Increasing hydroxyurea use in children with sickle cell disease at Kamuzu Central Hospital, Malawi

Tisungane Mvalo,^{1,2} Hillary Topazian,^{1,3} Portia Kamthunzi,^{1,4} Jane Chen,^{1,3} Isobel Kambalame,¹ Pilirani Mafunga,¹ Noel Mumba,¹ Msandeni Chiume-Chiphaliwali,⁵ Khadija Paseli,⁶ Nigel Key,⁷ Satish Gopal,^{1,4} Irving Hoffman,^{1,4} Ken Ataga,⁷ and Kate Westmoreland^{1,8}

¹University of North Carolina Project-Malawi, Lilongwe, Malawi; ²Department of Pediatrics, ³Department of Epidemiology, and ⁴Institute for Global Health and Infectious Diseases, University of North Carolina, Chapel Hill, NC; ⁵Department of Pediatrics, and ⁶Ministry of Health, Kamuzu Central Hospital, Lilongwe, Malawi; and ⁷Division of Hematology, and ⁸Division of Pediatric Hematology-Oncology, University of North Carolina, Chapel Hill, NC

Background

- Sickle cell disease (SCD) is the most common inherited hematologic disease in sub-Saharan Africa (SSA).
- In SSA, the rate of administration of hydroxyurea to patients with SCD is low because of the lack of accessibility and the lack of local evidence on safety and efficacy.
- Kamuzu Central Hospital (KCH) (Figure 1) is a national teaching hospital in Lilongwe, Malawi, where we have established a pediatric SCD clinic.

Objectives

- To examine the feasibility of introducing hydroxyurea in an SSA pediatric SCD clinic.
- To investigate the hematologic safety of hydroxyurea for children with SCD at KCH.

Methods

- This study was an observational, prospective cohort study at KCH that began in 2015 after the disease diagnosis was confirmed by hemoglobin electrophoresis.
- Patients made clinic visits every 1 to 3 months and study visits every 6 months.
- Study data included monitoring of complete blood count (CBC), serum renal function, liver function chemistries, and urinalysis.
- From 2015, low- to medium-dose (10-20 mg/kg/day) hydroxyurea began being administered to children with recurrent or major crises at KCH.
- From the last quarter of 2017, this clinic began prescribing hydroxyurea to all patients with the aim of having all SCD patients receiving hydroxyurea.

Capacity building

- This is one of the few clinics dedicated to providing care to SCD patients in Malawi.
- In the absence of monitoring high-risk SCD patients with transcranial Doppler ultrasound and performing prophylactic exchange transfusions, upscaling hydroxyurea therapy would benefit patients and reduce morbidity in SSA.
- Analysis of the occurrence of complications along with CBC parameters after initiating hydroxyurea therapy would provide medical evidence to support its use in SSA.

Results

Table 1. Characteristics of participants with recorded 6-month study visits taking hydroxyurea for 6 months or longer (N = 39)

Characteristic	No. (%)	Median	Range or IQR
Age at enrollment, y	—	7	0 to 16 (range)
Sex			
Female	20 (53)	—	—
Male	18 (47)	—	—
Length of follow-up time at KCH (months)	39	29	16-38 (range)
Hemoglobin since starting hydroxyurea (g/dL)	129*	7.4	6.5-8.1 (IQR)
Lactate dehydrogenase since starting hydroxyurea (U/L)	108*	664	525.5-769.0 (IQR)

IQR, interquartile range.

*All laboratory results for multiple patient visits combined.

Figure 1. Kamuzu Central Hospital.

Figure 2. Median laboratory results for all patients receiving hydroxyurea (N = 130; range per month, 2-32). Error bars show interquartile range.

Table 2. Complications of participants with study visits

Participant	hydroxyurea start date													Thrombo- cytopenia	Neutropenia	Pneumonia	Acute Chest Syndrome	Dactylitis	Stroke																			
	-12	-11	-10	-9	-8	-7	-6	-5	-4	-3	-2	-1	0							1	2	3	4	5	6	7	8	9	10	11	12							
1																											0	0	0	0	N	N	0	0	N	N	0	0
2																											0	0	0	0	Y	N	0	0	N	N	0	0
3																											0	0	0	0	N	N	0	0	N	N	0	0
4																											0	0	0	0	N	N	0	0	N	N	0	0
5																											0	0	0	0	N	N	0	0	N	N	0	0
6																											0	0	0	0	N	N	0	0	N	N	0	0
7																											0	0	0	0	N	N	0	0	Y	N	0	0
8																											0	0	0	0	N	N	0	0	N	N	0	0
9																											0	0	0	0	N	N	0	0	N	N	0	0

*Thrombocytopenia: platelets $<80 \times 10^3/\mu\text{L}$; neutropenia: neutrophils $<2.0 \times 10^3/\mu\text{L}$.

Conclusions

- The KCH pediatric SCD clinic has been successfully upscaling the administration of hydroxyurea in children since late 2017 and now has near universal coverage.
- Myelosuppressive effects of hydroxyurea in the patients at the SCD clinic have so far been shown to be transient.
- There are ongoing efforts to monitor clinical efficacy and myelosuppressive effects of hydroxyurea therapy in children with SCD as KCH continues to upscale administration of hydroxyurea.

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Authorship

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Correspondence: Tisungane Mvalo, University of North Carolina Project-Malawi, Lilongwe, Malawi; e-mail: tmvalo@unclilongwe.org.

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