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Published in final edited form as:

Am J Hematol. 2011 January ; 86(1): 85–87. doi:10.1002/ajh.21883.

Examining the characteristics and beliefs of hydroxyurea users and nonusers among adults with sickle cell disease

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Abstract

The attitudes of patients with sickle cell disease (SCD) toward the use of hydroxyurea (HU) therapy may contribute to the underutilization of HU in the United States, yet our understanding of these attitudes is limited. We examined the attitudes and beliefs of 94 adult SCD patients, comparing those who never used HU ($n = 37$), formerly used HU ($n = 23$), and were currently using HU ($n = 34$). Seventy percent of current HU users reported some level of improvement from the drug (“average” or “very much”) and 80% reported little or no trouble from side effects. Fifty-seven percent of former users reported taking HU for less than 6 months, with “doctor's recommendation,” or “not liking the way it made me feel” given as the most commonly reported reasons for stopping HU. Fifty percent of the never users reported receiving no information about HU from any source, and 85% of the never users thought that they would receive no improvement if they were to take HU. A deeper understanding of patient perspectives toward HU utilization is required as part of multipronged efforts to combat its underutilization in the treatment of SCD.

Sickle cell disease (SCD) is a serious, chronic, genetic disease that leads to the production of abnormal hemoglobin and is marked by many complications, including recurrent episodes of severe pain. Despite 100 years of SCD being a recognized clinical entity in Western medical literature, hydroxyurea (HU) is currently the only approved disease-modifying medication available for the treatment of SCD.

HU has been shown to be efficacious in the treatment of SCD [1]. Studies also suggest that treatment with HU may reduce the costs of health care for SCD, improve health outcomes, and decrease early mortality [2–10]. A recent independent panel convened by the National Heart, Lung, and Blood Institute concluded that the benefits of HU therapy for SCD outweigh its known risks [11–14].

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Conflict of interest: Nothing to report.

Unfortunately, despite its potential benefits, the clinical literature suggests that HU is underutilized as a treatment for SCD. Although multiple studies have examined provider-level barriers to HU use, evidence on SCD patient beliefs and attitudes about HU is limited [15,16]. Lack of patient knowledge about HU, misperceptions about its side effects, and poor health literacy are hypothesized as patient-level barriers [17]. Hankins et al. found that the perceived safety and efficacy of therapies were shown to be the two most important factors affecting treatment preference among parents and their children with SCD [16]. The aim of our study was to address the gap in current knowledge regarding SCD patient attitudes and beliefs about HU by examining surveys administered to adults with SCD who were taking part in a larger study assessing their experiences with health care.

Ninety-four adult patients (age 18 years and older) participated in our study and provided data about their HU utilization and attitudes. The distribution of HU use was as follows: 39% never users, 24% former users, and 36% current users. Table I describes the characteristics of our sample by HU use. Compared with those with current or former use, the never users had fewer sickle cell-related comorbidities and were less likely to report being on disability. When combined, those with current or former use experienced more hospital visits in the prior 12-month period than the never users (mean visits = 3.7 vs. 2.0, $P = 0.054$).

Seventy percent of current HU users reported some level of improvement from the drug (“average” or “very much”), and 80% reported “not at all” or “not much” trouble from side effects. Approximately, 83% of the former users reported taking HU for 1 year or less, with 57% taking HU for less than 6 months. The most commonly reported reasons given for stopping HU were their “doctor's recommendation” (39%) and “not liking the way it made me feel” (35%). Thirty-six percent of the never users reported that their doctors had previously suggested that they take HU. Fifty percent of the never users reported receiving no information about HU from any source. Eighty-five percent of the never users thought that they would receive no improvement if they were to take HU.

Thirty-three respondents (eight never users, nine former users, and 16 current users) described their concerns about HU in an open-ended manner. We labeled these concerns as representing three general categories (Table II): no perceived benefit, lack of knowledge, and side effects. Examples of specific concerns raised in each category are as follows:

No perceived benefit

Some respondents raised concern over a lack of perceived benefit from HU, or raised doubts about its effectiveness:

- “I am concerned about why it didn't work, and I continued to experience pain crises.”
- “Not sure if it works well because it's been 4 months and I'm still getting sick.”
- “I am concerned that I still have crises and it has not helped keep me out of the hospital.”

Lack of knowledge

Respondents expressed a lack of general knowledge concerning HU, or what type of medication it is:

- “Is HU a blood thinner?”
- “I have never heard about it.”

- “I would like to know more about it.”

