctor of Nursing Practice

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Abstract

Sickle cell disease (SCD) is a blood disorder that is inherited from both parents and affects millions of people globally. The symptoms of SCD may be debilitating and pose a significant challenge to nursing care. Hydroxyurea (HU), the Food and Drug Administration (FDA) approved treatment for SCD in adults is reportedly effective, but its usage is still minimal among adolescents with SCD. The purpose of this systematic review was to evaluate existing literature on the barriers to HU use in adolescents with SCD. The Johns Hopkins Nursing Evidence-based Practice (JHNEBP) Rating Scales guided this study. An extensive electronic search of Cumulative Index to Nursing and Allied Health (CINAHL), MEDLINE, Your Journal OVID, Academic search premier, and Cochrane Database of Systematic reviews of articles published in English from 2003 to 2013 was conducted. The 5 articles that met the inclusion criteria were organized, tabulated, and analyzed. The results suggest that inadequate knowledge about HU; physician concern about carcinogenic potential; lack of awareness of the National Heart, Lung, and Blood Institute (NHLBI) recommendations on HU use; and lack of belief in the benefits of HU contribute to providers' under-prescribing and minimal usage of the treatment. The implications for social change include knowledge useful for SCD patients, parents/guardians, care providers, and other researchers who are searching for direction in improving the quality of life of SCD patients. Long-term results may include increased HU usage, decreased pain episodes, fewer emergency room visits, and reduced patient mortality and morbidity.

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Dedication

This project is in memory of my loving father Rev Oyibo Victor Imegi; you laid the foundation of health care and nursing in the family by establishing a six-bed cottage hospital in Ogbogu Town, Rivers State Nigeria in 1950.

I am also dedicating this work to the memory of my late mother, Esther Ada Imegi; you are my dearest heart and my very best friend. Despite your limited education, you supported and encouraged me to go on to the highest degree there is in nursing. You were the wings beneath my wings. Your beautiful spirit shall forever be with us.

In memory of my baby brother Ndubueze Tony Imegi; you are my very special brother, and we were inseparable as we grew up. I will always remember you.

This project I also dedicate to all SCD patients, colleagues, mentors, and other interdisciplinary care providers who share the goal of improving the health-related quality of life of sickle cell patients.

Acknowledgments

I would like to thank Almighty God for guiding and supporting me through this journey. He gave me the strength, courage, health, persistence and the wisdom to complete this project. It would not have been possible without his mercy and grace.

To my loving husband, Ndubuisi Abaraoha, children, and grandchildren, I thank you all immensely for your patience, devotion, understanding, unending support, and encouragement. I love you all forever.

To my professor Dr. Mirella Brooks, my preceptor, mentor, and advisor Dr. Cassandra Dobson, you have supported, encouraged, and empowered me through this project. You are both highly appreciated.

Finally, to a host of other relatives and dear friends, who always asked after my progress in school and continuously offered moral support and prayers, I thank you all greatly.

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Section 1: Nature of the Project

Introduction

Sickle cell disease (SCD) is an autosomal recessive genetic blood disorder related to different kinds of defective hemoglobin (Hb) especially common among people with ancestral background from sub-Saharan Africa, South America, the Caribbean, Saudi Arabia, Turkey, Greece, and Italy (Centers for Disease Control and Prevention [CDC], 2014). Presently, researchers have identified more than 700 structural hemoglobin variants, but only three hemoglobins (Hb) S, C, and E) are widespread. Sickle cell disease is characterized by series of severely painful, recurrent episodes that result from occlusions of small blood vessels leading to frequent emergency room visits. Infections, damage of organs, stroke, and other complications are also common (Ballas, 2010). To date, SCD treatment has been symptomatic with a focus on pain relief with opioids. However, hydroxyurea (HU), the only Federal Drug Administration FDA approved breakthrough in the pharmacotherapy of SCD within the past 20 years, is reportedly capable of modifying the disease pathogenesis, transforming the treatment of sickle cell disease (Neville & Panepinto, 2011).

Despite reports that HU can decrease incidences of painful crises, is effective in treating acute chest syndrome, priapism, and increased levels of fetal hemoglobin (HbF) and reduces overall mortality rates in adult patients (Charache et al., 1995; Halsey & Robert, 1995; Saad et al., 2004; and Steinberg et al., 2003), there continues to be minimal use of HU in the management of sickle cell disease. The aim of this project was to perform a systematic review of the literature on the barriers that prevent adolescents aged

12-18 from being compliant with HU. According to the CDC (2014), the impact of SCD is not only on the patient but also on the family and society as a whole. The result of this systematic review will be used to recommend a rigorous education program on the effects of HU and to inform patients, their relatives and providers.

Background of Sickle Cell Disease

Sickle cell disease is an autosomal recessive blood disorder, meaning that the defective gene is on one of the first 22 pairs of chromosomes that do not ascertain gender. As such, SCD affects men and women equally. Getting one copy of the gene from each parent is essential to have the condition; as such, an individual with Hgb SS has acquired the genetic trait for SCD sickle cell disease hemoglobin S (HbS) from both parents (Myers & Eckes, 2012).

There are three types of genotypes. Healthy individuals have genotype which is the normal hemoglobin (Hb) AA, unaffected "carriers" have genotype hemoglobin (Hb) AS and are said to have the trait, and those with sickle cell disease have hemoglobin (Hb) SS. If two individuals with HbAS genotypes have children, one child will have a 25% chance of being healthy with HbAA. One child will have a 25% chance of having sickle cell anemia with HbSS genotypes. Two children will have a 50% chance of being an unaffected carrier with HbAS (Myers & Eckes, 2012) See Figure 1 for more information.

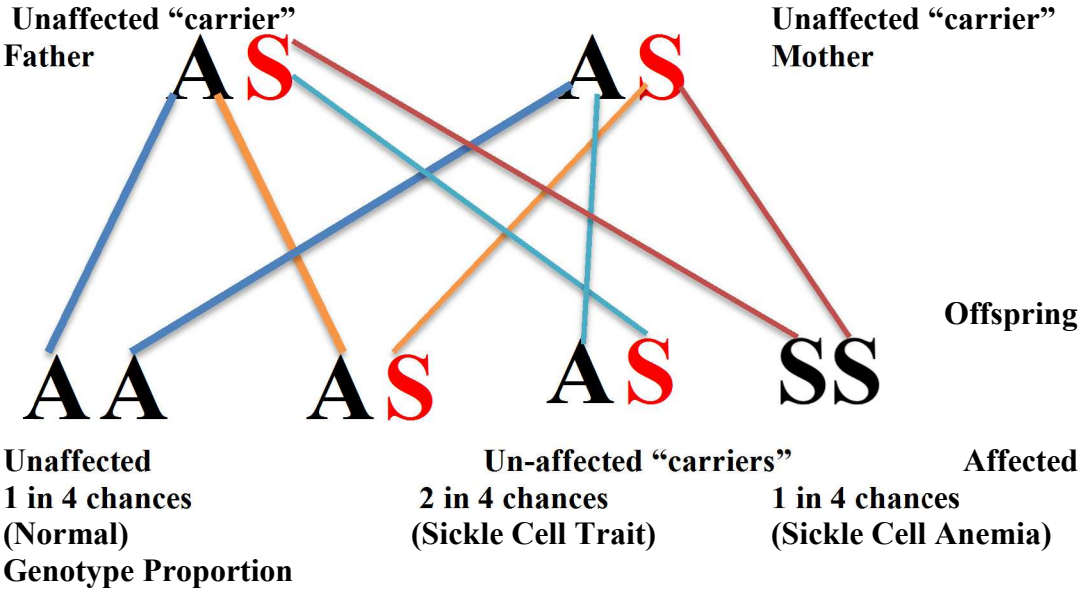

Figure 1. Distribution of hemoglobin genotypes.

