

Patterns of prescribing hydroxyurea for sickle cell disease patients from a central hospital, Saudi Arabia

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Abstract

Sickle cell disease (SCD) is a group of inherited disorders of hemoglobin synthesis. It is prevalent in different parts of the world, including the Kingdom of Saudi Arabia. The disease is associated with multiple acute and chronic life-threatening complications. Hydroxyurea (HU) is an effective preventive medication; its use has resulted in decreased morbidity and mortality. However, practice variability, including underutilization of HU, has been reported. No local publication has addressed this issue. The aim of this work is to consider the pattern of HU prescription for SCD patients. This is a retrospective study included patients seen in the outpatient clinics in a central hospital. Cases of medications unavailability or patient refusal to take the drug were not included. A total of 152 patients were included, of them 118 were prescribed HU and 34 were not. In 133 (87.5%) patients, the physician's decision was appropriate. Inappropriate decisions including both under prescription and, to much lesser extent, over utilization had been demonstrated in 19 (12.5%) cases. Impact of raising the healthcare providers' awareness and improving compliance with the updated SCD management recommendations and guidelines deserve further studying. In our local experience, although the majority of HU prescriptions were appropriate, both under prescription and to a lesser extent, overutilization was demonstrated.

Introduction

Sickle cell disease (SCD) is a group of inherited conditions of hemoglobin formation. It is associated with many acute and

chronic complications that cause significant morbidity and mortality.¹ The disease's prevalence in Africa is in the range of 1-2% in the north, while it is less than 1% in the south. In the United States, SCD affects around 72,000 people, while in the United Kingdom; 12,500-15,000 people have the disease.² In the Kingdom of Saudi Arabia (KSA) with a population of 20.4 million, the reported overall prevalence of the genotype SS (commonest genotype) is 1.06% with a trait of 7.3%.^{3,4}

Hydroxyurea (HU) is the first approved SCD modifying agent. It reduces the frequency of vaso-occlusive crises (VOCs), mortality, acute chest syndrome (ACS), blood transfusions, admission, length of stay, and opioid utilization during hospitalization.⁵⁻⁸ For SCD patients, the recommended indications for HU include the following: adults with three or more severe VOCs during any 12-month period, SCD pain or chronic anemia interfering with daily activities, severe or recurrent episodes of ACS and cerebrovascular stroke (CVS) with lack of possibility to implement a transfusion program.⁹

Practice variability in prescribing HU and underutilization, both have been reported from different parts of the world.^{9,10} No local study has addressed this issue before. The aim of this work is to study the pattern of prescribing HU from a central hospital in KSA.

Materials and Methods

This is a medical record-based retrospective study of 152 patients. The study covered SCD patients seen in the outpatient clinics at King Saud Medical City, Riyadh KSA, from May 2017 to January 2018. The inclusion criteria are: SCD patients at or above the age of 14 years, whether or not receiving HU. Cases with medication unavailability or patient refusal to receive the drug were not included. The study was approved by the Hospital Institutional Review Board.

Results

The basic characteristics of the patients are shown in Table 1. A total of 152 patients were included, 78 males and 74 females, with an age range of 14-40 years. HU was prescribed in 118 patients, while it was not prescribed in 34.

Regarding the patients for whom HU

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was prescribed ($n=118$), in 106 (90%) of them, there was at least one appropriate indication for prescribing the medication. VOC requiring hospital admission was the reason for HU prescription in 58 of these patients, with a range of 3-10 episodes per year. ACS was the indication in 12 patients, with a range of 1-3 episodes.

Other indications include anemia or painful episodes interfering with daily activity or patients with history of stroke who were not on regular exchange transfusion; these were evident in 4, 2, and 3 patients, respectively. Twenty-six patients had two indications; these were VOC and ACS, VOC and anemia interfering with daily activity, VOC and CVS, and ACS and CVS, which were present in 18, 4, 1, and 3 patients, respectively. One patient had VOC, ACS, and stroke.

In 12 (10%) patients in whom the HU was prescribed, none of the recommended indications were present (over utilized/inappropriate prescription; Table 2).

Considering the patients for whom medication was not prescribed ($n=34$), in 27 (79%) patients, there was no indication (appropriate decision), while in 7 (21%) cases, it was underutilized (inappropriate; Table 2). For the patients for whom the HU was underutilized, frequent admissions for VOC (3-4 episodes per year), one episode of ACS, and a history of CVS (not on regular exchange transfusion) were present in 4, 2, and 1 patient(s), respectively.

Table 1. Basic patients' characteristics.

Characteristic (n=152)	HU prescription	
	Prescribed (n=118)	Not prescribed (n=34)
Age range (years)	14-40	14-37
Male: female	63:55	15:19
Three or more admissions per year for VOC	58	4
History of acute chest syndrome*	12	2
Anemia interfering with daily activity.	4	0
Stroke, not on regular exchange transfusion	3	1
Painful episodes interfering with daily activity**	2	0
VOC and ACS	18	
VOC and anemia***	4	
VOC and CVS	1	
ACS and CVS	3	
VOC, ACS, and CVS	1	
No indication	12	27

HU hydroxyurea; VOC vaso-occlusive crisis; ACS acute chest syndrome; CVS cerebrovascular stroke. *Either severe or recurrent. **Other than moderate/severe or severe VOC. ***Interfering with daily activity.

Table 2. Pattern of HU prescription.

	Appropriate, <i>n</i>	Total inappropriate (over and underutilization)	
		Over utilized, <i>n</i>	Underutilized, <i>n</i>
Prescribed HU, <i>n</i> = 118	106	12	NA
Not prescribed HU, <i>n</i> = 34	27	NA	7
Total, <i>n</i> (%)	133 (87.5)		19 (12.5)

HU hydroxyurea. NA not applicable.

Discussion

HU constitutes a disease modifying agent for SCD with multiple advantages, including decreased morbidity and mortality. Our study has demonstrated variability in the prescription practice. Understanding such variability is needed for better adherence to the SCD treatment recommendations and guidelines.

Underutilization had been reported in more than one study.¹²⁻¹⁵ Among the contributing factors are lacking of awareness and poor compliance of the healthcare providers with the treatment guidelines and updates, their concern about patients' fertility and the theoretical carcinogenic potential on HU.^{11,14,15} Variability in practice between the different healthcare levels (community vs. university) has also been reported.¹⁰ In this study cases with medication unavailability or patient refusal to receive it, were not included.

In our study, most prescriptions were appropriate. However, both underutilization and much less frequent overprescribing practice were demonstrated (Table 2). To our knowledge, over prescription has not been previously reported.

The current study has shown the commonest indication was the VOC followed by ACS. These results are consistent with

previous publications.^{10,12} In contrast prescribing HU for the two more recently recommended indications, chronic anemia and frequent painful episodes that interfere with daily activities, is rare.⁹

A limitation of this study is including patients only from a central hospital, whereas primary health care and other more advanced centers might have different patient characteristics and physicians' practice.

Conclusions

In conclusion, in our study, although the majority of HU prescription practice is appropriate, both under prescription, and to a lesser extent, overutilization was demonstrated. The impact of raising the healthcare providers' awareness and improving compliance with the updated SCD management guidelines deserves further studying.

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