Side effects

The majority of respondents raised concerns regarding perceived or potential side effects from HU:

- Nonspecific side effects: “I am concerned about the side effects.”
- General safety: “There is no safety information past 10 years.”
- Reproductive effects: “I was told that HU causes birth deformities.”
- Cancer concerns: “My concerns are that it could lead to cancer, and it is dangerous for our bone marrow, it could harm us.”

Efforts to understand and overcome the barriers to the use of HU in treating SCD are an important area of inquiry. In this study, we sought to describe some of the characteristics, attitudes, and beliefs about HU among adult SCD patients. Nearly 83% of respondents who were categorized as former users of HU reported being on the drug for 1 year or less, with 56.5% being on it for less than 6 months. Many of these former users (39%) reported that they stopped because their doctor suggested it. We were unable to discern the reason why a patient's doctor may have suggested that they stop taking HU. It is possible that the patient was told to temporarily stop taking HU after experiencing some of the well-known short-term toxicities of the drug, such as leukopenia. A patient may also be told to stop taking HU if that patient demonstrates an inability or unwillingness to comply with the treatment regimen. In their studies of provider barriers to the use of HU for SCD patients, both Zumberg et al. and Lanzkron et al. found that provider concerns over patient compliance with the HU treatment regimen were the most endorsed reasons for not prescribing HU when it is otherwise indicated [18,19].

Thirty-five percent of the former users in our study reported that they stopped taking HU because they did not like the way that it made them feel, whereas the majority (80%) of current HU users in our study reported little to no difficulties from side effects. It is possible that these are self-selecting groups. That is, the former users may have experienced more short-term toxicities from HU, on average, than the current users. It is known that a clinical response from HU can take a minimum of 3–6 months to manifest. It is possible that our former users did not stay on HU long enough to experience a clinical benefit from the treatment which may have outweighed any short-term difficulties they may have experienced. This suggests the need for adequate patient pre-education about HU before the therapy is begun so that the patient may form realistic expectations for the course of therapy, particularly their expectations regarding when they might begin to experience benefit and what they might experience in the short-term before the benefits manifest.

Patient expectations may also explain why our respondents demonstrated doubts about the perceived benefits of HU. Many of our respondents expressed concern over the fact that they continued to experience pain crises or hospitalizations while on HU. If the outcome expectations of patients on HU are unrealistically high, then nonadherence with, or discontinuation of, the therapy would be unsurprising. Realistic expectations about HU must be promoted among this patient population.

Our study participants exhibited a lack of general knowledge about HU. LaVista et al. described the beneficial effects of a video-based educational intervention to raise patient interest in discussing HU with their physicians [17]. Similar interventions could be systematically used as part of any curriculum designed to educate SCD patients and their families about HU.

The most common concern about HU cited by our respondents was a concern over side effects. Although most respondents were nonspecific as to the nature of the bothersome side effects, the majority of those with a specific reason cited a concern over the general safety of HU. Although specific stated concerns over the potential reproductive effects of HU, or its potential carcinogenicity, were cited much less frequently in our study than are endorsed in studies of providers, it is possible that these concerns were encompassed in our respondent's nonspecific concerns over side effects and/or safety.

Care should be taken in attempting to generalize the results of our study to the wider adult SCD population in the United States. This was a small, single institution study involving patients receiving care at a comprehensive sickle cell center. Patients who receive their care outside of a specialty sickle cell center may have different attitudes and beliefs about HU, which may have important implications for the nature and type of HU educational interventions developed for SCD patients.

Barriers to a wider uptake of HU therapy among the SCD population exist at multiple levels, including at the level of the patient. Our study suggests that a general lack of knowledge about HU, doubts about its effectiveness, and concerns over its side effects are all patient-level barriers that need to be addressed. Furthermore, when patients do begin treatment with HU, it is important that their expectations about the drug and its effects are appropriately managed, particularly at the start of therapy, so that the patient and his or her medical team may give HU therapy an adequate chance to succeed.

Methods

Study design, setting, and sample

We conducted a cross-sectional study of 95 adults (age 18+) with SCD receiving care at an urban academic medical center from September 2006 to June 2007. Participants were recruited from the adult sickle cell and hematology outpatient clinics (49.5%) or those seeking acute care for the treatment of a vaso-occlusive sickle cell crisis from the Emergency Department (ED) or inpatient units (50.5%). Participating patients underwent a 15-min interview by a trained study team member and received \$10 for interview completion. Health status information was collected by self-report and abstraction from the patient's medical record. The academic medical center's institutional review board reviewed and approved the study procedures, and all participating patients gave informed consent.