Other forms of sickle cell disease can also occur if HbS is inherited from one parent and abnormal hemoglobin (for instance hemoglobin C (HbC) or thalassemia β is inherited from the other parent. This will give rise to HbSC or HbSβ respectively. The abnormality in the hemoglobin molecule results from mutation in the β-globin gene where a single nucleotide adenine to thymidine (A to T) in codon for amino acid 6. The change converts a glutamic acid codon (GAG) to a valine codon (GTG) (Cao, 2004). HbS has a unique property of causing polymerization (cellular aggregation) which changes normal red blood cells from smooth, round (like the letter "O"), and flexible state into a rigid, sticky, sickle-shaped cell (like letter "C"), causing clustering. This change makes movement in the blood vessels difficult. The cluster eventually leads to vaso-occlusion

and, as a result: pain crisis, tissue damage, susceptibility to serious infection, and organ failure (Cao, 2004; Ellison, 2007).

In the past, treatment of SCD was mainly symptomatic, with a focus on pain relief using opiates. Hydroxyurea (HU), the only FDA approved medication for SCD has been reported to reduce the damaging effect of SCD and improved some aspects of quality of life of the patients; however, its usage remains minimal (National Institutes of Health [NIH], 2008).

The purpose of this project was to carry out a systematic review of evidence concerning existing practices related to the barriers that are preventing this patient population from complying with this promising treatment. As a result of the findings, an educational program will be recommended to improve community knowledge concerning HU, which will make patients and their relatives' educated consumers.

Problem Statement

In the last 100 years, the treatment of SCD has focused on pain management with opioids, and folic acid for increasing fetal hemoglobin (HbF) which according to Ware (2010) is protective against clinical severity. Ware noted that low-percentage of HbF is linked to a higher risk of developing vaso-occlusive complications, organ damage, and early dearth. Neither of the early treatment approaches have had a significant impact in decreasing the crisis pain associated with SCD. Other treatments include blood transfusion and other palliative unapproved drugs.

Several studies reported the effectiveness of HU and showed significant results in increase fetal hemoglobin level, decreases in the frequency of painful attacks, decreases

in the number of emergency room visits, decreases in hospitalizations, and improved health-related quality of life (Al-Nood, Al-Khawlani, & Al-Akwa, 2011; Ballas et al., 2006; Charache et al., 1992; Panepinto, 2012).

The effectiveness of HU was noted even at low doses; the medication still appeared to raise fetal hemoglobin levels in sickle cell patients (Al-Nood, Al-Khawlani, & Al-Akwa, 2011), but this medication continued to be met with resistance. A systematic review of literature examined the different barriers that are preventing adolescents ages 12 – 18 with SCD from complying with HU. The review has identified barriers that prevent patients with sickle cell disease from being compliant with HU. Nurses are suited to provide health promotion in addressing this concern. Furthermore, the advanced professional nurse is equipped to provide education for patients and their families.

Purpose and Project Objective

The purpose of this project was to review and disseminate knowledge regarding the barriers that prevent adolescents ages 12-18 with SCD from being compliant with HU therapy. Additionally, this systematic review also recognized the stigma associated with HU and the lack of knowledge concerning the decreased use of HU in the SCD population

PICOT question

To examine the evidence, formulation of the clinical issue must be presented in a searchable and answerable question using the patient population (P), intervention or issue of interest (I), comparison intervention (C), status-outcome (O), and the time frame (T) for the intervention to achieve the outcome, in the (PICOT) format. The clinical question

was formulated in a structured and specific way to assist the reviewer in finding the appropriate evidence to answer the questions and decrease bias (Melnyk & Fineout-Overholt, 2011). The patient or population to whom the question applies for this review is adolescents ages 12-18 with SCD. The intervention or issue being considered is the barriers that prevent adolescents with SCD from being compliant with HU? The PICO question that guided this review was: what are the barriers that prevent adolescents ages 12 – 18 with SCD from being compliant with HU?

Frameworks for the Project

I used the JHNEBP for this systematic review of the literature. This evidence-based appraisal guide is a comprehensive manual that provides a novice or advanced nurses with specific guidelines about evidence-based practice (Newhouse, Dearholt, Poe, Pugh, & White, 2007). It further detailed a step by step appraisal on how to critique evidence-based studies and rating scales which provided information regarding the quality and strength of evidence used. This manual has a wealth of scholarly authors who are experts in the field of evidence-based practice.

This framework provided the basis for the analysis of evidence available on the barriers preventing SCD patients from using HU. This was achieved by using the model's application process of practice question, evidence, and translation (PET). This evidence-based practice (EBP) process conceptualizes asking a practice question, finding evidence, and translating the evidence into practice. It therefore, laid the foundation for gathering and assessing additional evidence that was revealed by following the specific steps of the application process. The JHNEBP model is a manual that has been referenced globally

for its succinct overview of EBP as well as providing an in-depth and broad structure that is comprehensive and user-friendly.

Nature of the Doctoral Project

A systematic review of the literature was carried out in an attempt to meet the project goals of identifying the barriers that prevent SCD patients from being compliant with HU. It also addressed stigma, lack of knowledge concerning treatment, and gaps that exist in the SCD population relating to HU. The search included articles published in English from 2003 to 2013, using the databases: CINAHL, MEDLINE, Pub Med, Academic Search Premier, Cochrane clinical trials, and National Library of Medicine. My search also included these literatures: Sigma Theta Tau International, Nurses Science Quarterly, and Journal of Blood. For inclusion criteria, the systematic review examined studies that included adolescents' ages 12-18 diagnosed with sickle cell disease and are being currently managed with HU therapy. Articles that identified specific barriers were also included.

History of Sickle Cell Disease

In 1910, Herrick was the first to identify sickle cell anemia when he published a description of peculiar and sickle-shaped red blood corpuscles in a case of a 20-year- old student from Grenada, West Indies. This young man was attending school in Chicago, where he complained of pain and was later diagnosed with severe anemia. No conclusion was drawn from his case until further microscopic examination of his blood work and other patients with similar complaints showed the same abnormal shaped cells (Herrick, 1910). Further investigations continued to surface regarding the shape of the corpuscles.

Over the years, several patients emerged with different symptomology. Doctors kept track of these patients and their case studies in an attempt to understand this cell disease.

In 1949, Dr. Linus Paulding and others discovered that the peculiar cell was due to an abnormal protein molecule. Dr. Paulding was later awarded for his work in linking genetic disorders and sickle cell disease together. This connection marked the birth of the molecular disease concept (Odievre, Verger, Silva-Pinto, & Elion, 2011).

Impact of Sickle Cell Disease

People with sickle cell disease experience chronic pain and acute pain episodes which result in frequent emergency room visits. Infection, organ damage, stroke, and other complications can also occur (Ballas, 2010). This disease also affects individuals psychologically, with affects ranging from depression, inappropriate coping strategies, lowered health-related quality of life, inability to perform activities of daily living, and role limitations, (Kofi, 2005). SCD is now recognized by world health organization (WHO) as a global health issue that has impacted society as a whole (Healthy People 2020, 2013).

The goal of Healthy people 2020 is to acknowledge that this disease has affected all people and all ethnicities. Individuals who are now living longer and healthier lives need health care that will improve their quality of life, healthy development, and healthy behaviors across all stages of life.

