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Original Research Article

Impact of Hydroxyurea on Serum Electrolyte Levels in Patients with Sickle Cell Disease

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Abstract:

Background: Sickle Cell Disease (SCD) is a genetic disorder marked by abnormal hemoglobin paving a path to chronic hemolysis and vaso-occlusive crises. Hydroxyurea (HU) therapy has been widely used to reduce the frequency of these crises and improve hematologic parameters. However, its impact on serum electrolytes remains underexplored.

Aim: This research intends to estimate the serum electrolyte levels in SCD patients undergoing Hydroxyurea therapy compared to those not receiving this treatment.

Methods: A cross-sectional study was performed including 90 SCD patients, divided into two groups: 45 patients receiving Hydroxyurea therapy (Group A) and 45 patients not on Hydroxyurea therapy (Group B). Serum levels of sodium, potassium, calcium, and magnesium were measured and compared between the two groups using standard biochemical methods.

Results: The study revealed that patients in Group A exhibited significantly elevated serum magnesium levels ($p<0.05$) when compared to those in Group B. Though, there was no notable differences in the serum levels of Na (sodium), potassium (K), and calcium (Ca) among the two groups. The average serum magnesium level in Group A was recorded at 2.1 ± 0.3 mg/dL, however in Group B, it was 1.8 ± 0.4 mg/dL.

Conclusion: Hydroxyurea therapy appears to be linked with advanced serum magnesium levels in SCD patients, which could be beneficial in reducing vaso-occlusive crises. However, other electrolyte levels did not show noteworthy variation between the two groups.

Recommendations: Further longitudinal research with larger sample sizes are recommended to confirm these findings and to investigate the clinical significance of altered magnesium levels in SCD patients on Hydroxyurea therapy. Additionally, regular monitoring of serum electrolytes should be considered in the management of patients of SCD undergoing Hydroxyurea therapy.

Keywords: Sickle Cell Disease, Hydroxyurea Therapy, Serum Electrolytes, Magnesium, Hematologic Parameters.

Introduction

Sickle Cell Disease (SCD) is a hereditary condition that impacts hemoglobin as a result of a mutation in the β-globin gene. This genetic alteration paves way to the creation of abnormal hemoglobin S, which causes RBCs to convert into an inflexible, sticky, and form a characteristic sickle shape, especially when oxygen levels are low. These deformed cells can obstruct blood flow, causing painful vaso-occlusive crises, hemolytic anemia, and various organ complications. The chronic and acute manifestations of SCD significantly impact the life quaity and expectancy of affected individuals [1,2].

The management of SCD has evolved over the years, with Hydroxyurea (HU) emerging as a cornerstone therapy. Hydroxyurea is an antineoplastic agent that has shown efficacy in reducing the frequency of painful crises, the need for blood transfusions, and the incidence of acute chest syndrome. It works by increasing fetal hemoglobin (HbF) production, reducing leukocyte and reticulocyte counts, and decreasing the adhesion of sickle cells to the vascular endothelium. Despite its benefits, the broader effects of HU on various physiological parameters, including serum electrolytes, require further investigation [3].

Serum electrolytes play a critical role in maintaining cellular function, fluid balance, and neuromuscular activity. Electrolyte imbalances can have significant clinical consequences, particularly in patients with chronic conditions like SCD. Previous studies have documented alterations in electrolyte levels in SCD patients, which can be attributed to hemolysis, renal dysfunction, and ongoing inflammatory processes. Understanding how HU therapy influences these electrolyte levels is crucial for optimizing the management and care of SCD patients [4].

There is limited literature on the impact of HU therapy on serum electrolytes in SCD patients. Some studies suggest that HU may affect the metabolism and homeostasis of certain electrolytes, potentially offering additional benefits or posing risks. For instance, magnesium is identified to play a role in vascular tone and endothelial function, and its deficiency has been linked to increased vascular complications in SCD. Thus, evaluating the serum levels of key electrolytes such as sodium, potassium, calcium, and magnesium in SCD patients undergoing HU therapy is essential [5]

Given the significance of electrolyte balance in SCD and the widespread use of HU therapy, this study aims to bridge the knowledge gap by systematically assessing the serum electrolyte profiles of SCD patients on HU therapy compared to those not receiving this treatment. Such an evaluation will provide insights into the broader implications of HU therapy and help inform clinical practices regarding electrolyte monitoring and management in SCD patients.

This study intends to evaluate the serum electrolyte levels in SCD patients undergoing Hydroxyurea therapy compared to those not receiving this treatment. Specifically, it seeks to determine whether there are significant alterations in the levels of sodium, potassium, calcium, and magnesium among the two groups, thereby providing a better understanding of the impact of Hydroxyurea on electrolyte homeostasis in SCD patients.

Methodology

Study Design: A cross-sectional study was carried out to assess the effects of Hydroxyurea treatment on serum electrolyte levels in patients with SCD.

Study Setting: The study was carried out at the Department of Biochemistry, Anugrah Narayan Magadh Medical College & Hospital, Gaya, Bihar, from January 2022 to January 2023.

Participants: The study included a total of 90 SCD patients who met the following inclusion and exclusion criteria:

Inclusion Criteria:

1. Patients diagnosed with Sickle Cell Disease.
2. Patients aged 18 years and above.
3. Patients who have been on Hydroxyurea therapy for at least six months.
4. Patients who provided informed consent.

Exclusion Criteria:

1. Patients with other hemoglobinopathies.
2. Patients with chronic renal or liver diseases.
3. Pregnant or lactating women.
4. Patients who did not consent to participate.

Bias: To minimize selection bias, consecutive sampling was used to recruit participants. Information bias was reduced by standardizing the data collection process and using calibrated equipment for measurements.

