Hydroxyurea adherence in adolescents and young adults with Sickle Cell Disease: An exploration of barriers to adherence in relation to health-related quality of life.

Fatma S Al-Zhrani, Solafa H Ghoneim, Manar Makin, Najd A Alsukhayri, Shahad A Alshaynawi

Department of pediatric, College of medicine, King Abdulaziz University, Saudi Arabia

Abstract

Background and objectives: Sickle cell disease (SCD) is a hereditary hematologic disorder that affects hemoglobin. With this disease, their health-related quality of life (HRQOL) significantly declines due to disease-related complications. Hydroxyurea is an oral medication recommended for the treatment of youth with SCD, as it is known to improve the HRQOL. However, adherence remains suboptimal. Reported barriers were forgetfulness, inability to obtain the medication, lack of knowledge about hydroxyurea, fear of side effects, and concerns about efficacy. This study aims to was to identify barriers to hydroxyurea adherence and their relationship to adherence rates and (HRQOL) among adolescents and young adults with sickle cell disease in a tertiary center, Jeddah, Saudi Arabia.

Method: A cross-sectional study used for patients with SCD (aged 15-24 years) in 2019. The study measures included Brief Medication Questionnaire (BMQ), Modified Morisky Adherence Scale 8-items (MMAS-8), visual analog scale (VAS), and Patient-Reported Outcomes Measurement Information System (PROMIS). A P value < 0.05 was considered to be statistically significant.

Results: A total of 40 participants (40% male, 60% female) had a mean age of 19 years reported the following barriers: negative belief (52.5%), recall barriers (35.0%), and access barriers (22.5%). Patients no significant difference was reported with adherence barriers a MMAS-8 score. However, a (p=0.038) with V AS. However, patients with negative beliefs demonstrated a significant difference (p=0.038) with respect to V AS. Conclusion: Patients who reported negative beliefs to hydroxyurea were more than those with recall and access barriers. No significant differences were reported with hydroxyurea adherence barriers. In future studies, a larger sample size with patients from all over Saudi Arabia would be recommended for more accurate, generalizable results.

Keywords: Hydroxyurea adherence, Barriers to hydroxyurea, Health-related quality of life.

Accepted December 07, 2020

Introduction

Sickle cell disease (SCD) is the most frequent monogenic disorder resulting from abnormal hemoglobin structure in red blood cells that generally responsible for making oxygen delivered to all tissues of the body [1]. Approximately (2-8%) of people around the world has the sickle cell anemia gene, considering it to be the commonest hemoglobinopathy [2]. Patients develop complications in their disease course, such as chronic anaemia, acute and chronic pain, severe chest infection, and long-term end-organ damage [3]. As these complications continue to occur throughout their lives, they experience a high reduction in health-related quality of life (HRQOL) [4].

Hydroxyurea (HU) was approved by the food and drug administration (FDA) in 1998 for the treatment of SCD patients [5]. It is an oral medication recommended for the treatment of youth diagnosed with SCD [6]. The drug causes an increase in fetal hemoglobin (HbF) levels in the circulation, which reduces the complications of SCD due to improved circulation [7]. It has benefits in improving morbidity, mortality, and domains of health-related quality of life [8-14]. Despite these therapeutic benefits, adherence in adolescents and young adults with SCD is often poor [15]. Several barriers contribute to hydroxyurea adherence including forgetfulness, inability to obtain the medication, lack of knowledge regarding hydroxyurea, worry of side effects, and efficacy concerns [16-21].

A study was done in Oman among 298 patients (aged 13 years and above) with SCD assessed the pattern of use, adherence, and safety of HU. Most patients were adherent to HU. However, 14 patients classified as non-adherent, and their major cause was forgetting medication. On the other hand, 128 patients taking HU discontinued the medication for many reasons including adverse drug reaction, contraindications, and no seen benefits [22]. Another cross-sectional study published in 2018 in the United States assessed the compliance to hydroxyurea by 34 youths and young adults (ages 12-22) with SCD. The study concluded that nonadherence to medication is because of the concern of oversiring the drug and fearing its harm. Those patients reported a worse quality of life compared to patients with low concerns about hydroxyurea [23].

A similar previous study done in 2017 involved 34 participants (ages 12-22 years) on hydroxyurea for 6 months or more, with no dose escalation for a minimum of 2 months, without chronic transfusions. The study explored the barriers that affect patients' adherence to hydroxyurea. A high HRQOL was achieved by patients who experienced fewer barriers, and those who adhered to the drug [24]. In addition, a cross sectional study was conducted in 2016 in Chicago involving 34 participants (12-22 years old) on a stable dose of hydroxyurea for a minimum of 2 months. They concluded that low adherence to hydroxyurea in SCD patients showed worse HRQOL. This included fatigue, pain, mobility, depression, and social isolation scores [25].
A cross-sectional study was done from August to September 2019 by using a survey. The included participants were adolescents and young adults between the ages (15-24) years with SCD (all genotypes). We excluded patients who underwent chronic blood transfusion and those with recent surgery.

A questionnaire was used to collect the data. Information included the Brief Medication Questionnaire (BMQ), which concentrated on their negative beliefs, recall barriers and access barriers. We considered negative beliefs if the patient answered concentrated on their negative beliefs, recall barriers and access barriers. We excluded patients who underwent chronic blood transfusion and those with recent surgery.

We used the Modified Morisky Adherence Scale 8-items (MMAS-8) and Visual Analogue Scale-dose (VAS dose) to evaluate adherence. In addition, Patient-Reported Outcomes Measurement Information System (PROMIS) was used in order to measure fatigue, pain interference, physical functioning mobility, physical functioning of upper-extremities, depression, and anxiety.