An average of 75,000 hospitalizations due to SCD reportedly occurred in the United States from 1989 through 1993. Medical expenditures during 2005 for children

with SCD averaged $11,702 for children with Medicaid coverage and $14,772 for children with employer-sponsored insurance (CDC, 2014.). The impact of SCD on the patient, his/her family, and society in general is significant. People with SCD are stereotyped with behaviors of drug dependency, as "frequent flyers" to the emergency department, unemployed, undereducated, and underserved (limited access to health care) (Ballas, 2010).

To counteract these negative perceptions, health care providers should be educated regarding the disease process, life-threatening complications, available treatment options, and psychosocial concerns of SCD. Most importantly, the individual with SCD must receive appropriate care when it comes to addressing their pain, as the complaint of pain is the hallmark of SCD (Ballas, 2010). There is a need to identify the barriers preventing the use of HU for the management of this patient population. This systematic review will be used to recommend rigorous education on the effects of HU to patients, patient families, caregivers, and health providers.

Risks and Benefits of Hydroxyurea

Hydroxyurea is an antineoplastic agent originally synthesized in Germany in 1869. Close to 50 years ago, HU was developed as an anticancer drug for the treatment of some types of leukemia, melanoma, myeloproliferative syndrome, and ovarian cancer (NIH, 2008). In 1984 HU was introduced as a treatment for sickle cell patients who meet the following criteria: diagnosis of HbSS or S β-thalassemia, ≥ 3 years of age, three or more severe vaso-occlusive pain events per year, or two episodes of acute chest syndrome per year (Jones et al., 2016; Sickle Cell Information Center, 2011). SCD

patients must take their medications, including HU, regularly in order to treat their disease and improve their health. Therefore, it is important to weigh the risks and benefits of such a treatment.

The FDA (2013) stated that when a medication's benefits outweigh its known risks, the agency deems it safe enough to approve it. With regards to HU, benefits recorded since its first testing on SCD patients include but are not limited to an increase in HbF, reduction in hospitalizations and pain crisis, reports of better overall HRQL, and better physical HRQL (Segal et al., 2008; Thornburg et al., 2011). HU has excellent bioavailability after oral administration and requires only once daily dosing, which enhances medication adherence. This benefit also makes it attractive for use in resource-poor countries, where there may not be widespread access to facilities to perform laboratory monitoring (Heeney & Ware, 2009; Strouse & Heeney, 2012).

On the other hand, recorded risks include reducing sperm count and motility with resultant abnormal morphology, HU-induced dermatomyositis, mild neutropenia, mild thrombocytopenia, severe anemia, rash, or nail changes (Grigg, 2007; Nofal, & El-Din, 2012). Despite the reported risks, HU has been shown to be helpful for sickle cell patients. The first major study of the treatment in 1995 was stopped early as it was clear that HU reduced the number and severity of pain episodes in patients with SCD compared with placebo (NIH, 2008). In 1998, HU was approved by the FDA for adults with SCD.

Although not yet approved for use on children, Heeney and Ware (2009) reported that HU was a powerful therapeutic drug with proven laboratory and clinical efficacy for children with SCD. One significant concern is the limited report on its toxicity and long term usage.

An observational follow-up conducted by Steinberg et al. (2003), on individuals with 9 years of treatment, concluded that adult patients taking HU for frequent pain episodes appeared to have reduced mortality. Similarly, to examine the risks and benefits of long-term HU usage, Steinberg et al. (2010) followed patients in their trial for 17.5 years and concluded that long-term HU use is safe and might decrease mortality. During the transition of HU in the treatment for SCD, there needs to be more research that will be carried out for appropriate management of HU use in SCD. In obtaining more reliable and valid data, there have to be more patients who are using HU to develop protocols that will be significant with a great emphasis placed on rigorous education on the effects of HU to patients, family, and providers.

Sickle Cell Disease and Quality of Life

The ultimate goal of health care providers is to maintain or improve the quality of life of individuals in general as well as, people with chronic and debilitating disease like SCD in particular. Traditionally, evaluating the disease burden and effect of treatment of SCD were mainly accomplished by determining laboratory values, calculating mortality data, the number of hospitalizations, and incidents of painful crisis (Charache et al., 1995; Platt et al., 1991; Platt et al., 1994).

Researchers of the last decade noted a significant increase in the development and use of tools to evaluate health-related quality of life (HRQOL) measures. These include pediatric health-related quality of life (PHRQOL) measurements or pediatric quality of life (PedsQL) for children and adolescents (Panepinto, Torres, & Varni, 2012).

There are generic HRQOL tools that can be used for any disease condition and also disease-specific tools which are necessary for understanding a particular disease condition. For example, PedsQL sickle cell module (PedsQL-SCD) is used to assess children with SCD (Dampier et al., 2010; Panepinto et al., 2008). Since the development of the PedsQL sickle cell module (PedsQL-SCD), studies have been shown that the tool is feasible, reliable, and valid to measure HRQOL in children with SCD. A multisite study by Panepinto et al. (2013) of 243 pediatric patients with SCD and 313 parents to report on the properties of the tool, noted that the PedsQOL-SCD module has shown acceptable measurement qualities for use on SCD. The report also demonstrated that use of the tool will foster understanding of the health and well-being of children with (Panepinto et al. 2013)

Definition of Terms

For the purpose of this systematic review, the following terms were defined as:

Health-related quality of life (HRQOL): is defined as the patient's perception of his/her well-being and level of functioning compared with a perceived ideal as affected by his/her health. Tools that measures HRQOL are multidimensional and include physical, emotional, and social components, as well as school/work functioning (Darbari & Panepinto, 2012).

Hemoglobinopathies: are a group of inherited disorders in which there is abnormal production or structure of the hemoglobin molecule. Examples include HbC, HbS-C, sickle cell anemia, and different types of thalassemia (National Library of Medicine (NLM), 2015)

Hydroxyurea (HU): is defined as an antineoplastic agent approved by FDA for the treatment of adults with sickle cell disease. It induces HbF production, increases erythrocyte hydration, and reduces cell adhesiveness among other things. It has also been reported to be a powerful therapeutic agent with proved laboratory and clinical efficacy for children with SCD (Heeney &Ware 2010).

Sickle cell crisis: is defined as the beginning of painful episodes in patients with SCD resulting from occlusion of blood vessels by sickle-shaped red blood cells. It is manifested as severe pain in the extremities, back, abdomen, or chest, and is usually associated with fever and the passage of dark or red urine (Serjeant & Serjeant, 2001).

Sickle Cell Disease (SCD): is defined as a chronic autosomal recessive hereditary disorder caused by the presence of hemoglobin S (HbS). This abnormality in the homozygote (SS) induces polymerization of some Hb, impeding movement blood circulation. It is characterized by chronic hemolytic anemia, acute vaso-occlusive crisis, and an increased risk for infection (Nzouakou, et al., 2010).

Assumptions

Upon review of the literature, my initial assumptions focused on the belief that SCD patients felt that HU was an experimental drug used primarily for the treatment for cancer patients. HU has been used for the treatment of many other diseases, including

SCD. The evidence has shown that there was limited research done on the long-term effects of the medication on SCD. Other patients believed that the drug is too harmful, and some would rather take the chance of just living without the use of HU. Because of the limited research completed on HU for SCD, there is little knowledge about the drug's effectiveness and toxicity (Heeney and Ware (2009). Due to the scant amount of patients that participated in the clinical trial for long term use of HU, there is not enough evident to show exactly how efficient HU use is for long-term management. Some research studies that were directly focused on HU tolerance found that the treatment had positive results in the treatment of SCD. In essence, many of the non-compliancy issues were found to be due to fertility concerns (Grigg, 2007).

