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Adherence to the Iron chelation Therapy Among Transfusion Dependent Beta Thalassemic Pediatric Patients - A Cross-Sectional Study At ATertiary Care Hospi-Tal In North India

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Abstract

Aims: This study was conducted to assess the adherence to iron chaletion therapy among transfusion dependent beta-thalassaemic children and to evaluate the causes for non-complaince.

Methods and Material: This cross-sectional study was conducted in thalassemia unit at a tertiary care centre in Punjab. A total of 55 thalassemia patients, who were on chelation therapy for atleast one year, were enrolled after a written consent. After receiving informed consent, patients were individually administered a questionnaire consist of personal and demographic information, questionnaire check compliance and pretested questionnaire called Morisky Medication Adherence Scale.

Statistical analysis used: The data was summarized using frequency distribution and descriptive analysis. Chi square test was used to find the association of categorical variables. The P value <0.05 was considered significant. All statistical analysis was performed using SPSS version 26.0.

Results: In our study 58.2% of the patients had compliance ≤90%. The mean ferritin was 3131.4±1271.3 µg/ml among the patients with compliance ≤90% then 2398.1±972.0 µg/ml with compliance >90%. Nearly half of the thalassemics on regular transfusion and chelation therapy have poor adherence to iron chelation treatment. Illiteracy, low socio economic status, female child and higher age of the child are linked to worse adherence.

Conclusions: Our study suggest that socio-economic and cultural conditions are important factors affecting adherence to treatment and outcome indicators in thalassemic children. This underlines the importance of a societal commitment and a need to focus on public strategies to support families with thalassemic children.

Keywords: Thalassemia, deferoxamine, Deferiprone and Deferasirox

Introduction

Thalassemia is a chronic inherited hematological disorder and a serious public health problem. It is a cause of life threatening hemolytic anemia throughout the Mediterranean region, Middle East, the Indian subcontinent, as well as in Southeast Asia. Advances in treatment have led to increased patient survival but with burden of chronic blood transfusion, chelation therapy and disease complications itself [1, 2]. The goal of treatment for transfusion dependent thalassemia patient is to maintain pre transfusion Hb 9g/dl to 10.5g/dl [3]. Adherence rate to chelation therapy in developed countries averages around 50% and is worse in developing countries [4]. Adherence to treatment is the extent to which a patient adheres to their prescribed therapeutic regimen and persistence is continuing to take the treatment for the prescribed duration [5]. Findings in untreated or poorly

transfused individuals with thalassemia , as seen in some developing countries, are growth retardation, anemia, jaundice, poor musculature, hepatosplenomegaly, leg ulcers, development of masses from extramedullary hematopoiesis, and skeletal changes that result from expansion of the bone marrow. Regular transfusion therapy leads to iron overload-related complications including endocrine complication (growth retardation, failure of sexual maturation, diabetes mellitus, and insufficiency of the parathyroid, thyroid, pituitary, and less commonly, adrenal glands), dilated myocardiopathy, liver fibrosis and cirrhosis therefore, improving compliance is the integral part to the treatment [6]. Deferoxamine, deferiprone and defrasirox are the three commonly used iron chelators for the treatment of iron overload. Published data suggests that compliance with Deferoxamine in typical clinical practice is 60 to 80% [7]. The oral chelators are easier to use, especially for pediatric and adolescent patients for whom compliance is a particular issue. Factors involved for the non-adherence are related to regimen, disease, psychological, social ,demographic and health system [8]. Previous studies suggested that compliance improves with use of oral chelation therapy , mean compliance of deferoxamine with addition of deferiprone , increased to 79 to 98 percent [7]. Nearly 90% of patients on deferasirox reported at least 90% adherence, compared to 75% of patients on deferoxamine [10]. One study concluded that adherence to deferasirox was very low (7.5%), with younger children being more adherent than older ones Illiteracy, higher age and joint family are the surrogate parameters of poor adherence to the medication [9]. For chronic conditions such as thalassemia major, even when free chelation therapy is available, support by an integrated team is a must to improve the compliance and this team includes a psychologist, nurse specialist working with the treatment center.. In India, very few studies have studied the factors that impact adherence to chelation therapy. Therefore, this study was conducted to assess the adherence to iron chaletion therapy among transfusion dependent beta-thalassaemic children and to look at the causes for non-complaince.

Materials And Methods

A cross-sectional descriptive design study that was conducted in thalassemia ward in Christian Medical College and Hospital Ludhiana, Punjab. 55 thalassemia patients were included in this study who gave written consent and had been taking chelation therapy for at least one year. Patients age < 1 year old and > 18years were excluded from this study. Compliance for oral chelators measured by calculation of number of doses administered in the last 4 weeks and on the basis of achieving 90% of medication administration. (patient report of chelator use as number of doses taken in the past 4 week out of those prescribed). Those who have taken 90% of dosage has been taken as good compliance. Patients and their parents were individually administered a structured questionnaire consisting of personal and demographic Information, self prepared questionnaire to check compliance and validated questionnaire called Morisky Medication Adherence Scale (MMAS-8) [11] MMAS-8 is composed of 8 items, out of which the items from 1 to 7 are yes/no questions (except item 5) where no answers receive a score of 1.0, and yes answers receive a score of 0. The score is reversed for item 5. Item 8 is measured based on a 1 to 5 Likert scale. The total scores range between 0 and 8, where 8 is considered as high adherence, 6–8 as moderate adherence, and <6 as poor adherences.

