Study on Serum Electrolytes in Sickle Cell Disease Patients on Hydroxyurea Therapy and Non-Hydroxyurea Therapy

Metta Madhuri[1], P Manoj[2], D.M.M. Rajkumari[3], A. Gopa Raju[4]

ABSTRACT

Introduction: Sickle disease is one of the oldest genetic disorders of medical science. Sickle cell disease affects millions of people worldwide. The morbidity and mortality associated with the disease, complications and sickle cell crisis is a significant health issue. Hydroxyurea is an anticancer agent, which proved to be the wonder drug in lower doses in sickle cell disease. Objective: To evaluate the serum electrolytes level in sickle disease patients and find out the effect of hydroxyurea.

Material and methods: Thirty sickle cell disease patients and twenty normal individuals as controls are included in the study. 11 patients on hydroxyurea therapy and 19 are non-hydroxyurea therapy. The serum levels of sodium, potassium, chloride, calcium, magnesium and phosphate were estimated in all the study subjects.

Results: There is significant difference observed among Total Bilirubin, Urea, and Creatinine and chloride levels among Sickle disease patients compared with normal individuals. No much significant results were observed among patients on hydroxyurea therapy and non- hydroxy urea therapy except for Total bilirubin and Sodium levels.

Conclusion: Electrolytes plays crucial role in the path physiology of sickle cell disease, but hydroxyurea therapy does not seem to alter the electrolyte levels in patients.

Keywords: Sickle Cell Disease, Hydroxyurea, Electrolytes

INTRODUCTION

Sickling of red cells in sickle cell anaemia patients is caused due to polymerization of molecules of deoxygenated haemoglobin - S into rigid, rod-like polymers. Fetal haemoglobin lacks beta-globin chain which inhibits sickling in vitro by interfering with the polymerization of haemoglobin-S. Many Clinical trials are conducted till date, the observed results suggested that increased fetal haemoglobin concentrations may have desired benefits in sickle cell anaemia.[1] Cytotoxic agents have a positive effect by stimulating the fetal haemoglobin.[2-3] Among them, hydroxyurea proved to be effective for clinical trials,[4] as it is easy to administer and relatively safe. Beyond the cytotoxic effects of hydroxyurea, it also reduces bone marrow production of neutrophils, reticulocytes and platelets which is an important mediator of inflammation. Because increased WBC has been associated with morbidity and mortality of Sickle cell anaemia.[5,6] lowering the WBC count in sickle cell anaemia is potentially therapeutic. Hydroxyurea is good inhibitor of ribo-nucleotide reductase, which has positive effect by increasing fetal haemoglobin in red blood cells and decreases the episodes of pain events; thereby enhancing the use of hydroxyurea is a promising approach to improve health outcomes among sickle cell disease patients.[7] Hydroxyurea, is a prototype known to promote HbF production indirectly by perturbing the maturation of erythroid precursors, is administered orally daily once, without any adverse effects and is effective for patients with sickle cell disease.[8,9]

Electrolytes are substances that act as ions in solution and have the ability to conduct electricity in human body. Studies involving sickle cell patients showed that there is increased loss of body fluids and electrolytes leading to dehydration and metabolic errors. Hence proper electrolyte balance is required for the normal functioning of cells in the human body[5] Electrolyte imbalance leads to complications i.e. if any electrolytes values are higher or lower than the normal.[10] The present study was carried out to evaluate and determine the relationship between electrolytes values in Sickle cell anaemia patients and observe the effects of hydroxyurea on serum electrolytes that are going through hydroxyurea therapy and non-hydroxyurea therapy. The serum electrolytes focused in this study are sodium, potassium, chloride, magnesium, phosphate and calcium.

MATERIAL AND METHODS

This cross sectional observational study was conducted in Biochemistry Department, Andhra Medical College, in collaboration with super-speciality ward under medicine department of, Andhra Medical College, Andhra Pradesh state in between April 2019 to September 2019. The study include three groups, one group on hydroxyurea therapy and other group which never had exposure to hydroxyurea therapy, third group with healthy controls. The study patients are selected randomly. Detailed information regarding the patients is taken by administering a semi-structured

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questionnaire and examination of the patients and the blood sample is taken after taking verbal and written consent from the patients.

Ethical Committee

Proposal of the study was kept before Andhra Medical College ethics committee for which approval was given after review and the study was conducted later from 1st April 2019.