Complete confidentiality of information obtained from the patients was achieved, and the information was only used for the benefit of the study. The participation was completely voluntary. Microsoft Excel was used for data entry and statistical analysis was performed by SPSS. A P-value < 0.05 was considered to be statistically significant.

**Results**

The sample size of our study was 40 patients, which include 24 (60%) females and 16 (40%) males. Their ages were between (15 and 24) years old. The mean age was $19.06 \pm 2.77$ years (Table 1). Most of the participants 33 (82.5%) regularly use hydroxyurea, while 7 (17.5%) patients did not use hydroxyurea. The majority of participants who reported barriers related to hydroxyurea were negative beliefs or motivational barriers (n=21, 52.5%), followed by recall barriers or forgetfulness (n=14, 35%), and access barriers such as paying for hydroxyurea and/or getting refills on time (n=9, 22.5%) (Table 2).

<table>
<thead>
<tr>
<th>Table 1: Demographic characteristics.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Adherence levels can be measured by MMAS-8 score that range from 0 and by VAS dose that range from 0 to 100%. Using MMAS-8, Patients with access barriers, recall bias, and negative beliefs showed no significant correlation with adherence criteria (MMAS-8) (p=0.836), (p=0.106) (p=0.079) respectively. In VAS dose, patients with negative beliefs was statistically significant (p=0.038), while those with recall bias and access barriers showed no relation (p=0.325), (p=0.727) respectively (Table 3).

Table 2: Frequency of patients with or without barriers to hydroxyurea adherence.

<table>
<thead>
<tr>
<th>Negative belief</th>
<th>Recall belief</th>
<th>Access barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent</td>
<td>Frequency</td>
<td>Percent</td>
</tr>
<tr>
<td>YES</td>
<td>32.5</td>
<td>21</td>
</tr>
<tr>
<td>NO</td>
<td>47.5</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>40</td>
</tr>
</tbody>
</table>

Anxiety and depression were more common with patients who have a negative belief (n=8) while some of them developed fatigue (n=4) and pain interference (n=3). Patients have a negative belief or without recall and access barriers did not show a significant relation to PROMIS scores (Table 4).

Table 3: Barriers to hydroxyurea adherence and health-related quality of life.

<table>
<thead>
<tr>
<th>BMQ Negative belief</th>
<th>BMQ Recall belief</th>
<th>BMQ Access barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
<td>P-value</td>
</tr>
<tr>
<td>MMAS-8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>12</td>
<td>0.079</td>
</tr>
<tr>
<td>Medium</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>High</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>VAS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>16</td>
<td>0.038</td>
</tr>
<tr>
<td>High</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

Discussion

This study aimed to identify barriers to hydroxyurea adherence and their relationship to adherence rates and and HRQOL among adolescents and young adults with sickle cell disease at a tertiary center, Jeddah, Saudi Arabia.

Of our participants, 82% regularly used hydroxyurea. Upon obtaining the frequency for each barrier affecting patients’ adherence to hydroxyurea, we found that negative belief was the most contributing factor, (52.5%) followed by recall bias (35.0%) then by access barriers (22.5%). We found in our study that negative belief was the most reported common barrier to hydroxyurea adherence. On the other hand, access and recall barriers showed no significance. Haywood et al. studied the reasons behind negative barriers to hydroxyurea adherence and summarized them as the patients’ belief that the drug is not working well, a lack of knowledge, and a fear of side effects [26]. Nevertheless, in our study, we did not focus on the possible reasons behind patients’ negative beliefs.

A study similar to our own published in 2017 by Badawy SM, found that the most barriers reported were recall barriers.
Hydroxyurea adherence in adolescents and young adults with Sickle Cell Disease: An exploration of barriers to adherence in relation to health-related quality of life.

(44%) [24]. The study also reported these significant results. The correlation between recall barriers and HRQOL was significant for pain (P=0.02), fatigue (P=0.05), and depression (P=0.05). Our findings showed no significance with these HRQOL domains. In addition, VAS and recall barriers reported significance (P=0.01) in the same study. While in our study, VAS and negative barriers showed significance (P=0.038). Finally, access barriers and MMAS-8 reported significance (P=0.02) in Badawy MS’s study. On the contrary, our study showed that negative belief was also not significant (p=0.079) [24].

In another study, they found patients taking hydroxyurea treatment with a high adherence rate have better HRQOL than those with a low adherence rate [25]. Moreover, Arlene Smaldone et al. reported that the more barriers to hydroxyurea, the poorer adherence to it, and the worse HRQOL could get [26]. However, we found no significance in our study between the barriers and HRQOL, and this may be due to our small sample size.

Since this study was a cross-sectional study, the most significant limitation we faced was dealing with a small sample size that can lead to bias. Also, our study was a single center as the population of young adults who participated in the study were all from one governmental hospital that limits the generalizability.

Conclusion

The most frequent barrier in this study was a negative belief (52.5%), while other barriers such as recall barriers were (35%) and access barriers (22.5%). The only significant difference reported was among patients with negative belief barriers and adherence rates to the VAS score (p=0.038). This indicated that the most common barrier in this study affecting adherence to hydroxyurea was negative belief. Furthermore, no association between barriers and HRQOL has been recognized in our study. Future studies are recommended to increase the sample size.

References


*Correspondence to
Fatma S Al-Zhrani
College of medicine,
King Abdulaziz University
Saudi Arabia
Telephone: 0567855009
Email: Falzahrani@kau.edu.sa