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Hematologists' Attitudes Toward Sickle Cell Disease Pain Management

Paul Saah

Milton High School

ABSTRACT

Sickle cell disease causes pain that can manifest in chronic or acute crises. In addition to other possible complications, this pain can frequently place sickle cell patients in the emergency room and hospital. The high volume of patient visits requires an analysis of the quality of care for this group and a conscious effort to improve the care from providers. This study aims to evaluate the attitudes of United States hematologists toward current SCD management guidelines established by the American Society of Hematology (ASH). No statistically convincing evidence was found to support the hypothesis that not all United States hematologists agree with each ASH sickle cell treatment guideline. However, there is a deeper level of contextual understanding and discussion necessary to confidently make this conclusion.

INTRODUCTION

Sickle cell disease (SCD), an inherited disorder that damages red blood cells and blocks blood flow, affects approximately 100,000 Americans and 1 in every 365 African American births (CDC, 2020). Sickle cell disease causes pain that can manifest in chronic or acute crises. In addition to other possible complications, this pain can frequently place sickle cell patients in the emergency room and hospital. Even though sickle cell results in frequent hospital visits, there are still misplaced stigmas around the community that has had negative impacts on the quality of care. Doctors Ballas and Ruta explain, "Although sickle cell pain is not a major feature within the pain community and its many societies and publications, paradoxically, SCD patients are often assumed to be associated with opioid abuse and addiction." (K. Ballas & S. Ruta, 2016). The high volume of patient visits requires an analysis of the quality of care for this group and a conscious effort to improve the care from providers. This study aims to evaluate the attitudes of United States hematologists toward current SCD management guidelines established by the American Society of Hematology (ASH).

Historical Context

Because SCD was relatively only recently discovered, a cure is yet to be found, and the best management methods are continually being developed. SCD is a relatively new disease, only first documented in 1910, which pales in comparison to conditions such as cancer or pneumonia discovered in 3000 and 460 BC, respectively. SCD was not given the name until 1921, and it was not until 1949 that Linus Pauling discovered abnormal hemoglobin was the cause of the disease. SCD affects most commonly people of African descent, including African Americans, a marginalized group that historically has struggled with receiving adequate health care throughout the world.

In the early 1970s, the civil rights movement called attention to racial inequality in health care. The immediate impact the attention brought to this inequality was the establishment of the Sickle Cell Disease Association of America to improve research, education, and health care for sickle cell patients. Additionally, the Sickle Cell Anemia Control Act was passed in the 1970s to allocate government funding for screening, research, and treatment

(American Society of Hematology, 2008). In 1995, hydroxyurea was found to help prevent complications in patients with sickle cell disease, but it still is not 100% effective and carries the possibility of severe side effects. Then in 1996, a bone marrow transplant study was carried out and demonstrated a cure. Unfortunately, bone marrow transplants can be inaccessible, financially impractical, and can cause major short and long-term complications. Although efforts have been made over time, there is still significant room for improvement in the management of SCD.

Literature Review

SCD is a relatively under-researched disease, but the literature outlines vital discoveries during the journey toward optimal SCD management. These studies research sickle cell from the perspective of both patients and providers and while this study evaluates providers' attitudes toward SCD management, the literature focuses heavily on the treatments from a patient perspective: where they have struggled with their medical staff and why. An example of this is a study that "found patients with SCD reported that nurses were not that caring with them compared to how the same nurses treated others with different medical conditions" (Dorsey et al., 2001). SCD affecting ethnically and culturally diverse communities is possibly a main factor behind this. A study utilizing the Service Perception Test (SPT) had results that consistently show Caucasian patients as receiving better service than Black patients (Chestnut, 1994).

A study done by EA Lorenzi that evaluated nurse/physician job satisfaction for care given to sickle cell patients in crisis looked to determine the effects of comprehensive nursing guidelines. While somewhat outside of the scope of the current study as it works with nursing guidelines, the overall goal of the Lorenzi study was to evaluate nurses and physicians congruently. They found "a statistically significant increase in job satisfaction in the areas of nurse/physician collaboration and having a broad knowledge base of sickle-cell disease." (Lorenzi EA, 1993). These findings show the potential influence that revisiting guidelines can have on quality of care for patients.