Limitations

During the initial onset of this project, there were limited articles that supported the purpose of this project, which was to review and disseminate knowledge regarding the barriers that prevent adolescents ages 12-18 with SCD from being compliant with HU therapy. Despite the key terms that were used, there were only articles that referenced the disease itself, and not many mentioned the barriers in using HU to treat SCD. Also, there were few articles on individuals between the ages of 12 and 18 using HU. After many discussions and re-evaluation of the search, it was decided to expand the search to include adults and children diagnosed with SCD. The search was broadened to include many other search engines and electronic databases, both nationally and internationally, that had EBP about the topic.

Significance of the Project

The implications for social change in HU treatment adherence by SCD patients include knowledge useful for this patient population, parents/guardians, care providers, and other researchers who are searching for direction in improving the quality of life of SCD patients. Also of significance would be motivating the patients' to be engaged in their healthcare management. The long-term results would include increased HU usage, decreased painful episodes, fewer emergency room visits, and reduced patient mortality and morbidity. HU therapy holds the promise of improving health outcomes, thereby closing adherence to the treatment which is necessary to maximize its efficacy (Drotar, 2010).

This review yielded information that would provide increased knowledge of the myths and barriers that are associated with the use of HU. The objective of this review was to identify the myths and the barriers that are associated with HU adherence, thereby disseminating information that would provide patients/guardians and health care providers with a better understanding of those barriers. Patients/guardians would be able to make an educated decision about the use of HU. Also, healthcare providers would be assisted in making the appropriate adjustment in the plan of care for the SCD adolescents who are resistant to the use of HU. Understanding the barriers preventing SCD patients from being compliant with HU treatment could bring about increased use of this revolutionary therapy.

Summary

SCD continues to be a complicated disease to manage, despite the innovations in treatment since its discovery in 1910. Although the trajectory of the disease has improved, with individuals living into their forties and fifties, there are many treatment approaches that need to be assessed to improve patients' quality of life.

Section 2: Review of Scholarly Evidence

Introduction

In this section the background for the proposed study is presented by briefly summarizing the literature on HU usage in the management of SC crisis, the effect of HU on the HRQL of SCD patients, and the state of knowledge in HU use on children with SCD. The literature describing adverse reactions, effectiveness, and toxicity of HU is considered. Studies exploring the concerns of the long term effects of HU are reviewed and critiqued. The limited studies to date of barriers preventing HU usage are evaluated, and the findings from this group of studies are synthesized and conclusions drawn regarding the gaps in knowledge that can be revealed by this systematic review. Additionally, this section discusses the literature search strategy, including the databases and libraries accessed, search engines used, the extent of the literature, and key terms utilized. This section further addresses the concepts, models, theories, and framework used and the reason for their selection.

Literature Search Strategies

The search engines used were CINAHL, MEDLINE, Academic Search Premier, Cochrane clinical trials, Google Scholar, and National Library of Medicine databases to access literature on the barriers preventing adolescents ages 12-18 with sickle cell disease from being compliant with HU treatment. The key terms and combinations of search terms that were used in the review of literature include: sickle cell disease, hydroxyurea, barriers, and adolescents. Only articles published in English from 2003 to 2013 was included.

Conceptual Framework

The evidence-based approach that was used in implementing the systematic review of literature was the JNEBP known as the PET This process has three phases and structures the activities of EBP. According to Newhouse, Dearholt, Poe, Pugh, & White (2007), the first phase is the identification of an answerable EBP question, the second phase is the systematic review and synthesis of both research and nonresearch evidence. This phase has five steps: (a) search for evidence, (b) appraise the evidence, (c) summarize the evidence, (d) rate the strength and quality of the evidence (see Tables 1 & 2), and (e) develop recommendations. The final phase is translation which is to communicate the findings.

Table 1

JHNEBP Strength of Research Evidence Rating Scale

	STRENGTH of the Evidence
Level I	Experimental study/randomized controlled trial (RCT) or meta-analysis of RCT
Level II	Quasi-experimental study
Level III	Non-experimental study, qualitative study, or meta-synthesis.
Level IV	Opinion of nationally recognized experts based on research evidence or expert consensus panel (systematic review, clinical practice guidelines)
Level V	Opinion of individual expert based on non-research evidence. (Includes case studies; literature review; organizational experience, e.g., quality improvement and financial data; clinical expertise, or personal experience

Table 2

JHNEBP Quality Rating Scale for Research Evidence

		Quality of the Evidence
A High	Research	Consistent results with sufficient sample size, adequate control, and definitive conclusions; consistent recommendations based on extensive literature review that includes thoughtful reference to scientific evidence
	Summative reviews	Well-defined, reproducible search strategies; consistent results with sufficient numbers of well-defined studies; definitive conclusions.
	Organizational	Well-defined methods using a rigorous approach; consistent results with sufficient sample size; use of reliable and valid measures.
	Expert Opinion	Expertise is clearly evident.
B Good	Research	Reasonably consistent results, sufficient sample size, some control, with fairly definitive conclusions; reasonable, consistent recommendations based on fairly comprehensive literature review that includes some reference to scientific evidence.
	Summative reviews	Reasonably thorough and appropriate search; reasonable, consistent results with sufficient numbers of well-defined studies; evaluation of strengths and limitations of included studies; fairly definitive conclusions.
	Organizational	Well-defined methods; reasonably consistent results with sufficient numbers; use of reliable and valid measures; reasonably consistent recommendations.
	Expert Opinion	Expertise appears to be credible.
C Low quality or major flaws	Research	Little evidence with inconsistent results, insufficient sample size, conclusions cannot be drawn.
	Summative reviews	Undefined, poorly defined, or limited search strategies; insufficient evidence with inconsistent results; conclusions cannot be drawn.
	Organizational	Undefined, or poorly defined methods; insufficient sample size; inconsistent results; conclusions cannot be drawn.
	Expert Opinion	Expertise is not discernable or is dubious.

Review of the Evidence

Research in the area of HU and the management of sickle cell crisis (SCC) has evolved over the last 10 decades. Research now includes more clinical experience, accumulating for more than 25 years (Ware, 2010). Some studies examined the effect of HU on the HRQOL in individuals with SCD, outcomes reported by patients with hemoglobinopathies, and the difference in the HRQOL in children with SCD receiving HU and those that were not.

According to Thornburg, Calatronic, and Panepinto (2013), who conducted a retrospective cohort study of children with SCD who had completed the HRQL, found that children who received HU had a higher median (IQR) on the PedsQL than children who did not receive HU. Panepinto et al. (2008) conducted a cross-sectional study to determine the feasibility and the validity of HRQL. The authors used the statistical application of Cronbach's alpha, which showed that the HRQL was reliable. Another study by Dabari and Panepinto (2012), found that HU contributed to improving the HRQL scores of children with SCD; in that the subjects had improvement in psychological coping ability. Panepinto (2012) found that using the specific HRQL for patients with SCD can be useful inside and outside of the clinical setting to provide a better understanding of the health and well-being of patients with SCD.

Various researchers discussed the mechanism of action of HU in relieving symptoms of SCC and improving the patient's QOL. Charache et al. (1992) reported that, although HU is effective in the increase of HbF, it can also pose a problem in causing painful attacks in patients with high hematocrit (Hct). Furthermore, Singh et al. (2010)

stated that gene expression is the result of increased HbF. Also, Akinsheye et al. (2011) investigated different aspects of this subject. The authors also concluded that both clinical and laboratory characteristics of SCA HbSS are weighted by the concentration of HbF. And when that happens, there is a significant increase in the percentage of HbF from 12.83 to 19.17% after a year's treatment with HU.

