Sickle Cell; Gestational Chronic High ESR[1'2] caused by Entamoeba Histolytica[3] (Protozoa) Leads to Point Mutation in β-Globin

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ABSTRACT

Sickle cell anemia is not a hereditary hemoglobinopathy1-[4], point mutation in β- globin that promotes the polymerization of deoxygenated hemoglobin leading to RBC distortion and ischemic tissue damage is caused by chronic high ESR "GESTATIONALLY" because of chronic infection of Entamoeba histolytica "transmitted CONGENITALLY[5]" from GI tract to bone marrow.

Treating Entamoeba histolytica leads to reduction of chronic high ESR, consequently improvement in sign and symptom of sickle cell.

Keywords: Sickle Cell, Chronic ESR, β-Globin, Entamoeba Histolytica, iv Metronidazole/Tindazole, HbS

DESCRIPTION

Sickle cell anemia is a disordered disease[6] based on the phenomena of "defect due to effect" concept i.e. chronic high ESR caused by Entamoeba histolytica leads to point mutation in β-globin, affects millions of children throughout the world in terms of heterozygosity and homozygosity.

Babies being born with sickle cell disease are facing sick-like feeling for whole life, dactylitis, whole body pain, all of sudden acute pain in chest and back makes the life miserable. Statics and data interprets that it is growing by the rate of more than 40% in last twenty years.

Researches on sickle cell are based on post happening of disease, while analyzing, apparently it looks like herediatery hemoglobinopathy caused by point mutation in β- globin but specificity in point mutation in beta- globin is also not clear because it is seen several hundred different hemoglobinopathies[7] caused by mutation in globin genes are known.

Till date currently such biomarkers which can directly measure HbS polymerization in RBC do not exist as per medical record, it is also not clear whether any direct relation exist between SCD phenotypes diversity and different rates of HbS polymerization[8].

It is quoted in the text that 8% to 10% African Americans are heterozygous for HbS , a largely asymptomatic condition known as sickle cell trait, reason for this heterozygousity is unfolded.

Population studies in various researches have shown that sickle cell hemoglobin mutations has arisen independently at least six times in area in which falciparum malaria is endemic[9], correlating sickle cell anemia with falciparum malaria and further it is quoted that it provides clear evidence of strong Darwinian selection of HbS which is unacceptable because till date sickle cell is a strikingly variable condition varies markedly both with time in same individual and between different individuals, variability and unpredictability is seen with most other serious complications that leads to premature death. Contrary to Darwin theory percentage of sickle cell trait transmission i.e. heterozygosity/homozygosity is described in various studies concluded as hereditary disease but surely of transmission is unpredictable[10].

It is seen in retrospective cohort study, area in which falciparum malaria is endemic is also seriously endemic with Entamoeba histolytica infection[11], Insufficient data gives ≥ 50% of population of African American in infected by Entamoeba histolytica but also more than 8% of population is seropositive[12] , it is clearly seen in poor socioeconomic condition countries /communities, this types of population is simulataneously suffering from chronic high ESR[13] caused by chronic infection of Entamoeba histolytica that gives manifestation of sickle cell traits in and their parents.

It is also seen that every patient of sickle cell is suffering from Entamoeba histolytica associated with chronic high ESR simultaneously mild, moderate and severe rise of CRP[14], which is worth pondering.

Entamoeba histolytica is transmtted gestationally[15] (from mother to new born baby during gestation) and sexually[16] from husband to wife and vice versa, since mother is already infected and suffering from chronic infection of Entamoeba histolytica, severity and intensity of chronic infection of new born baby leads to point mutation in β-globin as a result apparently look herediatry disease and value of chronic ESR at the time of birth of baby leads to heterozygous or homozygous sickle cell. Depending upon the value of chronic ESR of sickle celled parent, it is categorized as minor or major, higher the value of chronic ESR greater is the probability of β-globin mutation for sickle cell.

We can easily have better prognosis method of heterozygous and homozygous sickle cell on the basis of value of chronic

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ESR caused by Entamoeba histolytica :-

Mild chronic infection	→Chronic ESR 6mm-10mm/hr	→hemoglobin 11-12gm	→normal
Moderate chronic infection	→ chronic ESR 15-18mm/hr	→hemoglobin 9-10gm	→ heterozygous SC
Severe chronic infection	→1-chronic ESR 25-55 mm/hr	→hemoglobin 5-8gm	→ homozygous SC
2-chronic ESR ≥60 mm/hr	→ hemoglobin 4-6gm	→HbSα- thalassemia or	→HbSβ-thalassemia

More than 95% of pathologies give false report in diagnosing Entamoeba histolytica in stool examination, beside this cross checking of ESR is also very important for better prognosis of disordered disease (hemoglobinopathy)

Treating Entamoeba histolytica with IV metronidazole/ tinidazole /orniazole ± quinolone leads to reduction of chronic ESR gives improvement of sign and symptoms of sickle cell.

"Duration of treatment is monitored with the reduction of chronic ESR".

CONCLUSION

Sickle cell anemia is chronic inflammatory[17] infectious disordered disease[18] caused by chronic high ESR because of Entamoeba histolytica, treating Entamoeba histolytica with IV metronidazole/tinidazole/orniazole ± quinolone leads to improvement of sign and symptoms of sickle cell.

Mode of action of Sickle cell

Gestational transfer of Entamoeba Histolytica (protozoa)

(From mother to new born baby congenitally)

↓

Infection of Entamoeba histolytica from G I Tract to bone marrow[19]

↓ release of inflammatory mediators

↓ I L-1α,IL-1β,IL-6,I L-8, TNF-α Chronic rise of ESR

↓

Chronic inflammation of whole body including bone marrow

↓

1-reduction of Erythropoiesis due to diminish production of RBC precursor

2-Chronic high ESR causes point mutation in β-globin

↓

Depletion in β-globin chain synthesis

↓

Ineffective erythropoiesis

↓

Sickle cell disease

Treatment of Sickle cell anemia (Disordered disease) (MOA)

Entamoeba histolytica infection (from GI tract to Bone marrow)

Treatment ↓→Metronidazole /Tinidazole + Diloxinate furate ±quinolone

↓

Reduction of inflammatory mediators

↓

Reduction of chronic ESR

↓

Reduction of inflammation of bone marrow (Red cell precursors)

↓

Effective erythropoiesis

Note- Intravenous therapy is more effective in reducing chronic ESR compare to orals – for deep seated infection in "bone marrow"

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