Because sickle cell disease is uncommon and under researched it can be difficult to create comprehensive and universal guidelines. Guidelines are instituted and validated using primarily clinical trials, but because it is such an uncommon disease, this can be difficult to do. Dr. Michael DeBaun explains, "Given the importance of evidence-derived guidelines, particularly for management of an uncommon disease, adherence to rigorous methodology is critical for their credibility." (DeBaun, 2014). In addition to developing guidelines being the initial difficulty, DeBaun also finds that it is becoming increasingly difficult to add to guidelines and have it endorsed by relevant societies such as the American Society of Hematology (ASH), the American Academy of Pediatrics, and the American Society of Pediatric Hematology/Oncology. Recommendations whether necessary or not will not be implemented without extremely strong evidence (DeBaun, 2014). This evidence can take additional time even if the recommendation carries enough validity in the opinion of others to be added to the guidelines. DeBaun claims "There are a number of clinical areas in which the SCD guideline could have provided additional information." (DeBaun, 2014). This is not to say the stringent nature of the guidelines is unnecessary, only speaks to the lack of resources available to sickle cell research.

Research Gap

While various studies have been performed to research the quality of care for patients with SCD, there is still a clear gap regarding United States providers thoughts on the guidelines established for their practice. This study aims to determine what attitudes and opinions United States' Hematologists demonstrate regarding the American Society of Hematology guidelines for SCD management. This additionally aims to evaluate any potential correlations between attitudes and various demographic factors. Thus, establishing the following research question: **to what extent do United States hematologists' attitudes toward sickle cell pain management align with current treatment guidelines?** The resulting data will potentially allow providers an additional platform and opportunity to provide their

thoughts and have them be heard. The results will provide those in positions to influence guidelines additional reason to change them for the better.

Hypotheses

H_0: All United States hematologists agree with each American Society of Hematology sickle cell treatment guideline.

H_A: Not all United States hematologists agree with each American Society of Hematology sickle cell treatment guideline.

MATERIALS AND METHODS

The study was approved by the Milton High School institutional review board as well as the Emory University board. The boards determined that although this experiment involves human subjects, it is a voluntary survey designed for quality improvement purposes and did not require informed consent forms from participants. The survey research method was developed based on one published model study: *Self-reported practices in opioid management of chronic noncancer pain: A survey of Canadian family physicians.* The study served as the structural base for this research, as it analyzed variables regarding physicians' practices in relation to the Canadian guideline (Allen et al., 2013). The Allen study reported correlational results based on the quantitative data collected.

Study Participants

This cross-sectional survey was conducted with a sample of primary care physicians (n=24). The ideal n value for credibility in the field is 100, but due to lack of time and resources, 24 was the final number of participants. Primary inclusion criteria included current practice as a hematologist. All surveys were filled, and one survey was excluded as the specialty of the respondent was internal medicine and not hematology.

Research Method

A survey was determined to be the most appropriate method for this study due to its successful implementation in the aforementioned study analyzing similar variables. Additionally, surveys are a common form of correlational research in this field. Participants were asked to complete a ten-minute Likert scale survey evaluating their attitude toward ASH guidelines regarding sickle cell pain management in addition to pertinent demographic information. With the help of an expert advisor, physicians across the country were contacted about participating in the study. Through this structure, the data gathered was analyzed collectively to compare observed values with expected values. The Allen study had 710 Canadian family practice physicians complete a questionnaire developed with reference to the recommendations of the Canadian guideline to evaluate knowledge regarding opioid use in chronic noncancer pain, factors affecting decision making when prescribing opioids, and **frequency of following recommended practices before starting patients on opioids**. The section evaluating recommended practice held relevance to my study and was the model. Allen provided three answer options of "<25% of the time", "25% to 50% of the time" and ">75%" of the time. This study was similar except because it can be difficult to recall an exact percent of the actions taken, a Likert-scale (one-to-five) style was determined to be better employable as it better gauges one's attitudes and better aligns with the focus of this study. The current study excluded questions analyzing variables regarding knowledge of opioid use (in this case sickle cell treatment) as it is outside the scope of the research question. The study also excluded questions regarding factors affecting decision making as it is also outside of the scope of the research question. The current study has a sample size incomparable to the Allen study meaning conclusions are to be made with caution. Unlike the Allen

study, gathering data on a five-point Likert scale allowed for the creation of relevant graphical depictions which positively contribute to the results and discussion. Measuring all variables on a consistent Likert scale also allowed for the implementation of goodness-of-fit analysis to answer the research question. The Allen study was published in the *Pain Research & Management* journal, a peer-reviewed academic journal concerning all aspects of research on pain management.