In another study, however, Cummings and Anie (2003) suggested that there is a need to investigate HU therapy patients' QOL as well as their psychosocial status. A multicenter study of the effects of sickle cell conducted by Ballas et al. (2006) showed that oral HU reduced painful SCC by 50% and had significant results on the HQOL scale in the areas of daily pain and frequency. Further research by Ferster et al. (1996) noted the treatment of SC patients with some improved aspects of QOL that is similar to those reported by Ballas, et al. (2006). The findings indicated that HU increases the production of HbF, thereby improving HRQOL, and may decrease the length of hospital stay for SCD patients.

HU is not yet approved for use in children with SCD. Its toxicity and the lack of longitudinal studies concerning its effect on the adult population have been concerns. HU use on children was based on the effective results obtained from its use on the adult, eight years later in 1993. And it was reported to be effective (Ohene-Frempong, Horiuchi & Bulgarelli, 1993). Several studies were conducted globally and all reported low toxic levels, as well as the clinical and laboratory effectiveness of HU (Festa et al. 2001; Montalambert et al. 1999; Oury, Hoyoux, Dresse, & Chantraine, 1997). Although it has been shown to be effective in adults, the concerns regarding whether this medication

should be used in children continues to be discussed. Recent studies have reported some efficacy in the use of HU in children. These few studies have shown some significance in increasing HbF (Braga et al., 2005).

In 2005, an open-label uncontrolled prospective study by Braga et al., of nine children, to assess efficacy and safety of HU concluded that the medication was effective, increased HbF levels and decreased hospitalization. Another study by Smith et al. (2011) examined the association between HU treatment and pain intensity, analgesic use, and utilization in ambulatory SCD patients. Smith et al. (2011) concluded that HU treatment led to significant reduction in daily pain and analgesic usage in adults. More studies of adults and children are needed to provide more information for providers to make their decision concerning HU usage.

Few studies on managing SCD with HU have been supportive of the treatment. Some studies reported no adverse reaction (Al-Nood, Al-Khawlani, & Al-Akwa, 2011; Singh et al., 2010) while others recorded effectiveness with some side effects (Grigg, 2007; Lanzkron et al., 2008; Stouse et al., 2008).

There continues to be concern related to the efficacy and safety of HU. This concern exists among patients, health care providers, and researchers. Many researchers are still not sure about HU use or its long-term effects in the management for SCD patients. There seems to be some concern with regards to the seriousness of the side effects associated with the drug. One study reported that the side effects were so serious that the research had to be held until laboratory results were stabilized, and labs such as

those for thrombocytopenia and neutropenia were stabilized before restarting the dose (Jones et al., 2016).

In another study of 15 patients by Yates et al. (2013), HU was effective in increasing the HbF and resulted in a significant decrease in episodes of chest syndrome, pain, and hospitalizations. However, there were significant side effects recorded, including; thrombocytopenia, which resulted in treatment being discontinued for one patient. Nonetheless, the study concluded with suggestions that HU is efficacious and safe for long term use in children with SCD.

In regards to fertility, the fear of reduced sperm count and abnormal pregnancy are of great concern to patients of childbearing age, and there is evidence to confirm their fears. Grigg (2007) carried out a retrospective review of four adult men who had semen analysis while on hydroxyurea. Three cases upon cessation of treatment concluded that one-out of the three cases had azoospermia, however, spermatogenesis returned after treatment had stopped. However, the other two cases have been reported to show impairment of sperm morphology and motility which continues to be of concern to both patients and researchers.

As a result of his observation he recommends that men planning to have long treatment of HU should: (a) sperm bank before starting treatment, (b) monitor sperm count annually, and (c) use contraception if not azoospermic for at least three months if sexually active with a fertile partner during HU therapy(Grigg, 2007). A second experiment on effect of HU on male fertility was conducted by Jones et al. (2009) to determine if the adult male transgenic SC mouse exhibits the patterns of reproductive

endpoints (hypogonadism) characteristic of men with SCD and also whether HU aggravates this condition. The experiment concluded that HU treatment exacerbates the already SCD-induced hypogonadism to gonadal failure.

Another rare adverse reaction has also been reported. Nofal and El-Din (2012) reported a case study of a 68-year-old woman on HU treatment for chronic myeloid leukemia diagnosed 9 years prior. The patient's symptoms were reported to be gradual, with a non-pruritic erythematous rash on the dorsum of the hands and graduated to extremely disabling painful ulcers that interfered with walking. The authors reported that the dermatitis could be induced by different medications, but HU is the most commonly implicated.

Summary and Conclusion

To summarize, SCD is one of the hemoglobinopathies that has an effect on the Hb in the body. As a result, the entire body is affected, due to anemia and hypoxia, causing painful episodes. There have been many innovations in the treatment of SCD; however, hospital admission and fatality still continue to be a problem for SCD patients. In 1998, HU was approved by the FDA, and researchers hoped that it would improve the QOL for the SCD patients.

Data showed that the use of this medication would increase the HbF of the SCD patient, thereby decreasing painful SCC, acute chest syndrome, mortality and morbidity. Despite these findings, the report has shown that patients with SCD are not adherent to or compliant with HU use (Yates et al., 2013). There continues to be a very low percentage of patients who adhere to taking HU. Other reports show that patients are not well

informed about the risks and benefits of HU. Thus, fear and confusion continue to be additional barriers to taking this medication (Lebensburger et al., 2013).

Due to the lack of education and fear of adherence to HU, advanced nurses are in line to educate the SCD population on how to be compliant with HU. Thereby nurses will make an impact on the proper utility of HU globally, thus improving patients' QOL, as well as reducing co-morbidity in SCD through education and positive EBP. As an advanced nurse practitioner, this writer is passionate about the well fair and the care of the SCD population. SCD continues to be a disease where there is a vast disparity in health care, education and research. It is my view that this gap in treatment for this population needs much more to be done. Therefore, this writer will continue to be a force that will assist in improving the health and education of SCD patients.

As this relatively new drug is monitored more closely to note its efficiency and efficacy for the treatment of SCD; then the evidence will show how HU will improve the overall lives of SCD patients, thus the gaps that were identified in the literature, regarding the barriers will be reported in the method section. The findings will be disseminated to the SCD community which will assist in improving the trust relationship among patients and health care providers. As a result, there hopes to be an increase in the use of HU among SCD patients. This systematic review provided evidence needed to connect the gaps in the literature and the methods by illustrating what the findings revealed.

Section 3: Approach/Project Design and Methodology

Introduction

The purpose of this project was to carry out a systematic review of evidence to determine the barriers preventing adolescents ages 12 – 18 with SCD from complying with HU treatment. The major parts of this section are: (a) the EBP guideline used for the project implementation and rationale for using it, (b) the method used to search for evidence including search engines used, the process utilized for the selection of evidence that met criteria, and (c) how selected studies were evaluated for strength and quality.

Institutional Review Board

A systematic review of literature is used to identify, appraise, and synthesize studies to answer a specific clinical question and draw a conclusion about the data gathered (Melnyk & Fineout-Overholt, 2011). The reasons a literature review may be performed include but are not limited to: discovering what is already known and new knowledge about a topic, as well as assisting in designing new research studies (Oermann & Hays, 2011). A systematic review is a research study that requires an Institutional Review Board (IRB) approval. The IRB for Walden University consists of staff and faculty members from each of the major research areas, and they are responsible for making sure that all of the University's research studies comply with the university's ethical standards as wells as federal regulations. It is a requirement of all Walden students and faculty members conducting research studies involving the collection of data and analysis to request an IRB approval (Walden University, n.d.). The IRB approval for this DNP project was assigned the following number: 09-24-15-0336323.