Inclusion Criteria

Samples collected from patients attending the super speciality ward under General Medicine department of Andhra medical college, who are diagnosed as sickle cell anaemia.

Exclusion Criteria

Patients with any other hemoglobinopathy, those who did not give consent and patients not willing to participate in the study, any recent blood transfusions

Sample Collection

Five ml of blood was collected, sample kept under room temperature for half an hour time. From the clotted blood sample, serum was separated by centrifuge and that collected serum was taken for electrolyte analysis.

STATISTICAL ANALYSIS

The values are expressed as mean +/- standard deviation and t-test was used wherever necessary for calculating the significant differences at $p < 0.05$

RESULTS

50 individuals are selected randomly for the study. Mean age of SCD patients was 16.21+/-9.80 and healthy controls was 23.05+/-5.18.Out of which thirty sickle cell disease patients

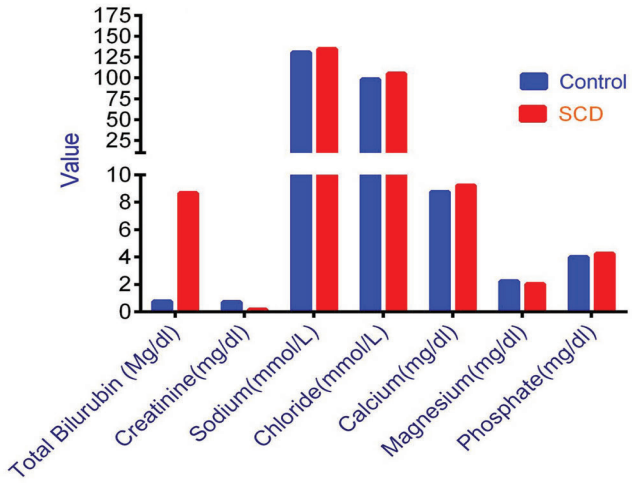

Figure-1: Comparasion of study parameters which are significant

Variables	Sickle Cell Patients (n= 30)	Control (n = 20)	p-Value
Age	16.21 ± 9.80	23.05 ± 5.18	0.001
Sex (M :F)	14:16	7:13	0.03
Total Bilirubin (Mg/dl)	8.68 ± 2.94	0.76 ± 0.57	<0.001
Direct Bilirubin (Mg/dl)	1.35 ± 1.78	0.18 ± 0.094	0.0006
AST(IU/L)	23.91 ± 31.41	15.74 ± 4.62	0.17
ALT(IU/L)	33.11 ± 24.53	19.25 ± 10.94	0.009
Urea (mg/dl)	13.84 ± 6.67	24.24 ± 5.46	<0.001
Creatinine(mg/dl)	0.17 ± 0.028	0.71 ± 0.012	<0.001
Sodium(mmol/L)	134.64 ± 3.93	130.61 ± 3.59	0.005
Potassium (mmol/L)	3.99 ± 0.95	3.80 ± 0.32	0.31
Chloride(mmol/L)	105.09 ± 3.97	98.32 ± 3.23	<0.001
Calcium(mg/dl)	9.22 ± 0.61	8.75 ± 0.69	0.009
Magnesium(mg/dl)	2.04 ± 0.32	2.24 ± 0.11	0.003
Phosphate(mg/dl)	4.25 ± 0.40	3.99 ± 0.29	0.03

Table-1: Comparison of study variables between sickle cell patients and Control

Variables	Hydroxyurea (n= 11)	Without Hydorxyurea (n = 19)	p-Value
Age	21.35 ± 12.73	13.81 ± 7.81	0.04
Sex (M :F)	5:06	8:11	
Total Bilirubin (Mg/dl)	2.35 ± 0.81	1.66 ± 1.11	<0.001
Direct Bilirubin (Mg/dl)	1.03 ± 0.36	1.46 ± 0.65	0.01
AST(IU/L)	43.33 ± 15.98	16.64 ± 5.85	0.0001
ALT(IU/L)	22.11 ± 22.35	24.88 ± 9.71	0.7
Urea (mg/dl)	15.33 ± 6.27	12.99 ± 4.02	0.28
Creatinine(mg/dl)	0.45 ± 0.25	0.52 ± 0.18	0.45
Sodium(mmol/L)	133.17 ± 6.73	138.21 ± 3.57	<0.001
Potassium (mmol/L)	4.04 ± 1.05	4.21 ± 0.46	0.63
Chloride(mmol/L)	105.63 ± 2.12	106.56 ± 4.87	0.47
Calcium(mg/dl)	9.31 ± 0.55	9.66 ± 0.69	0.13
Magnesium(mg/dl)	2.02 ± 0.16	2.24 ± 0.44	0.06
Phosphate(mg/dl)	4.46 ± 0.48	4.38 ± 0.26	0.61