Procedure

All methods and instruments underwent IRB approval prior to the commencement of the study. The survey (See Appendix A) was hosted through REDCap, a secure web application for building and managing online surveys and databases and disseminated via email. The email contained a portion requesting that participants share the survey with fellow colleagues (See Appendix B). It is unclear exactly who participated in this step and the initial email list was obtained from expert advisor. Given the lack of a discrete sampling frame and varied methods of contacting hematologists, a non-probability convenience sample was obtained. Responses were collected over the course of two weeks and a follow-up email with a reminder was sent after one week. The study was completely voluntary, and participants could choose to answer or not as they please. A total of 25 responses were collected, and one response was disregarded as the respondent's specialty was internal medicine and not hematology which could potentially skew the data.

Data Analysis

Although the Allen study utilized Pearson's analysis to determine links between variables, all of which are interval, the present study used a chi-square goodness-of-fit test to determine the likelihood of the variable coming from the specified distribution. As the study seeks to find a level of agreement amongst the population of US hematologists, the interpretation of to "agree" was "agree" or strongly agree" while to "not-agree" was considered as "neutral" "disagree" or "strongly-disagree". "Agree" and "not-agree" were collapsed into 1 and 2 respectively for statistical analysis.

RESULTS

Responses

After excluding respondents who were not United States hematologists, 24 responses were received for analysis. It is not possible to determine a precise response rate because this was a convenience sample with no formal frame to draw on and the snowball element is an additional layer of complication for the purpose of response rate determination.

Demographics

Relevant demographics are shown in Table 1. Mean years of experience among respondents was 10.6 and the majority of respondents had >20 years of experience. Responses according to specialty were Hematology/Sickle Cell-Peds (17), Hematology/Oncology-Peds (5), Hematology/Sickle Cell-Med/Peds (2). About 96% of respondents claim to be aware of the 2020 ASH guidelines for sickle cell disease for treating chronic pain.

Significant Question Results

The question regarding use of SNRI/SSRI for adults with SCD who have chronic pain from SCD-related avascular necrosis had the lowest level of agreement. Table 2 shows the results from this question that yielded the highest chi-square value. About 67% of respondents agreed with this guideline, leaving 33% not in agreement and a x^2 value of 2.66. The question regarding shared decision making for the continuation of COT (chronic opioid therapy) and its benefit for adults and children with chronic pain from SCD had the highest level of agreement. Table 3 shows the results from this question that yielded the lowest chi-square value. About 96% of respondents agreed with this guideline, leaving 4% not in agreement and a x^2 value of 0.042.

Figure 1

What is your specialty area? *(specialty_area)*

Total Count (N)	Missing*	Unique
25	0 (0.0%)	4

Counts/frequency: Hematology/Sickle Cell - Adult (0, 0.0%), Hematology/Oncology - Adult (0, 0.0%), Hematology/Sickle Cell - Peds (16, 64.0%), Hematology/Oncology - Peds (5, 20.0%), Hematology/Sickle Cell-Med/Peds (2, 8.0%), Hematology/Oncology-Med/Peds (0, 0.0%), Other____ (please describe) (2, 8.0%)

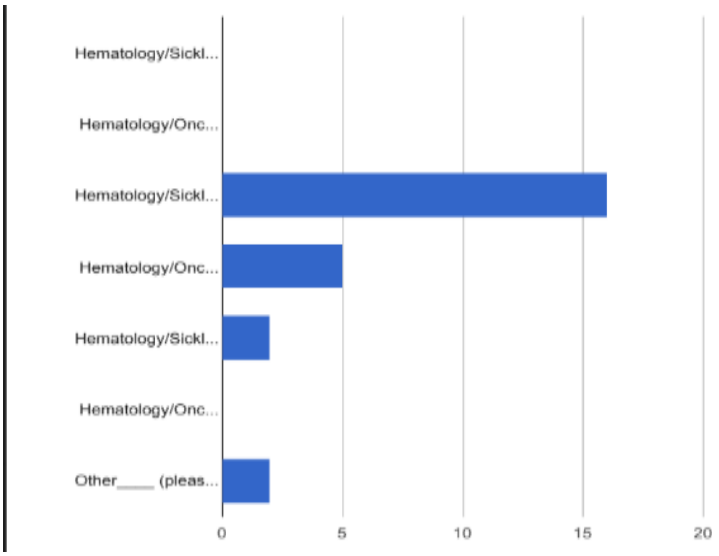
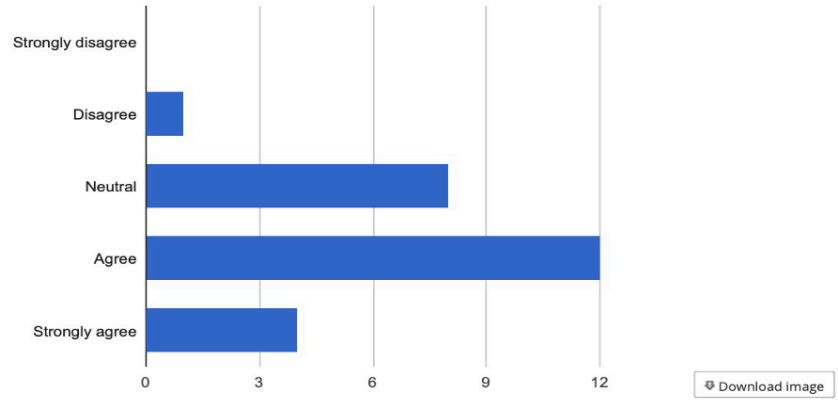


