International Journal of Research in Medical Sciences
Gosai DK et al. Int J Res Med Sci. 2014 May;2(2):695-698
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: 10.5455/2320-6012.ijrms20140561

Research Article

Study of ocular manifestations in children of thalassemia

Dhara K. Gosai[1]*, K. M. Mehariya[2], Jigarkumar B. Gosai[3]

[1]Assistant Professor, Department of Pediatrics, B J Medical College, Ahmedabad, Gujarat, India
[2]Professor & Head, Department of Pediatrics, B J Medical College, Ahmedabad, Gujarat, India
[3]Assistant Professor, Department of Emergency Medicine, B J Medical College, Ahmedabad, Gujarat, India

Received: 12 March 2014
Accepted: 25 March 2014

***Correspondence:**
Dr. Dhara K. Gosai,
E-mail: drdharagosai@yahoo.co.in

ABSTRACT

Background: Purpose of current study was to study the ocular manifestations in beta-thalassemia major patients and assess the ocular side-effects of iron chelating agents.
Methods: Cross sectional study included 45 β Thalassemia major patients from age group of 6months to 12 years were taken. Full medical history, thorough physical examinations were done to all patients groups, and ophthalmological examination to determine the prevalence of ocular manifestations for all patient groups and to correlate these manifestations or changes with iron chelating agents.
Results: In 45 patients (22 males and 23 females) with age ranging between 2 years to 12 years, ocular involvement is seen in 35% in the form of decreased visual acuity 26%, tortuous blood vessels in 4.5%, disc hyperemia in 4.5%, heterochromia in 2.5%, retinal pigment epithelium mottling in2.5% and this involvement were more with older age group.
Conclusion: Most of the ocular changes of beta thalassemia are attributed to the course and severity of the disease. Reduction in serum iron and serum Ferritin levels by iron- chelating agents and regular ocular examination to look for side-effects of such agents can aid in preventing or delaying ocular complications.

Keywords: Thalassemia, Ocular manifestation

INTRODUCTION

Thalassemias are the most common single gene disorder worldwide.[1] The incidence of thalassemia is very high, It is estimated that there are 35 million carrier of Thalassemia i.e. 1 in 25. Around 10 - 15,000 babies with haemoglobinopathies are born in India every year. Blood transfusions therapy on continuing bases represent the primary treatment for β Thalassemia. Repeated blood transfusion leads to massive tissue deposition of iron &subsequently on long term basis causes multi organ dysfunction as a complication of it.[2]

Mechanism of ocular manifestation in thalassemia is multifactorial. Thalassemia patients are taking regular blood transfusion therapy which causes iron overload. Iron chelating agents chelate other metals such as copper, zinc, nickel and cobalt essential for normal retinal function causing several ocular abnormalities. Deficiency of micronutrients like zinc, vitamins like vitamin B12 can also lead to ocular manifestations. Ocular effects in patients of thalassemia commonly seen are: visual acuity changes, cataract, pigmentary retinopathy, optic neuropathy, thinning and tortuosity retinal vessels, & vitreoretinal haemorrhages.[3,4]

METHODS

This study was conducted in the thalassemia clinic, department of pediatrics, civil hospital, Ahmedabad for duration of 1 month. This study was cross sectional study of forty five children, diagnosed as β thalassemia major patients were visited thalassemia clinic for transfusion

therapy in the month of October. The study was aimed at finding ocular manifestations in thalassemia patients with special reference to age, duration of disease, serum ferritin & to study the ocular manifestations in relation to dose and duration of deferasirox.

All children enrolled have been receiving treatment in the form of packed red cell transfusion at a dose of 10 ml/kg body weight transfusion in order to maintain their hemoglobin concentration between 9-11 gm/dl. Iron chelating agents were started if the serum Ferritin level was above 1000 µg/dl. An informed consent for participation was obtained from parents or legal guardians. Patients with any congenital ocular abnormalities were excluded.

Data was collected in form of detailed medical history, Iron chelating agents: dose, duration and compliance, Serum Ferritin level. (Average of last 4 readings) & examination in form of thorough physical examination & Ophthalmological examination by an ophthalmologist included: Near and distance visual acuity assessment, external examination with diffuse illumination, slit-lamp examination, direct and indirect ophthalmoscopy & fundus fluorescent examination was done in selected patients.