Table-2: Comparison of study variables between hydroxyurea and non-hydroxyurea

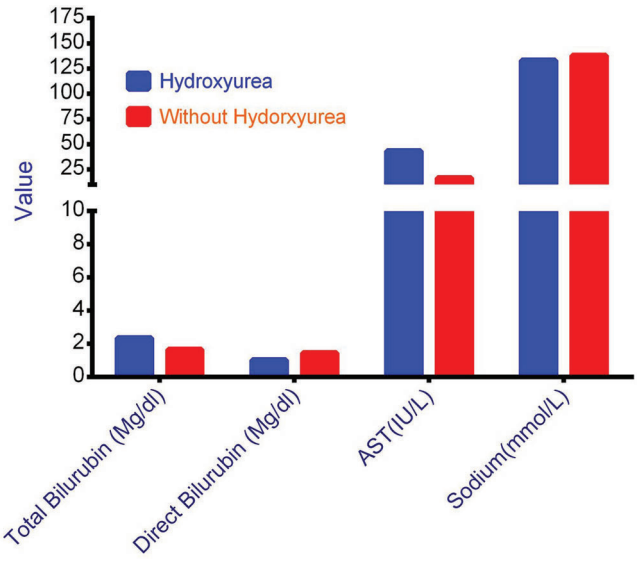

Figure-2: Comparasion of study parameters which are significant

and twenty healthy individuals as controls are included in the study. 11 patients on hydroxyurea therapy and 19 are non-hydroxyurea therapy.

The serum electrolyte levels are significantly high in sickle cell anaemia patients than the values of the normal individuals, significant difference observed among Total Bilirubin, Urea, and Creatinine and chloride levels among Sickle disease patients compared with normal individuals. (Table 1)

No much significant results were observed among patients on hydroxyurea therapy and non- hydroxy urea therapy except for Total bilirubin and Sodium levels. (Table 2)

DISCUSSION

In this study, the serum chloride levels were found to be significantly higher in the sickle cell disease patients; this was in contrast with the findings of Agoreyo etal.[10] Serum AST and ALT levels are grossly elevated which are not statistically significant (p = 0.17 and 0.09) when compared with the controls. From results of the present study, calcium was found higher in the serum of sickle cell patients as compared to control but not statistically significant (p = 0.009).The previous finding supported this in which increased levels of calcium in sickle patients were found when compared to control by Ataga K etal.[11] The magnesium levels were found to be lower in the sickle cell patients than the controls but the difference was not significant (p = 0.03). Some findings supported the study, in which magnesium levels were found in decreased concentration in sickle cell patients, Nnodim JK et al.[12] From the study, phosphate levels were found significantly higher in sickle cell patients compared to control (p < 0.03),the same was also reported by Oladipo et al.[13] Serum potassium levels are also elevated when compared with the controls that is 3.99 +/- 0.95 whereas in control group was 3.80+/- 0.32 which was statistically not significant and similar observation was made by Clark et al[14], who put forward that dehydration and deoxygenation caused excessive potassium losses, resulting in cation depletion. This later gets accumulated in the extracellular environment giving abnormally elevated values in sickle patients. The magnesium levels were found to be lower in the sickle cell patients than the controls but the difference was not significant ($p = 0.003$). Some findings supported the study, in which magnesium levels were found in decreased concentration in sickle cell patients.[12] Digban also reported that the levels of magnesium were found in decreased values in sickle cell patients.[15]

Limitations

The sample size of the study was small, hence cannot be projected on whole population.2. Follow up cases can give better insights into the serum electrolytes values and other variables in this study.

CONCLUSION

Serum electrolytes play a vital role in the patho - physiology of sickle cell disease and their complications. Dehydration induces sickling. From the current study, it was evident that the serum levels of most of the electrolytes vary significantly between sickle cell disease patients and controls but among the sickle cell patients with hydroxyurea and without hydroxyurea here is no statistical significance found.

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