Clinical Profile of Patients of Sickle Cell Disease on Zinc Therapy

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ABSTRACT

BACKGROUND

Sickle cell disease is an inherited multisystem disorder, characterized by chronic hemolytic anemia and recurrent painful episodes which relates to presence of mutant sickle hemoglobin within red blood cells. Studies regarding zinc level estimation in sickle cell disease are in plenty. However, studies regarding zinc therapy in sickle cell disease are very few. In this study we compare the clinical presentation of patients of sickle cell disease on zinc therapy with those who were not on zinc therapy.

AIM

To study clinical profile of patients of sickle cell disease, who were on zinc therapy with respect to anemia, crisis, infections and hospital admissions and compare them with control i.e. patients of sickle cell disease who were not on zinc therapy.

MATERIAL AND METHODS

Total sample size computed for this study was 100(50 cases and 50 controls).Cases were patients of sickle cell disease(SS pattern) who were taking zinc regularly (50 mg elemental zinc OD) for 6 or more than 6 months and controls were patients who were not taking zinc.20 normal healthy persons were included to estimate zinc level in normal persons.

All patients were followed every monthly for 6 months in sickle cell clinic as well as whenever they were admitted in medicine wards. Data was analyzed by using Chi-square statistics and ANOVA on Statistical Software STATA Version 8.0.

RESULT

After a follow up of 6 months average no. of crisis/patient in control was 2.46±0.64 and in cases was 1.18±0.59 (p=0.0000).Average no. of infection/patient in control was 1.54±0.58 while that in cases 0.68±0.51 (p=0.0000). Average no. of admission/patient in control was 2.52±0.65 while that in cases 1.22±0.62 (p=0.0000).

CONCLUSION

There was significant reduction in no. of crisis, no. of infection and no. of hospital admission in patient of sickle cell disease who were on zinc therapy as compared to those who were not on zinc therapy.

Keywords

Clinical Profile, Sickle Cell Disease, Zinc Therapy

INTRODUCTION

Sickle cell disease is an inherited multisystem disorder, characterized by chronic hemolytic anemia and recurrent painful episodes which relates to presence of mutant sickle hemoglobin within red blood cells[1]. The management of this disease has been essentially symptomatic and largely unsatisfactory. Search of ideal anti sickling agent is still on[2]. Use of zinc as antisickling agent has sound laboratory support. In laboratory studies, it has been shown that zinc increases the filterability of partially deoxygenated sickle cell in vitro.[3] It also has a membrane stabilizing effect and antagonizes calcium binding of haemoglobin "s"[4, 5, 6]. Zinc also reduced irreversible sickle cell (ISC) count within as low as 14 days of therapy.[7]

Serum zinc level and electro kinetic potential are

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significantly low in sickle cell anemia. The diminution of the EKP of erythrocyte in sickle cell disease may cause reduction of repulsive forces on the surface of these erythrocytes so that thrombotic crises are facilitated by agglomeration of RBCs.[8] Beneficial effect of zinc is also seen in cell mediated immunity. Zinc supplementation decreased the incidence of infection in patients with sickle cell disease[9].

Studies regarding zinc level estimation in sickle cell disease are in plenty[10-20]. However, studies regarding effect of zinc therapy in sickle cell disease are very few21-24. Hence, we were stimulated to carry out this study to compare the clinical presentation of patients of sickle cell disease on zinc therapy with those without zinc therapy.

MATERIAL & METHOD

This cohort study was conducted at tertiary care hospital (Govt. Medical college and Hospital, Nagpur) from June 2006-November 2007.Total sample computed for this study was 100(50 cases and 50 controls) with following inclusion and exclusion criteria.

A) Inclusion criteria

- **Cases:** Adult patient of sickle cell disease (SS pattern) who were on zinc therapy (elemental zinc 50 mg OD) for minimum 6 month of more.

- **Control:** Patients of sickle cell disease (SS pattern) who were not on zinc therapy.