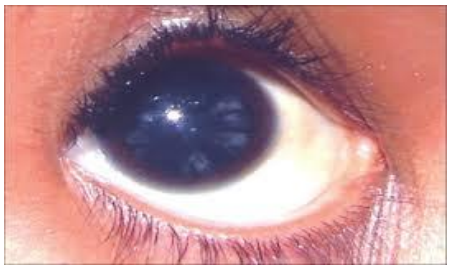

Figure 1: Lenticular opacity.

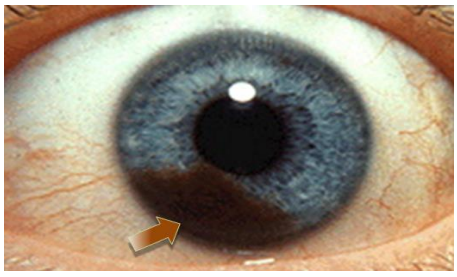

Figure 2: Iris pigmentary changes.

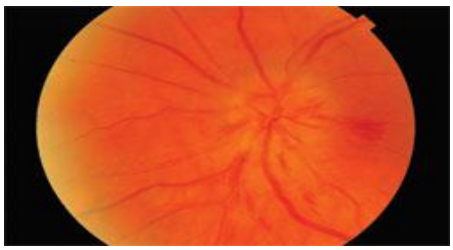

Figure 3: Disc hyperemia.

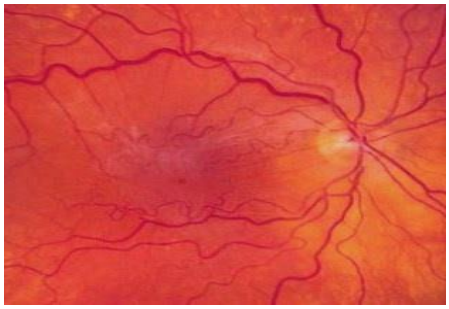

Figure 4: Retinal tortuosity.

RESULTS

In our study ocular involvement was seen in 35.5% of patients of thalassemia, out of which 26% were having decreased visual acuity 26%, disc hyperemia 4.5%, tortuous retinal blood vessels 4.5%, retinal pigment mottling 2.5%, heterochromia 2.5%. Out of all patients, ocular manifestations present in 7 out of 15 males patients & 9 out of 14 patients with P value of 0.84, which was statistically not significant.

Table 1: Manifestations based on age.

Age	No. of subjects (n=45)	Ocular involvement
Less than 4 years	9	2 (22.2%)
5-8 years	22	6 (27.3%)
9-12 years	14	8 (57.1%)

Age-wise distribution of patients with ocular manifestation was: 22.2% of <4 years, 27.3% of between 5-8 years & 57.1% of 9-12 years. Thus incidence of ocular toxicity increases as age increases.

Table 2: Relation to serum ferritin.

Serum ferritin	No. of subjects (n=45)	Ocular involvement
Less than 1000	6	0 (0%)
1000-2999	18	6 (33.3%)
3000-4999	16	7 (43.75%)
5000 or more	5	3 (60%)

Incidence of ocular involvement is seen in patients with S. ferritin levels >5000, which is 60%,while in group with S Ferritin level 3000-4999 it was 43.75% & 33.3 % in <3000. Ocular involvement was seen in 9 out of 12 in patients who have received chelation therapy for less than 5 years while in 7 out of 11 patients who received for more than 5 years with P value of 0.9, which is statistically not significant. So prolonged iron chelation therapy is not having direct causative effects on ocular involvement.

Table 3: Effect of dose of deferasirox.

Dose of deferasirox	No. of subjects (n=39)	Ocular involvement (41%)
<20mg/kg/day	10	4 (9.7%)
20-30mg/kg/day	13	5 (12.8%)
>30mg/kg/day	16	7 (17.9%)

Incidence of ocular involvement was 17.9% in patients on deferasirox >30 mg/kg/day which correlate with high ferritin level in patients as compare to 12.8% in patients receiving @20-30 mg/kg/day.

DISCUSSION

Thalassemias are the most common single gene disorder worldwide. Mutations involving the beta globin gene in beta-thalassemia cause disruption in red blood cell maturation leading to ineffective erythropoiesis and multi-system involvement. Multiple/repeated blood transfusions lead to siderosis. Adverse ocular changes may occur as a result of the disease itself or as side-effects of iron chelators and include cataract, optic neuropathy, retinal pigment epithelial (RPE) degeneration, RPE mottling, retinal venous tortuosity, vitreoretinal hemorrhages and obliteration of iris pattern.