Figure 2

The use of SNRI/SSRIs for adults with SCD who have chronic pain from the SCD-related identifiable cause of avascular necrosis for management is of benefit in the context of a comprehensive disease and pain management plan. *(ash_q2)*

Total Count (N)	Missing*	Unique
25	0 (0.0%)	4

Counts/frequency: Strongly disagree (0, 0.0%), Disagree (1, 4.0%), Neutral (8, 32.0%), Agree (12, 48.0%), Strongly agree (4, 16.0%)



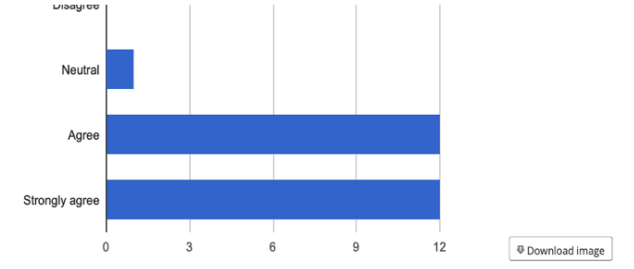
$X^2=2.66$

Figure 3

The use of shared decision-making for the continuation of COT is of benefit for adults and children with chronic pain from SCD who are receiving COT, are functioning well, and have perceived benefit. *(ash_q10)*

Total Count (N)	Missing*	Unique
25	0 (0.0%)	3

Counts/frequency: Strongly disagree (0, 0.0%), Disagree (0, 0.0%), Neutral (1, 4.0%), Agree (12, 48.0%), Strongly agree (12, 48.0%)



$X^2=0.042$

Table 1

X^2	13.276
p-value	0.10269957

ANALYSIS AND DISCUSSION

Revisiting Hypothesis

Now that data is present, the null hypothesis can be revisited and either rejected, supported, or partially supported.

H_0: All United States hematologists agree with each American Society of Hematology sickle cell treatment guideline.
H_A: Not all United States hematologists agree with each American Society of Hematology sickle cell treatment guideline.

The study fails to reject the null hypothesis as the p-value was found to be .103. The widely accepted significance value in the field and in this study is .05, so because the p-value is greater than the significance value, there is no convincing evidence that not all United States hematologists agree with each American Society of Hematology sickle cell treatment guideline.

Discussion

This study provides new information on the attitudes of United States hematologists toward guidelines for sickle cell treatment. There was a high degree of concordance among physicians' opinions on most all guidelines, somewhat disproving a need for further analysis of the guidelines. Most of the disagreement was found in topics related to the use of SNRI/SSRIs and antidepressants for pain management. The disagreement regarding antidepressants and SNRI/SSRIs may not be widely shared by all hematologists as a study published in 2018 found "Interdisciplinary teams are effective in creating a guideline to assess and treat depression and effects on pain and QoL (quality of life) in patients with SCD." (Simo & Siela, 2018). The discrepancy found between the studies is likely due to the demographic makeup of the current study along with other factors. The highest concordance was found in practices regarding cognitive and behavioral pain management, integrative approaches, and chronic opioid therapy (COT). The results of the cognitive and behavioral pain management is consistent with other available literature. A study comparing hydroxyurea (a widely accepted drug for sickle cell treatment) and cognitive behavioral therapy found, "both CBT and hydroxyurea appear to help improve quality of life in patients with SCD. CBT seems to have the additional advantage of increasing psychological coping ability, and may therefore be beneficial adjunctive to hydroxyurea." (O & Ka, 2003). The reason for the high level of concordance among respondents regarding the use of COT is unclear considering "its effectiveness is unproven in sickle cell disease (SCD)" (Carroll et al., 2016).