B) Exclusion criteria

Pediatric age group, Chronic infections like TB, AIDS etc., Organ failure patients, Patients with diabetes, cirrhosis of liver, alcoholic liver disease, inflammatory bowel disease, malabsorption syndrome and leprosy, Patients on hydroxyurea, Females with pregnancy, Patients who were irregularly taking zinc.

The approval of ethical committee Govt. Medical College and hospital, Nagpur was obtained. A written informed consent was obtained from every patient in prescribed proforma. All cases and controls were subjected to detailed history and thorough clinical examination. Zinc levels were estimated in 20 normal persons and also in cases and controls by using kit method. Details of zinc therapy regarding type of zinc preparation, doses and duration was noted. Patients were followed every monthly for 6 months in sickle cell clinic as well as whenever they were admitted in medicine wards for biochemical parameter, no. of infections(documented and clinical), no. of crisis and no. of admissions. Clinical infections were those where cultures were negative but showed clinical evidence of infection such as upper respiratory tract infections, bronchitis etc. while Documented infections were those where infections were confirmed with positive bacteriological cultures Emphasis was given that in cases they were taking zinc regularly in adequate doses and strict vigilance was kept on them regarding zinc therapy during follow up.

Data was analyzed by using Chi-square statistics and ANOVA on Statistical Software STATA Version 8.0.

RESULTS

The age range in control and cases was 13 – 34 years with mean age 21.4 ± 5.79 years and 13 – 32 years with mean age 21.26 ± 5.38 years respectively. Maximum cases and controls were in the age group of 15 – 19 years. Out of 50 control studied, 30(60%) were males and 20 (40%) were females. The male: female ratio was 1.5: 1. Out of 50 cases studied, 24 (48%) were males and 26 (52%) were females. The male: female ratio was 1.2: 1.3.Out of 50 controls, 46 (92%) patients belongs to Mahar and Nav Buddha and 4 (8%) belongs to other communities which include Kunbis, Telis, Muslims and others. Out of 50 cases, 42 (84%) patients belongs to Mahar and Nav Buddha and 8 (16%) belongs to other communities**. (Table 1)**

Range of normal serum zinc level as per kit was 70-150 µg/dl with mean of 110 µg/dl. In our study range of serum zinc level in normal healthy person was 105-126 µg/dl with mean of 115.5±10.5 µg/dl. In control group (zinc deficient) the mean serum zinc level was 80.05 ± 10.90 µg/dl. In cases (patients who were on zinc therapy) the mean serum zinc level was 137.6 ±15.08 µg/dl. This difference was found to be highly significant. (P = 0.0000)**.(Table 2)**

Mean hemoglobin level in controls (patients who were zinc deficient) was 5.95 ± 0.57 µg/dl while in cases (patients who were regularly on zinc therapy) the hemoglobin level was found to be 7.30 ± 1.22 µg/dl. This difference was found to be highly significant (P = 0.0000). Mean serum bilirubin in controls was 2.57 ± 0.85 mg/dl. The mean serum bilirubin level in cases was 1.99 ± 0.77 mg/dl. The difference was found to be significant. (P = 0.0005)The mean unconjugated bilirubin in controls was 1.82 ± 0.57 mg/dl while in

cases it was 1.39 ± 0.55 mg/dl. This difference was found to be statistically significant (P = 0.0002) **(Table 3).**

Total no. of crisis during follow up period of 6 month in controls was 123 while that in cases it was 59. This difference was found to be highly significant. (P = 0.0000)In controls, out of total 123 crisis, 83 (67.47%) were vasoocclusive, 27 (21.95%) were mixed, 13 (10.56%) were hemolytic whereas sequestration and aplastic crisis were not noted during follow up. In cases, out of total 59 crisis, 45 (76.27%) were vasoocclusive, 10 (16.94%) were mixed, 4 (6.77%) were hemolytic whereas sequestration and aplastic crisis were not noted in cases also during follow up. The mean no. of crisis per patient in control was 2.46 ± 0.64 whereas in cases 1.18 ± 0.59. This difference was found to be highly significant. (P = 0.0000)**(Table 4)**