Measures

HU history, beliefs, and attitudes—Patients who self-reported that they were not currently taking HU were categorized as “never” or “former” HU users. “Current” users were subsequently asked to assess how much they thought taking HU had helped them (not at all to very much) and the extent to which they have been bothered by side effects from taking HU (not at all to very much). Former users were asked to estimate the length of time they were on HU (<6 months to 5+ years) and to provide the reason that they stopped taking HU. Never users were asked to recall if a doctor had ever suggested that they take HU (yes/no), to gauge the amount of information they have received about HU (none to too much), and to postulate how they thought taking HU would make them feel relative to their current assessment of their condition (much worse to much better). Additionally, patients were given the opportunity to describe in their own words any concerns that they may have had about HU. Thirty-three of the 95 participating patients provided responses to this open-ended question.

Patient characteristics—We assessed a number of patient demographic and clinical characteristics by patient self-report, including the patient's level of education (<high school, high school/GED, some college, college or beyond), annual household income (<\$10,000; \$10,000–\$35,000; and >\$35,000+), current employment (employed/unemployed), and current receipt of disability benefits (yes/no).

Using the patient's medical record, we assessed the following demographic and clinical variables: patient age, patient sex, the patient's sickle cell genotype (HbSS/HbSC/SbThal/Other or Unknown), the number of sickle cell-related comorbidities ever experienced by the patient (out of five possible: acute chest syndrome, avascular necrosis, renal disease, pulmonary hypertension, and iron overload), and the number of hospital visits by the patient in the prior 12 months.

Statistical methods—Bivariate associations between patient characteristics and HU use status were conducted using the chi-square test, Fishers exact test, Student's t-test, and one-way analysis of variance as appropriate. Two investigators (CH and SL) reviewed the responses to the open ended questions about the reason for stopping HU use (among “former” users) or any concerns that any respondent expressed about HU, and coded these responses into smaller categories. Disagreements between the investigators regarding the coding were resolved through discussion. The frequencies with which these smaller categories were mentioned are presented as simple tabulations and percentages in Table II. Analyses of quantitative data were conducted using Stata 10 software [20].

Acknowledgments

Contract grant sponsor: Johns Hopkins Blaustein Pain Research Fund; Contract grant sponsor: National Heart, Lung, and Blood Institute; Contract grant numbers: 5F31HL082037-02 and 5K23HL083089-02; Contract grant sponsor: Johns Hopkins Clinical Research Scholars award; Contract grant number: #5KL2RR025006-03; Contract grant sponsor: Agency for Healthcare, Research, and Quality; Contract grant number: 5K08HS013903-04.

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Table I**Patient Characteristics by Self-Reported Hydroxyurea Use**

Patient characteristics	Hydroxyurea use			P-value
	Never (n = 37)	Former (n = 23)	Current (n = 34)	
Age, mean(sd)	32.7 (11.9)	32.9 (8.8)	33.3 (10.1)	0.972
Female	59.5%	65.2%	52.9%	0.646
Sickle cell type				0.093
HbSS	54.1%	50.0%	82.4%	
HbSC	16.2%	27.3%	5.9%	
SbThal	24.3%	18.2%	8.8%	
Other/Unknown	5.4%	4.5%	2.9%	
Hospital visits, mean(sd)	2.0	3.7	3.6	0.203
Sickle comorbidities, mean(sd)	1.02 (0.99)	1.69 (0.97)	1.73 (1.1)	0.008
Education				0.774
Some HS	13.5%	13.0%	5.9%	
HS grad or GED	29.7%	43.5%	41.2%	
Some college	35.1%	21.7%	26.5%	
College or beyond	26.5%	21.7%	26.5%	
Unemployed	59.5%	69.6%	76.5%	0.303
On disability	43.2%	73.9%	67.6%	0.030
Household income				0.999
<10k	32.4%	31.8%	29.4%	
10k to <35k	32.4%	31.8%	32.4%	
35k+	35.3%	36.4%	38.2%	

Table IINumber of Adult Sickle Cell Patients Describing Concerns About Hydroxyurea ($n = 33$)

Concern	No. (%) ^a
Side effects	25 (75.8)
Nonspecific	14 (56)
Safety	8 (32)
Reproductive effects	2 (8)
Carcinogenic	1 (4)
No perceived benefit	8 (24.2)
Lack of knowledge	4 (12.1)

^aConcerns are not mutually exclusive.