Evaluation of Avascular Necrosis and prescribing patterns of Hydroxyurea for pediatric patients with Sickle Cell Disease

Precious Uwaezuoke, FNP, APRN, CNE; Angel Anthamatten, DNP, FNP-BC; Misty Evans, DNP, APRN, CPNP-AC
Vanderbilt University School of Nursing

SCHOOL OF NURSING
VANDERBILT UNIVERSITY

Key Points

- Hydroxyurea (HU) is an important therapy for sickle cell disease (SCD) that reduces disease severity and progression.
- This project analyzed prescribing patterns for HU and adherence to an institutional clinical practice pathway (CPP) for patients with SCD with or without AVN.
- A retrospective chart review was completed for children with SCD who received care between 2018-2021 (n=50).
- Most patients had a AVN diagnosis (72%), with average age of diagnosis being 12.2 years (SD 3.8).
- The average age of HU initiation was 7.3 years (SD 4.3).
- Of these 50 children with SCD, 22 had achieved maximum tolerated dosing (MTD). However, maintenance of MTD over a 12-month period occurred in only 18 (36%) of these 50 children.
- Hydroxyurea dose was modified during 29 (58%) of 50 encounters, but only 22 (44%) were adjusted according to the institution's CPP.
- This project revealed opportunities to optimize HU utilization and dosing.
- Next steps can include exploring strategies to ensure HU doses are appropriately titrated toward MTD when in escalation range, according to evidence-based recommendations.
- Though this project revealed a lack of optimization of HU, it served as an essential first step in shining light on an area which could improve current quality of care.

PURPOSE

- In 2015, a team of experts at a large children's hospital in the southern region of the United States developed a protocol that outlined best prescribing practices for HU for children with sickle cell disease (SCD).
- Since the implementation of this clinical practice pathway (CPP), provider adherence to the institution's prescribing protocols has not been evaluated.
- This important step of the quality improvement process can facilitate optimization of the care delivered to the children with SCD who receive medical services at this institution.
- This project aimed to analyze prescribing patterns for HU and adherence to an institutional CPP for pediatric patients with SCD with or without AVN.

Sex	Male (62%) Female (38%)
SCD Genotype	HgbSS (80%) HgbSC (12%) HgbSbeta0Thalassemia (8%)
AVN diagnosis	With (72%) Without (28%)
Method for detecting AVN	X-ray (72%) MRI (28%)
Average age of AVN diagnosis	Mean= 12.2 years (SD 3.8)
Average age of HU initiation	Mean= 7.3 years (SD 4.3)
Documentation of initial caregiver hesitancy regarding HU initiation	Yes (14%) No (86%)

Table 1. Demographics of a cohort of children with Sickle Cell Disease (n=50)

BACKGROUND

- A dangerous hallmark of SCD is recurring occlusions of blood vessels secondary to the disorder's pathophysiology.[8]
- Avascular Necrosis (AVN) results from disruption of blood flow to the bone, causing the eventual collapse in bone structure.[5]
- There have been many advances with SCD management (such as immunizations, HU, and penicillin prophylaxis), which has led to increased survival for persons with SCD.[6-7]
- The success of improved lifespan presents another important sequela: AVN prevalence is expected to increase since there is greater time for disease progression.
- It is essential to identify and implement strategies that can help delay the onset of this complication, and an important one is proper utilization of HU.

METHODS

- ICD codes identified participants with the following diagnoses: sickle cell disease with vaso-occlusive crisis, sickle cell disease without crisis, HgbSS, HgbSC, HgbSbeta0Thalassemia, hemoglobinopathy, HgbSbeta+, avascular necrosis, osteonecrosis, ischemic necrosis, aseptic necrosis, and like terms.
- Fifty pediatric patients with SCD with or without radiologic findings of AVN seen at this institution during the August 2018 to August 2021 period were included in a retrospective chart review. All participants with AVN and who were managed with HU were included to assess how HU had been optimized in this high-risk cohort.
- Data collection included: gender, genotype, presence of AVN, whether there was multi-focal AVN, age at AVN diagnosis and HU initiation, identification of caregiver hesitancy with HU use, ability to maintain MTD with HU, and evaluation of HU dosing adjustments.
- Optimization was determined by the ability to meet MTD lab parameters and maintain these results throughout a cycle of four months (either May-August period of 2019 or 2021) and over 12 months of therapy (August 2018-2019 or August 2020-2021).

Lab Parameter	Toxicity level	Level for escalation	Considered MTD
Absolute Neutrophil Count	<1000	>3000	1000-3000
Hemoglobin	Hgb <7g/dL if ARC <100,000	Hgb >8g/dL or ARC >100,000	
Absolute retic count	ARC <80,000 unless Hgb>8g/dL	ARC >100,000 or Hgb >8g/dL	80,000-100,000
Platelets	<80,000	>100,000	80,000-100,000

Table 2. Hydroxyurea dosing parameter guidelines[12]

Reason for not following clinic protocol? (N=28)

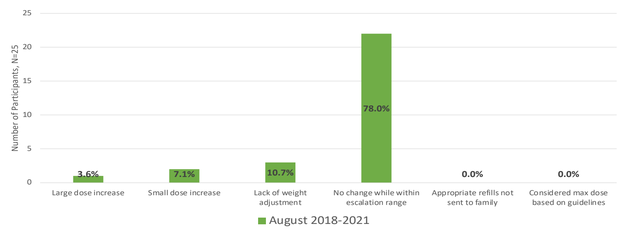

Table 3. Reason for HU dose adjustment not following clinic protocol

RESULTS

At MTD with HU?	n=50
Yes	22 (44%)
No	28 (56%)

Maintained MTD over 12 months?	n=50
Yes	18 (36%)
No	32 (64%)

HU dose adjustment during 12-month period?	n=50
Yes	29 (58%)
No	21 (42%)

HU dose adjustment aligned with protocol?	n=50
Yes	22 (44%)
No	28 (56%)

CONCLUSIONS

- Findings revealed a lack of implementation of HU dose optimization.
- There is an opportunity to explore strategies to ensure HU doses are appropriately titrated toward MTD when lab parameters are in escalation range, according to evidence-based recommendations.
- Next steps could also include exploring strategies to avoid delay in initiation of HU therapy for children with SCD.
- Root cause analyses may provide insight into factors contributing to the suboptimal prescribing adherence to evidence-based recommendations and stimulate identification of strategies to overcome barriers to this quality initiative.

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