Although, the results of this study may require further evaluation as Dr. Nadirah El-Amin's study, International Differences in Outpatient Pain Management: A Survey of Sickle Cell Disease, found "significant variations in how different parts of the world manage pain in the outpatient setting for SCD" (El-Amin et al., 2019). Assuming the results of El-Amin's study are true, then regardless of whether United States hematologists agree with ASH guidelines or not, sickle cell guidelines need revisiting worldwide. El Amin says, "Given the wide geographic differences in

prescribing habits, there is a significant need for safe and efficacious multinational guidelines."(El-Amin et al., 2019). These multinational guidelines could vary from continent to continent, or even regions within continents, but a focus on collaboration among physicians across the world is imperative to optimization of sickle cell treatment. An additional example is found in Matthew Smeltzer's 2021 study where he identifies further inconsistency in sickle cell care from providers compared to another guideline created by The National Heart Lung and Blood Institute (NHLBI). The study found that around 33% of providers were unaware of these guidelines (Smeltzer et al., 2021). They additionally found barriers to providing care for patients that results in poor mental health that may be explained by a lack in the guidelines. Because of variability in resources available to providers, differences in populations of patients, and more, there may be common practices among some providers across the world that are completely unknown to the United States physicians that could be utilized.

The results from the study executed by Dorsey and their team aligns with the alternative hypothesis from the current study. The Dorsey study found "Participants with SCD reported lower satisfaction with nurses' caring behaviors than those with other medical conditions" (Dorsey et al., 2001). If patients take issue with the quality of care from their providers, then there may be an issue in the training for physicians or maybe the guidelines. While this conclusion is statistically backed by a p-value of 0.03 which is smaller than the significance level of 0.05, there are limitations to drawing a parallel to the current study. Firstly, the study is relatively outdated, being published over twenty years ago. Additionally, their study had a relatively small sample size of 29 participants making it difficult to generalize to the entire population. Lastly the author specifies that they used convenience sampling which potentially carries inherent biases that could alter results. Another detail to take note of is the fact that due to sampling bias in the current study, the entire sample consists of some type of pediatrician (refer to table 1) when Dorsey's study worked with only adult patients. This could explain a difference in results. Additionally, the current study works with physicians and Dorsey's study evaluated nurses. This is further reason to compare the two studies with caution.

IMPLICATIONS & LIMITATIONS

Because of the critical nature of sickle cell management, constant improvement on care for patients is crucial. While improvements have been made over time, there is still plenty of room for impactful change. Though the results of this study do not show an active disagreement between hematologists and the ASH guidelines in place for them, there are variations in guidelines throughout the United States and the world that could result in different attitudes from different populations of hematologists. Comparing the results of this study with the vast sum of available literature creates new ideas and evidence for why more universal guidelines must be established. Understanding specifically where hematologists agree and disagree within guidelines provides the base of further research.

This survey, like all surveys has the inherent limitation of putting reliance on reported behavior rather than actual behavior. Answering based on what providers feel is true in the context of their practice may not always align with their techniques on a daily basis. The purpose of a Likert scale is to provide quantitative data, but without qualitative data, this study lacks further insight to the opinions of providers and an explanation of their answers. The generalizability of the findings is unclear as regional differences in practice may not be represented in the study making it difficult to compare to others. In addition to regional differences, the demographic makeup of the study is not representative of all hematology subspecialties. Lastly, the relatively small sample size as compared to other studies in the field adds further speculation to the generalizability of the findings.

CONCLUSION & FUTURE DIRECTION

The current study demonstrates physicians' attitudes toward ASH sickle cell management guidelines. There was little to no debate among most guidelines, the most disagreement found in topics related to the use of SNRI/SSRIs

and antidepressants for pain management. The highest concordance was found in practices regarding cognitive and behavioral pain management, integrative approaches, and chronic opioid therapy. The study showed an overall agreement between United States hematologists with the ASH guidelines, but any conclusions are to be made with extreme caution considering the outlined limitations to the study. To corroborate the results of this study, it should be replicated on a larger scale including more participants that are more representative of the entire population of United States hematologists. A stratified random sample rather than a convenience sample would aid in the lack of even representation found in this study. Furthermore, there was additional secondary data not included in the paper (follow up free response text) due to its insignificance and low participation rate. As an extension, those results could be analyzed in conjunction with the results presented to note any potentially key influences. Any further studies should emphasize finding qualitative data alongside quantitative to provide deeper insights.

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