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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.

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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 VAS. However, Patients with negative beliefs demonstrated a significant difference (p=0.038) with respect to VAS.

Conclusion: Patients who reported negative beliefs to hydroxyurea were more than those with recall and access barriers. Negative beliefs also showed strong significance with VAS. 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.

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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 overusing 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].

No studies were conducted in Saudi Arabia, especially in the western region to determine barriers to hydroxyurea adherence. It's important to identify barriers to avoid the complications of the sickle cell disease. Therefore, our study aimed to identify barriers to hydroxyurea adherence and their relationship to adherence rates and HRQL among adolescents and young adults with sickle cell disease at a tertiary center, Jeddah, Saudi Arabia.

Research Methodology

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 that HU does not work or has side effects. Recall barriers if they did not remember dosage amount and access barriers if they said it was difficult to refill or to pay for HU.

We used 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 ± 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 1: Demographic characteristics.

Sample size	Frequency	Percent	Age's minimum	Age's maximum	Mean	Standard deviation
Female	24	60	15	24	19.075	2.7678
Male	16	40				
Total	40	100				

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

	Negative belief		Recall belief		Access barriers	
	Percent	Frequency	Percent	Frequency	Percent	Frequency
YES	52.5	21	35	14	22.5	9
NO	47.5	19	65	26	77.5	31
Total	100	40	100	40	100	42

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 3: Barriers to hydroxyurea adherence and levels of adherence.

	BMQ Negative belief			BMQ-Recall belief			BMQ-Access barriers		
	Yes	No	P-value	Yes	No	P-value	Yes	No	P-value
MMAS8									
Low	12	6	0.079	7	11	0.106	4	14	0.836
Medium	8	6		6	8		4	10	
High	0	1		1	0		0	1	
VAS									
Low	16	9	0.038	10	15	0.325	6	19	0.727
High	4	3		3	4		2	5	

Anxiety and depression were more common with patients 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 4: Barriers to hydroxyurea adherence and health related quality of life.

HRQOL Domains	BMQ-Negative Belief			BMQ-Recall Barrier			BMQ-Access Barriers		
	Yes (n=21)	No (n=19)	P. value	Yes (n=14)	No (n=26)	P. value	Yes (n=9)	No (n=31)	P. value
Fatigue	4	16	0.787	3	22	0.631	2	26	0.672
Pain Interference	3	17	0.72	3	24	0.21	1	27	0.886
Physical Function: Upper Extremities	1	16	0.246	1	23	0.658	1	28	0.9
Physical Function: Mobility	2	17	0.916	1	23	0.658	0	27	0.256
Anxiety	4	18	0.188	2	23	0.802	2	28	0.316
Depression	4	18	0.188	3	24	0.21	1	27	0.886

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

(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. Further studies are recommended to increase the sample size.

References

1. Ashley-Koch A, Yang Q, Olney RS. Sickle hemoglobin (HbS) allele and sickle cell disease: a HuGE review. Am J Epidemiol 2000; 151: 839-45.
2. Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. Bull World Health Organ. 2008; 86: 480-7.
3. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. The Lancet. 2010; 376: 2018-31.
4. Panepinto JA, Bonner M. Health-related quality of life in sickle cell disease: past, present, and future. Pediatr Blood Cancer 2012; 59: 377-85.
5. https://www.fda.gov/consumers/consumer-updates/fda-encourages-new-treatments-sickle-cell-disease
6. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. 2014; JAMA 312:1 033-1048.
7. McGann PT, Ware RE. Hydroxyurea for sickle cell anaemia: What have we learned and what questions still remain? Curr Opin Hematol 2011; 18: 158-165.
8. Thornburg CD, Calatroni A, Panepinto JA. Differences in health-related quality of life in children with sickle cell disease receiving hydroxyurea. J Pediatr Hematol Oncol 2011; 33: 251-4.
9. Wang WC, Oyeku SO, Luo Z, et al. Hydroxyurea is associated with lower costs of care of young children with sickle cell anemia. Pediatrics 2013; 132: 677-83.
10. Wang WC, Ware RE, Miller ST, Iyer RV, Casella JF, Minniti CP, et al. Hydroxycarbamide in very
11. Strouse JJ, Lanzkron S, Beach MC, et al. Hydroxyurea for sickle cell disease: a systematic review for efficacy and toxicity in children. Pediatrics 2008; 122: 1332-42.
12. Thornburg CD, Files BA, Luo Z, et al. Impact of hydroxyurea on clinical events in the BABY HUG trial. Blood 2012; 120: 4304-10.
13. Ballas SK, Barton FB, Waclawiw MA, et al. Hydroxyurea and sickle cell anemia: effect on quality of life. Health Qual Life Outcomes. 2006; 4:59.
14. Nwenyi E, Leafman J, Mathieson K, et al. Differences in quality of life between pediatric sickle cell patients who used hydroxyurea and those who did not. Int J Health Care Qual Assur 2014; 27: 468-81.
15. Loiselle K, Lee JL, Szulczewski L, et al. Systematic and meta-analytic review: Medication adherence among pediatric patients with sickle cell disease. J Pediatr Psychol 2016; 41: 406-18.
16. Thornburg CD, Calatroni A, Telen M, et al. Adherence to hydroxyurea therapy in children with sickle cell anemia. J Pediatr 2010; 156: 415-9.
17. Badawy SM, Thompson AA, Liem RI. Technology access and smartphone app preferences for medication adherence in adolescents and young adults with sickle cell disease. Pediatr Blood Cancer 2016;63: 848-52.
18. Walsh KE, Cutrona SL, Kavanagh PL, et al. Medication adherence among pediatric patients with sickle cell disease: a systematic review. Pediatrics 2014; 134: 1175-83.
19. Haywood C, Beach MC, Bediako S, et al. Examining the characteristics and beliefs of hydroxyurea users and nonusers among adults with sickle cell disease. Am J Hematol 2011; 86: 85-7.
20. Brandow AM, Panepinto JA. Monitoring toxicity, impact, and adherence of hydroxyurea in children with sickle cell disease. Am J Hematol 2011; 86: 804-6.
21. Jose J, Elsadek RA, Jimmy B, et al. Hydroxyurea: Pattern of use, patient adherence, and safety profile in patients with sickle cell disease in Oman. Oman Medical Journal 2019; 34: 327–335.

22. Badawy SM, Thompson AA, Liem RI. Beliefs about hydroxyurea in youth with sickle cell disease. Haematology Oncology and Stem Cell Therapy 2018; 11: 142-148.

23. Badawy SM, Thompson AA, Penedo FJ, et al. Barriers to hydroxyurea adherence and health-related quality of life in adolescents and young adults with sickle cell disease. Eur J Haematol 2017; 98: 608-14.

24. Badawy SM, Thompson AA, Lai JS, et al. Health-related quality of life and adherence to hydroxyurea in adolescents and young adults with sickle cell disease. Pediatr Blood Cancer 2016; 64.

25. Haywood C, Beach MC, Bediako S, et al. Examining the characteristics and beliefs of hydroxyurea users and nonusers among adults with sickle cell disease. Am J Hematol 2011; 86: 85-7.

26. Smaldone A, Manwani D, Green NS. Greater number of perceived barriers to hydroxyurea associated with poorer health-related quality of life in youth with sickle cell disease. Pediatr Blood Cancer 2019; 66: e27740.

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