In controls, out of 77 total number of infections, clinical infections were 63 (82%) with average no. of clinical infection per patient was 1.26 ± 0.69. In cases out of 34 total number of infections, clinical infections were 29 (85%) with average number of clinical infection per patient was 0.58±0.49. This difference was found to be statistically significant. (P = 0.0000) In controls, out of 77 total number of infections, 14 (18%) were documented (i.e. infections that were culture positive) with average number of documented infection per patient was 0.28 ± 0.45. In cases out of 34 total number of infections, 5 were documented infections with average number of documented infection per patient was 0.1 ± 0.38. This difference was also found to be statistically significant. (P = 0.0217**) (Table 5).**

Total no. of admission in controls were 126 while that in cases they were 61. This difference was found to be highly significant. (P = 0.0000)The mean no. of admission per patient in controls was 2.52 ± 0.65 while that in cases it was 1.22 ± 0.62. This difference was highly significant. (P = 0.0000**) (Table 6)**

To sum up, average no. Of crisis/patient in control was 2.46 ± 0.64 whereas in cases 1.18 ± 0.59. Average no. of infection/patient in control was 1.54±0.58 while that in cases 0.68±0.51. In controls average no. of admission per patient was 2.52 ± 0.65 while that in cases it was 1.22 ± 0.62. This difference was found to be significant. (P = 0.0000**) (Table 7)**

DISCUSSION

Thus, it has been observed that, patients who were zinc deficient (mean serum zinc level 80.05 ± 10.90 µg/dl) were more anemic, have more number of crisis, more number of infections and more number of admissions as compared to cases i.e. patients who were regularly taking zinc in adequate doses(mean serum zinc level 137.6 ± 15.08 µg/dl) and this was statistically significant.

It was found that zinc therapy definitely helps patients of sickle cell disease in reducing severity of hemolysis, thereby decreasing their hemolytic crisis and indirectly anemia by its anti sickling action. By treating anemia, hypoxia is reduced, thereby reducing vasoocclusive crisis. Hence their frequent admissions due to anemia and vasoocclusive crisis are decreased by zinc therapy.

Similarly zinc therapy also helps these patients of sickle cell disease in reducing number of infection and number of admission to hospital, as zinc increases their cellular immunity, but this requires detailed study of their immunological status of large number of patients of sickle cell disease.

Elemental zinc 50 mg daily increases the level of zinc in zinc deficient patient of sickle cell disease within a period of as low as 14 days to 4 months7,11. The anti sickling action of zinc start with 14 day therapy has been proved experimentally in sickle cell disease patients7. However whether zinc should be continued lifelong or exact duration of zinc therapy cannot be commented.

Sergeant GR (1970)21 studied 34 patient of sickle cell anemia with leg ulcers. Zinc was supplied in a form of zinc sulphate in a dose of 220 mg three times daily. . Apparent healing of leg ulcer on oral zinc sulphate raises the possibility that zinc deficient state contribute to etiology.

Chaubey BS and Gupta VL (1987)11 studied 30 patients of sickle cell disease who were put on zinc therapy and were followed up for a period of one and half year. In pretherapy follow up, total number of crisis was 128, mean duration of hospital stay and loss of working days/crisis was 3.9 and 4.9 respectively. In the post therapy follow up, total number of crisis was 59, duration of hospital stay was 4.3 days, the loss of working days was 3.4 days/crisis.

Chaubey BS and Gupta VL (1995)22 studied 130 patients who were randomized to receive zinc sulphate

capsule in control and intervention groups. After a follow up 1.5 years. In control group, total number of crisis was 344, total number of infection was 204.In intervention group, total number of crisis was 160, total number of infection was 108.[2]

Ananda S Prasad et al (1999)26 studied 11 patients of sickle cell disease which were followed for one year (baseline), the number of hospital admission at this base period was 7.18 ± 3.4 following they received zinc for 3 years at the end of 3 years the number of hospital admission was reduced to 3.36 ± 3.0.