Approach and Rationale

The evidence-based practice guideline that was used for the implementation of this systematic review was the JHNEBP model simply described as the PET process. There are three parts and several steps to this EBP process. The steps include but are not limited to: (a) identify an EBP question, (b) extensively search for evidence, appraise the evidence, summarize the evidence, rate the strength of the evidence, and (c) develop recommendation for change based on the strength of the evidence (Newhouse, Dearholt, Poe, Pugh, & White, 2007).The aim of this approach was to provide the best possible research evidence on the existing knowledge of the barriers to HU use; thus, closing the gaps that exist in the management of this disease in the SCD population.

Defining Structured Question

The identification of a practice question, issue, or concern begins the process of translating evidence into practice. According to Newhouse, Dearholt, Poe, Pugh, & White (2007), this is one of the crucial steps, because the rest of the process is driven by how the question is asked. According to Newhouse et al. (2007), several steps are included in applying the best evidence to practice and using the PICO format. This format focuses on the search and saves an undue amount of time in searching the literature for an answer to the question. To yield the most relevant information and best evidence for this project, the PICO approach was utilized to identify a specific EBP question. Using the PICO format clarified and organized the following:

1. P – Patient population of interest: adolescents ages 12 – 18 with sickle cell disease

2. I – issue of interest: compliance with hydroxyurea.

3. C – Comparison of interest: noncompliance with treatment regimen
4. O– Outcomes of interest: improvement of HU use and the barriers that prevent usage described in the literature.

Method

A systematic and comprehensive search for evidence was performed using the search engines of CINAHL, MEDLINE, OVID, Academic search Premier, Cochrane clinical trials, and Cochrane database of the systematic review from 2003 to 2013. The period covered ten years of relevant literature on the topic, and only articles published in English were identified. The following search terms or a combination of words were used: hydroxyurea, sickle cell disease, hydroxyurea therapy, sickle cell crisis, barriers to hydroxyurea therapy, sickle cell disease, sickle cell management and hydroxyurea. The text words contained in title and abstract, as well as in the index terms used for the description of the article were analyzed. Using all identified keywords and index terms, a second search was done across all databases. All studies that met inclusion criteria were retrieved for review and analysis. The intent of this review was to identify available evidence on barriers that prevent SCD patients from adhering to HU therapy.

Inclusion Criteria

This systematic review examined studies that included adolescents' ages 12-18 years old, who were diagnosed with SCD and were being managed with HU therapy. Articles that identified specific barriers were also included.

Exclusion Criteria

Articles that included title, keywords, or abstracts that were vague and not related to the research question were excluded.

Selection

The goal of this search approach was to retrieve both published and unpublished studies. Using a three-step strategy, an initial search of CINAHL and MEDLINE was done to form a list of keywords, next was the analysis of the text words contained in title and abstract, as well as in the index terms used for the description of the article. Using all identified keywords and index terms, a second search was done across all included databases. All studies that met inclusion criteria were retrieved for review. Finally, the reference list of all identified reports and articles were searched for additional studies

The initial search located *N*=19,932 potential relevant articles. The articles that had the key words HU and SCD (*N*=99), based on the title, or abstracts were reviewed. There were (*N*=31) articles that were specific to different types of SCD, including the thalassemias, minor and major as well as sickle cell disease Hgb C. Finally, there were only, (*N*=5) articles that reported on barriers specific to HU use: from the providers', patients', and families' perspectives. These five articles have shown the different kinds of barriers specific to the use of HU and are illustrated in Table 4. The remaining 26 articles were vague and did not identify the effects of HU for SCD. These articles only briefly mentioned HU as in innovative treatment, but failed to report any significant findings as they relate to the efficacy and safety of the drug. As a result, these articles did not meet

the inclusion criteria. The results of the electronic literature search and strategy are shown in Table 3 and Figure 2.

Summary

The utilization of the JHNEBP evidence rating scale for strength and quality during the implementation of the systematic review provided a methodology to analyze the literature. This EBP guideline also helped to acquire a better understanding of the barriers preventing SC patients from complying with HU. The extensive search yielded only five articles for synthesis. This systematic review of the literature did not require human subjects. As such, the IRB application that was sought through Walden University IRB was only used as a requirement for program completion.

Table 3

SCD and HU Electronic Database Search

Keywords	CINAHL	Ovid MEDLINE	Your Journals@ OVID	Academic Search Complete	Cochrane Database of Systematic Reviews	Cochrane Central Register of Controlled Trials
SCD	1,399	4,721	0	1,935	30	0
HU	499	10,388	0	708	4	0
SCD and HU therapy	13	65	2	31	0	0
SC Crisis and HU therapy	1	1	1	2	0	0
Barriers to HU and SCD	1	1	0	4	0	0
SC Mgt. and HU	22	97	0	7	0	0
Total:	1,935	15,273	3	2,687	34	0