Desferrioxamine and deferriprone, which are used to avoid systemic complications of siderosis cause chelation of metals such as iron, copper, zinc, cobalt and nickel in the retina. These metals are essential for normal retinal function.[3,4] The aim of the study was to know the ocular manifestations in multiple transfused beta-thalassemia major patients and assess the ocular side-effects of iron-chelating agents.

There are very few studies which consider the ocular side effects of thalassemia. Frequency of ocular involvement in our study was 35.5%, Gartagantis et al.[5] reported figures of 41.3%, Gaba A et al.[6] reported ocular involvement in 71.4% while Taneja et al.[7] reported figures of 58% of subjects in their respective studies. Visual acuity was affected in 26% patients while in Gaba et al.[6] study, the figure was and Taneja et al.[7] study, this figure was 67%.

In our study, increased serum ferritin is associated with increased ocular anomalies which are consistent with other studies. Duration of deferasirox has no direct relation with thalassemia. We found a larger number of thalassemic children to have ocular abnormalities despite only moderate doses of deferasirox and in the presences of high serum ferritin levels, which implicate a role of iron in ocular pathology in thalassemia. We recommend a larger study to evaluate the role of iron in ocular abnormalities in these patients. The reversibility of ocular changes should also be studied by changing the chelating agent or altering its dose.

A longer follow-up period is required to analyze and comment on how ocular changes may evolve. A limitation of the present study is that it cannot conclusively establish whether ocular changes are a result of the disease per se or due to iron-chelating agents. This requires stoppage of chelation therapy. It may be kept in mind though that iron overload and iron-chelating agents both may be mutually confounding factors in the causation of ocular changes of thalassemia. Also, patients enrolled in our study were already following a fixed thalassemia treatment regimen from elsewhere. In order to study the ocular manifestations of thalassemia in these patients and the ocular side-effects of iron-chelating agents, it was imperative that the treatment regimens being followed at presentation be continued.

A limitation of the present study is that it cannot conclusively establish whether ocular changes are a result of the disease or due to iron- chelating agents. This requires stoppage of chelation therapy which was not possible. It may be kept in mind though that iron overload and iron chelating agents both may be mutually confounding factors in the causation of ocular changes of Thalassemia.

CONCLUSION

Ocular changes of beta thalassemia are attributed to the course and severity of the disease. Serum ferritin is an important proxy indicator for ocular manifestations in thalassemia. Reduction in serum ferritin levels by iron-chelating agents is useful for preventing adverse effects associated with iron overload and regular annual ocular evaluation is important to look for side-effects of such agents can aid in preventing or delaying ocular complications.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Lokeshwar MR. Thalassemia. In: Lokeshwar MR, Shah N, Kanika S, Manglani M. IAP, eds. Textbook of Paediatrics. 3rd ed. New Delhi: Jaypee Publishers; 2006. Thalassemia; pp. 622–30.
2. Bloomfield SE, Markenson AL, Miller DR, Peterson CM. Lens opacities in thalassemia. J Pediatr Ophthalmol Strabismus. 1978;15:154-6.
3. Orton RB, de Veber LL, Sulh HM. Ocular and auditory toxicity of long term high dose subcutaneous desferrioxanine therapy. Can J Ophthalmol. 1985;20:153-6.
4. Olivieri NF, Buncic JR, Chew E. Visual and auditory neurotoxicity in patients receiving subcutaneos desferrioxamine infusions. N Eng J Med. 1986;314:869-73.

5. Garataganis SP, Zoumbos N, Koilopoulos JX, Mela EK. Contrast sensitivity function in patients with beta Thalassemia major. Acta Ophthalmol. 2000;78: 512-5.
6. Gaba A, Souza PD, Chandra J, Narayan S, Sen S. Ocular abnormalities in patients with beta Thalassemia. Am J Ophthalmol. 1998;108:699-703.
7. Taneja R, Malik P, Sharma M, Agarwal MC. Multiple transfused thalassemia major: ocular manifestations in a hospital-based population. Indian J Opthalmol. 2010;58:125-30.

DOI: 10.5455/2320-6012.ijrms20140561
Cite this article as: Gosai DK, Mehariya KM, Gosai JB. Study of ocular manifestations in children of thalassemia. Int J Res Med Sci 2014;2:695-8.