Thus, Zinc therapy may prove boon to these patients of sickle cell disease and reduce their agony of painful crisis and frequent admissions to hospital.

IMPLICATION OF STUDY

This study has definitely proved beneficial effect of zinc therapy in patient of sickle cell disease. It not only improved the anemia in this patient but also reduces their frequent admissions by reducing rate of vaso-occlusive crisis and various infections in them.

Limitation of study

Out study is only of 6 months follow up. This requires large multicentric trial of zinc therapy in large number of sickle cell disease patients.

Table 1: Baseline characteristic of patient groups

AGE	**Control Group (N=50)**	
Range	13 – 34	13 – 32
Mean	21.4 ± 5.79	21.26 ± 5.38
SEX		
Males	30 (60%)	24 (48%)
Females	20 (40%)	26 (52%)
CAST DISTRIBUTION		
Nav Buddha & Mahar	46 (92%)	42 (84%)
Others	4 (8%)	8 (16%)

Table 2: Serum zinc level in control and cases

Groups	**No. of cases**	**Range (µg/dl)**	**Mean ± SD (µg/dl)**	**P value**
Normal healthy person	20	105-126	115.5 ± 10.5	0.0000
Controls (patients without zinc therapy)	50	59.8-100.1	80.05 ± 10.90	
Cases (patients on zinc therapy)	50	106.32-170.1	137.6 ± 15.08	

Table 3: Lab parameter in controls and cases

	Lab parameter	**Controls (n = 50)**	**Cases (n = 50)**	**P value**
a)	Hb% (gm/dl)	5.95 ± 0.57	7.30 ± 1.22	0.0000
b)	Serum Bilirubin (mg/dl)	2.57 ± 0.85	1.99 ± 0.77	0.005
i)	Direct	0.76 ± 0.3	1 0.61 ± 0.25	0.0075
ii)	Indirect	1.82 ± 0.57	1.39 ± 0.55	0.0002

Table 4: Distribution of type and No. of crisis in control and cases during follow up				
	Type of Crisis	**No. of Crisis (Control)**	**No. of Crisis (Cases)**	**P value**
	Vasoocclusive	83 (67.47%)	45 (76.27%)	
	Mixed	27 (21.95%)	10 (16.94%)	
	Hemolytic	13 (10.56%)	4 (6.77%)	
	Sequestration	0 (0%)	0 (0%)	
	Aplastic	0 (0%)	0 (0%)	
	Total	**123 (100%)**	**59 (100%)**	**0.0000**
	No. of Crisis/Patient	**2.46 ± 0.64**	**1.18 ± 0.59**	**0.0000**

Table 5: No. of clinical and documented (positive bacteriological culture) infection in control and cases.			
	No. of Infection (Control)	**No. of Infection (Cases)**	**P value**
Clinical	63 (82%)	29 (85%)	
No. of clinical infection/patient	1.26 ± 0.69	0.58 ± 0.49	0.0000
Documented (Bacteriologically culture positive)	14 (18%)	5 (15%)	
No. of documented infection/patient	0.28 ± 0.45	0.1 ± 0.38	0.0217
Total	**77 (100%)**	**34 (100%)**	

Table 6: No. of hospital admissions in controls and cases during follow up			
	No. of admission (Controls)	**No. of admission (Cases)**	**P value**
Total	126	61	0.0000
No. of admission/patient	2.52 ± 0.65	1.22 ± 0.62	0.0000

Table 7: Correlation of serum zinc level and clinical parameters in controls and cases			
Parameters	**Controls**	**Cases**	**P value**
Mean serum zinc	80.05±10.90	137.6 ± 15.08	0.0000
Average no. of crisis/patient	2.46 ± 0.64	1.18 ± 0.59	0.0000
Average no. of infection/patient	1.54 ± 0.58	0.68 ± 0.51	0.000
Average no. of admission/patient	2.52 ± 0.65	1.22 ± 0.62	0.0000

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