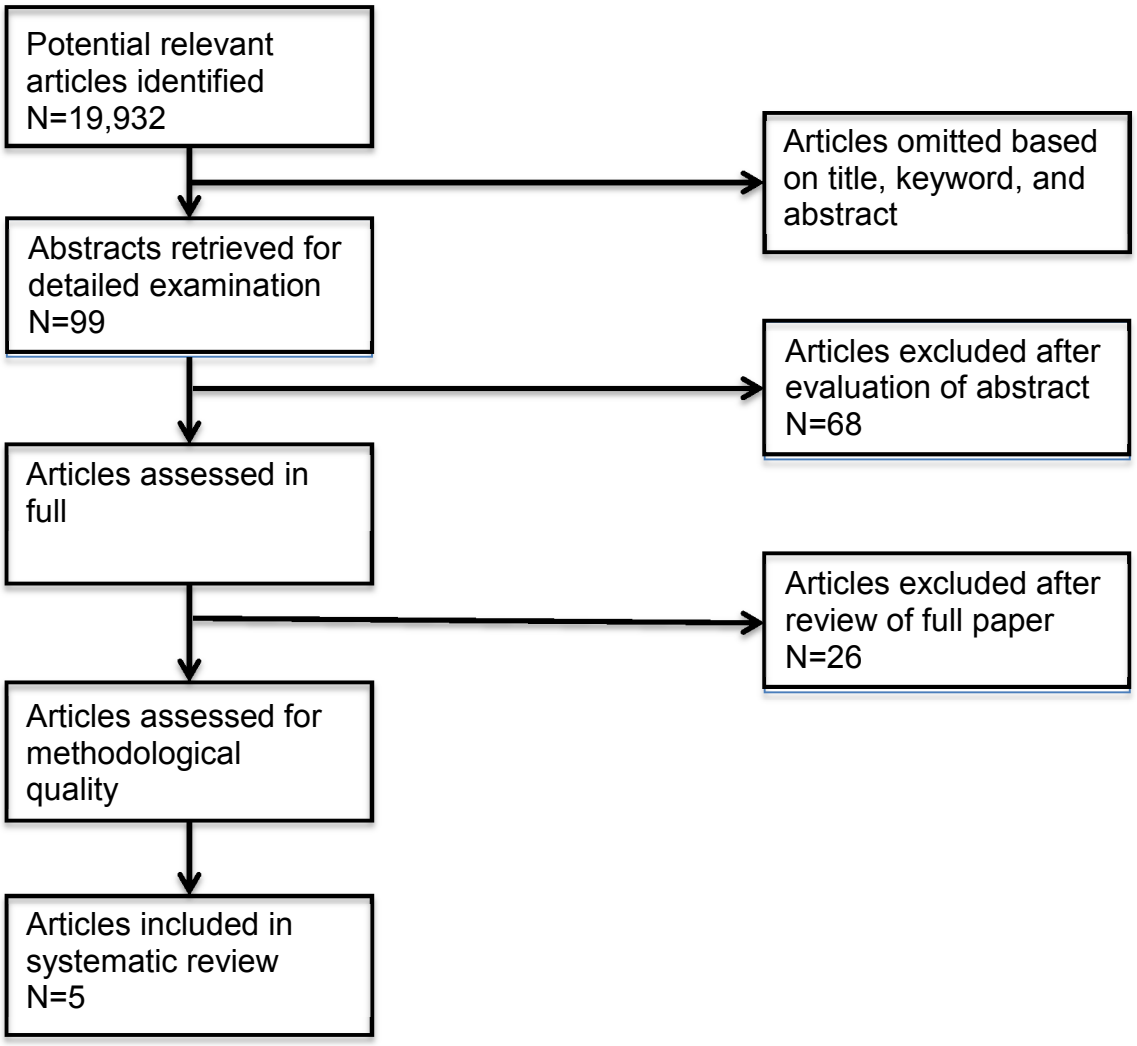

*Figure 2.*SCD and HU literature search.

Section 4: Discussions and Implications

Introduction

The overall purpose of this systematic review was to identify the barriers that have prevented adolescents ages 12-18 with sickle cell disease from being compliant with HU therapy. Such barriers have been reported to stem from the patient, health care providers, and the system; financing, limited access to care, and problems of transitioning from pediatric to adult care (Heeney, 2012). Therefore, these multidimensional concerns that pose the current challenges to the SCD population need to be investigated. This project was guided by the question: what are the barriers that prevent patients with SCD from being compliant with HU? The evidence was evaluated using the JHNEBP evidence-based rating scale. This tool is described in Section 3, which established the criteria on which to base the strength and the quality of the studies reviewed.

Findings

The identified articles were evaluated with the JHNEBP guidelines for strength and quality. This reference provided a framework for analyzing EBP, in which specific indicators provided rating scales and the quality of the tool. This format provided levels of the strength of the evidence. This prioritized the research based on its rigor, systematic approaches, and the type of clinical trials conducted. This kind of leveling differentiates between experimental studies and nonexperimental studies, such as cohort studies, case studies, qualitative studies and quasi-experimental studies (see Table 4).

Table 4

JHNEBP Evidence Rating Scales: Strength and Quality of the Evidence

STRENGTH & QUALITY	STUDY	DESIGN AND SAMPLE	RESULTS	LIMITATIONS
3/Good	Exploring Barriers and Facilitators to Clinical Trial Enrollment in the Context of Sickle Cell Anemia and Hydroxyurea Lebensburger et al., 2013	A qualitative phenomenology Exploratory study design Sample size: N=6-8: average age (31-56 year). All participants were African- Americans.	Three main themes emerged as related to barriers: 1-General Barriers: Practical issues cost time; parents rather to take the meds than the child. 2- Randomized trials Medications vs. placebo How are patients randomized 3- HU Too costly] Long-term effect Acute side effects.	. Each focus group was intended to include eight participants; however there was reduction in attendance which had reduced the diversity of the sample population and introducing the possibility of response bias. The demographic data was collected after informed consent, so differences in the parent population were not known.
4/Good	Hydroxyurea for the treatment of Sickle Cell Disease: Efficacy, Barriers, Toxicity, and Management in Children Strouse and Heeney, 2012	A recommended guideline N = 227	The evidence showed that HU reduce painful events and hospitalization in children of all ages with HbSS. The evidence is not sufficient enough to convince the authors to start HU in all children with SCD.	The United States was one of the only countries that carried out a large clinical trial of HU in pediatric SCD which represent >1% of the global burden of SCD
4/Good	How I use hydroxyurea to treat young patients with sickle cell anemia Ware, 2010	Observational data design N= 500	There need to be means of how healthcare providers can improve the adherence of HU usage. There has to be appropriate monitoring and support given due to the perceive complication of HU. Healthcare providers have to provide accurate information to patients and families who are interested in starting on HU therapy.	A limitation of the findings is from expert opinion who has observed hundreds of patients with SCD, who participate in the HU trial. However, needed randomized clinical trials to be done.to provide statistical evidence on the efficacy and safety of HU for SCD management.

STRENGTH & QUALITY	STUDY	DESIGN AND SAMPLE	RESULTS	LIMITATIONS
4/Good	Provider Barriers to Hydroxyurea Use in Adults with Sickle Cell Disease: A Survey of the Sickle Cell Disease Adult Provider Network. Lanzkron, et al., 2008	A survey design: a 45-item questionnaire. Sample size: N-148 names of people, including, nurse, practitioners, nurses and others.	Ninety-four percent of patients' with SCD had read or heard about the recommendation of using HU. Providers had many concerns regarding prescribing HU. Such as patients not being compliant with needed blood tests. Not being compliant with taking HU. Another concern by physicians' is that patients do not have enough information on HU, also the concern about carcinogenic effects.	Low response rate. There was a 47% response rate, which is consistent with other surveys. Another limitation is the physicians who were selected to participate in the study. In that, they do not represent the providers that typically treat SCD patients
4/Good	Hydroxyurea Therapy for Sickle Cell Disease in Community-Based Practices: A Survey of Florida and North Carolina Hematologists/Oncologists. Zumberg, et al., 2005	Survey design N=848 mailed N=506 Telephone contacts	The use of HU needs to be better advertised and disseminated within the SC communities. Further tools need to be developed to educate the community at large. Evidence showed that barriers to wider use of HU include physician concerns about the carcinogenic potential of HU, doubts about the drug's effectiveness, perceived patient apprehension about adverse effects, concern about the lack of contraceptive use, and patient compliance.	The survey was limited to Florida and North Carolina and as such not an adequate representation of the SCD population.

Discussion

There has been limited research conducted on HU therapy for managing SCD, and the barriers to its use. However, published evidence supports the argument that HU induces the production of HbF, decreases the hospitalization rate, and decreases the infection rate of adolescents with SCD. The lack of data concerning adults taking this therapy or the long-term effects of this treatment on children is a major concern. It will be difficult to arrive at a conclusion because of limited evidence.

Two of the five articles included in this review arrived at final decisions based on a minuscule number of studies carried out in this field. The researchers, Lebensburger et al. (2013), had some concerns when using African-Americans (AAs) in research studies. Focus group attendance was low, reducing diversity and addressing the common beliefs regarding how AAs see the participation in research. The report of how AAs feel about participating was very obvious. The study identified three main themes related to barriers to clinical trial enrollment: (a) general barriers to health related research; practical issues, emotional issues, mistrust of doctors or studies, (b) concerns of trial design; randomization, and (c) concerns of HU; long term unknown risks. Despite the small number of participants, focus group *n=3*; parents/guardian *n=14*, saturation was achieved, leading to significant contributions to the development of strategies for the recruitment of AA children in clinical studies (Lebensburger, et al. 2013).

Ware (2010), who reported on HU use for young children with SCD, had15 years of experience with the use of HU for SCD patients. He observed hundreds of patients with SCD who participated in the HU trial. The study identified barriers to the use of HU

to include provider's inadequate knowledge about HU, patients and family not offered treatment, and when offered refuse due to unrealistic fears. Data from randomized controlled trials (RCT) will be needed to provide statistical evidence of the efficacy and toxicity of HU in the management of SCD.