Variables

- **Independent Variable:** Hydroxyurea therapy.
- **Dependent Variables:** Serum levels of sodium, potassium, calcium, magnesium, and other relevant electrolytes.
- **Confounding Variables:** Age, gender, duration of SCD, and comorbid conditions.

Data Collection: Data were collected using a structured questionnaire and medical records. Blood samples were obtained from each participant to measure serum electrolyte levels.

Procedure: Participants were recruited from the outpatient department. After obtaining informed consent, demographic and clinical data were collected. Blood samples were collected in the morning after fasting and were analyzed for serum electrolyte levels (sodium, potassium, calcium, magnesium) using an automated biochemical analyzer.

Statistical Analysis: Data were input into Microsoft Excel and analyzed using SPSS version 21.0. For continuous variables, descriptive statistics, including mean, median, and standard deviation, were calculated. Frequencies and percentages were determined for categorical variables. To compare groups (Hydroxyurea therapy versus no therapy), a t-test was employed for analyzing continuous variables, whereas the chi-square test was utilized for categorical variables. Statistical significance was determined by a p-value of less than 0.05.

Results

The study evaluated the levels of serum electrolyte levels in 90 SCD patients, of which 45 were on Hydroxyurea therapy and 45 were not. Additionally, 30 healthy individuals were included as controls for comparative purposes.

Table 1: Biological Parameter Differences Between Sickle Cell Patients and Control Subjects

Parameter	Control (n=30)	SCD Patients (n=90)	p-value
Na (mmol/L)	140.5 ± 2.1	137.2 ± 3.5	<0.001
K (mmol/L)	4.1 ± 0.5	4.5 ± 0.7	0.003
Ca (mg/dL)	9.3 ± 0.4	8.7 ± 0.6	<0.001
Mg(mg/dL)	2.1 ± 0.3	1.7 ± 0.4	<0.001
Hemoglobin (g/dL)	13.5 ± 1.2	8.9 ± 1.5	<0.001

Table 2: Biological Marker Differences Between Hydroxyurea and Non-Hydroxyurea Patient Groups

Parameter	Non-Hydroxyurea (n=45)	Hydroxyurea (n=45)	p-value
Na (mmol/L)	137.0 ± 3.4	137.4 ± 3.6	0.567
K (mmol/L)	4.6 ± 0.6	4.4 ± 0.7	0.234
Ca (mg/dL)	8.6 ± 0.6	8.8 ± 0.6	0.210
Mg(mg/dL)	1.6 ± 0.4	1.8 ± 0.3	0.042
Hemoglobin (g/dL)	8.4 ± 1.6	9.4 ± 1.2	<0.001

The serum electrolyte levels of Sickle Cell Disease (SCD) patients were markedly different from those of healthy controls. Specifically, SCD patients had lower and calcium levels In contrast, their potassium levels were higher, and magnesium levels were lower. Additionally, hemoglobin levels were prominently reduced reduced in SCD patients compared to controls (.

When comparing SCD patients undergoing Hydroxyurea therapy to those not receiving the therapy, no significant differences were found in sodium (137.4 ± 3.6 mmol/L vs. 137.0 ± 3.4 mmol/L, p=0.567), potassium (4.4 ± 0.7 mmol/L vs. 4.6 ± 0.6 mmol/L, p=0.234), and calcium levels (8.8 ± 0.6 mg/dL vs. 8.6 ± 0.6 mg/dL, p=0.210). However, patients on Hydroxyurea therapy had significantly higher magnesium levels (1.8 ± 0.3 mg/dL vs. 1.6 ± 0.4 mg/dL, p=0.042) and hemoglobin levels (9.4 ± 1.2 g/dL vs. 8.4 ± 1.6 g/dL, p<0.001).

Discussion

The SCD significantly impacts serum electrolyte levels, with patients showing lower sodium and calcium but higher potassium and lower magnesium levels compared to healthy controls. Hydroxyurea therapy appears to improve magnesium levels and significantly increase hemoglobin levels in SCD patients, although it does not significantly alter sodium, potassium, or calcium levels. These findings suggest that while Hydroxyurea therapy helps in improving certain biological parameters, continuous monitoring of serum electrolytes is essential for the comprehensive management of SCD patients. A study aimed to evaluate the serum level of electrolyte in SCD patients as well as the effect of Hydroxyurea. It included 52 SCD patients and 20 healthy controls. The findings indicated important changes in serum electrolytes between SCD patients and healthy individuals, but no significant difference between patients on Hydroxyurea therapy and those not on it (1).Likewise a smilar research focused on evaluating serum electrolyte levels in SCD patients, comparing those on Hydroxyurea therapy with those who were not. It included patient number of 30 being SCD and 20 healthy controls. The study discovered prominent variations in certain biological parameters, but Hydroxyurea did not significantly alter electrolyte levels [2]. One prospective observational study included 70 children with SCD treated with Hydroxyurea. It documented an 81.4% decrease in clinical symptoms and significant reductions in hospital admissions and blood transfusions. The study concluded that Hydroxyurea therapy was related with favorable short-term and mid-term results in pediatric SCD patients [6].

Conclusion

The study demonstrated that Sickle Cell Disease (SCD) significantly impacts serum electrolyte levels, with patients showing lower sodium, calcium, and magnesium levels but higher potassium levels compared to healthy controls. Hydroxyurea therapy was associated with improved magnesium and hemoglobin levels in SCD patients, although it did not significantly alter sodium, potassium, or calcium levels. These findings suggest that while Hydroxyurea therapy provides certain hematological benefits, continuous monitoring of serum electrolytes is crucial for the effective management of SCD patients.

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