Additionally, the survey done by Zumberg et al. (2005) identified barriers to the broader use of HU, which include: (a) physicians' concern about carcinogenic potential, (b) doubts about HU effectiveness, (c) perceived patient apprehension about adverse effects, (d) concerns about the lack of contraceptive use, and (e) non-compliance of patients. The survey was limited to Florida and North Carolina, and as such was not sufficient representation of the sickle cell population. Zumber et al. (2005) addressed the risks of HU use that cannot be disregarded, but rather provide the consumers with needed information necessary to make the best decisions. Zumber et al. reported that a decrease in the neutrophil count is associated with HU which exposes the patient to infection.

Strouse and Heeney (2012) recommended treatment guidelines for the use of HU in treating children with SCD. Their recommendations were based on the evidence that HU reduces painful events and hospitalization in children of all ages with HbSS. The evidence is not sufficient enough to convince the authors to start HU in all children with SCD. Because limited research was done for children with SCD, little is known about the efficacy and the complete interactions of HU. However, active research and investigation continue in order to validate the effects of HU use in children with SCD (Lanzkron et al. 2008). Poor adherence was identified as the primary reason that HU therapy is ineffective in the treatment of children with SCD. Lack of knowledge about HU

continues to be a challenge. The review of evidence illustrates that there is a need for future research on the use of HU.

Implications

I have demonstrated that research is limited in the area of HU therapy and the non-compliance of therapy among adolescents ages 12 – 18 with SCD. The reason for this is multifaceted. According to Heeney (2012), some reasons for the nonadherence are systemic barriers, patient and family/caregiver barriers, and provider barriers. The care of this patient population cannot be carried out adequately until the reasons related to the limited usage of HU are addressed.

Further research needs to address the barriers that are preventing the SCD patients to adhere to the HU medical regimen. Several studies (Ballas et al., 2006; Dabari & Panepinto, 2012; Lanzkron et al., 2008; Platt, 2008)) indicate that the use of HU has been beneficial in the decrease of painful sickle cell crises when HU is maintained. Therefore, it would be beneficial for nurses to identify the causative agents involved in decreased use of HU in SCD patients.

Strengths and Limitations of the Project

Strengths

This DNP project had several strengths. First, the project addressed a major concern in the SCD community. Research has shown HU to be beneficial for SCD patients, but usage remains limited; uncovering the barriers to the minimal use is needed. Secondly, the project is a systematic review of the literature and I will use the outcome to recommend an educational program that nurses can utilize in their practices to provide

evidence-based care. Thirdly, identifying the barriers to HU usage allows for an understanding of the different types of barriers to HU use that originate with patients, patient relatives, system; financing, health care disparity, and providers.

Limitations

This project had its limitations. The review only included articles written in the English language. This was a limitation to the study because this could have eliminated other important research studies that were done in other languages. Another limitation of note is the fact that all articles were retrieved only from online resources and as such credible studies in paper format could have possibly been left out. Restricting the study to 10 year period is also a limitation, as several articles that could have illuminated the barriers to HU use were excluded. Focusing on the patient population of interest (adolescents' ages 12-18) with SCD could also have eliminated studies focusing on adults and children.

Analysis of Self

Scholar

Before undertaking this project, I did not know how encompassing and overwhelming a systematic review can be. Retrospectively, I underestimated the project. However, the DNP curriculum at Walden prepared me with the skills needed to understand and navigate any unforeseen obstacles and challenges that I encountered. The experience of this endeavor has taught me to have a clear goal and a vision of the outcome, and what it will take to reach the target. According to American Association of Colleges of Nursing [AACN] (2013), scholarship and research are the hallmarks of

doctoral education. My DNP project epitomizes the scholarship of discovery and integration which, according to Boyer (1990), reflects the investigative and synthesizing traditions of the academic life. This competency is Essential III of the eight DNP Essentials ([AACN], 2013, p.11).

Practitioner

This project has increased my knowledge of SCD in ways I never imagined. Working on this topic area for over two years has given me confidence and the ease to talk about many aspects of SCD. I am enthusiastic about discussing the new knowledge with my colleagues. I hope to arouse their interest in this patient population and the management of their condition. This project has improved my ability to synthesize and critique the literature faster than before this study.

Project Developer

This systematic review of evidence afforded me the opportunity to identify the different barriers to HU use. Such barriers ranges from institutional involvement, patient/family/caregiver fears', and healthcare providers limited knowledge regarding the outcome of HU use. With this information, I will recommend rigorous education programs that will increase professional knowledge and awareness of this practice problem. Additionally, I would like the sickle cell disease population to realize the need and possible benefits of incorporating HU therapy into their disease management. Adding this promising medication to their treatment regimen can reduce pain crises, infections, decrease emergency room visits, and improve overall QOL for SCD patients.

Summary

Despite the significant findings of the effects of HU, many barriers to treatment still exist. Some restrictions prevent patients from achieving the effects of a drug that may have increased benefits: decrease crises pain, reduce emergency department visits, increase HbF levels and improve polymerization of the cells, causing less sticking of cells. Despite limited use in children ages < 3, the review of literature also revealed that HU may contribute to the improvement of HRQL of adolescents with SCD. Due to morbidity and mortality associated with SCD, efforts to improve their QOL are of great concerns. The minimal usage of HU continues to be a gap that was identified by this review. Further research needs to be conducted to better understand the barriers that prevent the SCD patients from using HU.

Section 5: Scholarly Product

Project Dissemination

According to Oermann and Hays (2011), the dissemination of research findings that have examined the different interventions accessible to the health care system, support EBP endeavors and are effective means to build healthcare knowledge. This project was undertaken to review and synthesize all evidence available on the barriers preventing adolescents ages 12 – 18 with SCD from being compliant with HU. The SCD population could benefit from this review as the findings from this project could further promote best practices or change of practice that this patient population needs. To bring about change with this systematic review of the literature, I must disseminate the result to the SCD communities, caregivers, and providers nationally and internationally through publication, poster presentations, manuscripts, etc.

Subsequently, I intend to circulate this research study through poster presentations and publications. The reason for this choice is that poster presentations have the potential to reach a broader audience that could easily reach sickle cell patients, their families, health care practitioners, and providers in the Bronx, New York, the tristate area, as well as nationally and internationally. The publication of the results of this systematic review could be used to improve the care of SCD patients. Education programs addressing the identified barriers can be implemented that will change behaviors and improve the knowledge base of the community as a whole.

Due to the findings of this systematic review, the evidence has shown that many unanswered questions exist on the management of SCD with HU. Many patients

continue to be resistant to taking HU, despite all of the comprehensive research that has been done to show its effectiveness in cases of SCD. Comprehensive education must be provided for all ages and all cases of SCD patients to support the impact that HU has on SCD patients.

Education must be geared towards identifying the barriers and clearing up the myths that exists for HU. By providing mass media of information on HU, this will decrease the barriers and improve the compliance rates of HU. Education should exist on the risks and benefits of HU, as well as on the current research and the findings from experts regarding the effectiveness of HU. Obtaining feedback from the audience; patients, their families, and health care providers after an education session is essential, in that further clarification can be made to decrease the fear of taking HU. I will make additional efforts to provide education in community based organizations with people who are afflicted with SCD, as well as churches where there is a high incidence of SCD within the community. Brochures and pamphlets on the effectiveness of HU will also be disseminated throughout the communities with high incidence of SCD. Future development of educational applications for smartphones and tablets will also be considered as a means of providing educational information on the use and effectiveness of HU.

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