Results

55 thalassemic patients were included in this study. The baseline characteristics of the study population are mentioned in Table 1. The mean serum ferritin was 2824.7±1202.5 µg/ml. In our study 58.2% of the patients had compliance ≤90%. The mean ferritin was 3131.4±1271.3 µg/ml among the patients with compliance ≤90% then 2398.1±972.0 µg/ml with compliance >90%. The most common reason for non- compliance was problem in remembering medicine, that was seen in 71.9% of the patients with p value <0.001. 37.5% of the patients had problems in sticking themselves to the medications (p value= 0.001) and 25% had problems with buying the drugs due to non availability or cost of the drugs. 60% patients are male. 89.1% of the study population belonged to urban area. 54.5% of the study population belonged to lower middle class.

High adherence was seen in 41.8% of the patients. MMAS-8 score of <6 was reported by 32.7% (n=18) of the study population, 25.5% (n=14) had the score of 6-8, 41.8% (n=23) had a score of >8. The

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maximum adherence with iron chelation therapy was found in the age group of 5-8 years (34.8%) and the adherence was lesser in the elder patients (p=0.325) (Table 2). The adherence in males (65.2%) was found to be higher as compared to that in females (34.8%); however, the difference was not statistically significant (p=0.503). The adherence was more in urban population(95.7%) as compared to rural population (p=0.383).(Table 2) The mean ferritin level is low in compliant patients as compared to non compliant patients with p value of 0.024. The common reasons for poor adherence was problem in remembering(77.8%) and sticking to the therapy (55.6%) with p <0.001.

MMAS-8 score >8 was maximumly seen in 5-8 year of age group(34.8%), statistically nonsignificant. MMAS-8 score > 8 was seen in males (65.2%) as compared to female (34.8%) (p = 0.572). 43.5% of lower middle and 21.7% of upper middle had MMAS-8 score >8 which was not statistically significant, with p value of 0.659.(Table 3) The mean ferritin was 2398.1±972.0 µg/ml, 2651.4±1067.4 µg/ml and 3504.7±1318.5 µg/ml with MMAS-8 score >8, 6-8 and <6 respectively with p value 0.009. It was observed that 77.8% of the patients with MMAS-8 score < 6 had problem in remembering and 55.6% had problem with sticking, which was statically significant with p value <0.001. 27.8% patients had problem with buying the drugs and11.1% had side effects of the chelation therapy.

Discussion

Iron chelation is one of the mainstays of treatment of iron overload in thalassemics on regular blood transfusion therapy and compliance to chelation therapy needs to be ensured to minimize the complications of the same. We observed that amongst children visiting our thalassemia centre, 58.2% were less than 90% complaint while 41.8% were more than 90%complaint to chelation. It has been observed that males tend to have better compliance to chelation therapy. This was observed in a study by Kakkar et al and we observed a similar trend [12]. We also observed a slightly better compliance in the urban families, though not statistically significant. One may consider literacy and a more frequent contact with the health centre as opportunities for better understanding and thereby compliance amongst the urban population. A rural placement adds the additional stress of travel to a suitable centre for transfusion and chelation and might affect the assimilation of the information affecting compliance to chelation in return. More often than not the rural population is not financially as sound and lack of an awareness in the community also affects family support. Low family income, poor family support along with side effects of chelators have been implicated as reasons affecting compliance to chelatin therapy by researchers [13,14,15]. We also observed a better compliance among the families belonging to upper and lower middle class income groups. Other authors have also pointed at the lower family income and support as reasons for poorer compliance [18,19].

Trachtenberg and Rashid found that adherence to chelation therapy is better in younger children compared to adults [10,16]. Jordan et al also observed lower adherence amongst older children and felt that was because of poorer parent monitoring [17]. Younger children who are under better parental control versus older children on the brink of teenage rebellion may be expected to have better drug compliance. We found a higher compliance rate among the 5-8 years old. However, statistical significance was not established.

The commonest reason given for poor compliance was problem in remembering to take medication in 71.9% children followed by 37.5% had problem with sticking themselves and 25% had problem with buying the drugs, while none of them had problems in taking the medication. Kakkar noted that a higher proportion of non-adherent patients felt there were too many medications and found it difficult to consume the medications.

The mean serum ferritin levels were lower in thalassemics with good compliance. This shows that better compliance to chelators decreased the ferritin levels in the body. Similar results were reported by a study done by Trachtenberg et al [19] Krisada Theppornpitak et al also showed similar results in his study High adherence level of patients correlates with better controlled serum ferritin levels [18]. However, Lee et al. reported that there was no correlation between self-reported adherence with serum ferritin levels [20].

Too many medicines to be taken daily and difficulties in drug administration, remembering it and sticking

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to those medicines were the important reasons cited by the non-compliance patients. Various other authors have also shown the role of situational psychological factors, busy work schedule, illiteracy, social stigma, poor socio-economic status and poor family support as reasons for non-adherence to chelators [21,22].

Medication adherence has been shown to be a problem in several long-term conditions in both adults (diabetes; schizophrenia; heart disease; asthma) and children (HIV, diabetes, juvenile arthritis and asthma) [23]. Jochmann A et al observed improvements among asthmatic children with ≥80% adherence compared to no improvements were seen among patients with adherence to the therapy <60%. [24] Grey et al. suggested that parenteral support and guidance increase adherence and help adolescents with T1DM achieve success in metabolic control over 1 year of follow-up. [25] Among approximately 63% of pediatric patients of chronic illness 50% to 88% of children and adolescents are non-adherent to their prescribed regimens [26,27]. Non adherence among pediatric patients have a greater impact on health care use than adult patients as self-management behaviors are often developed in childhood and adolescence. Non adherence increases hospital admissions, health care use and increases morbidity and mortality [27].

Conclusion

Poor adherence was seen in 58.2% of our study participants. Illiteracy, higher age, low socio-economic status and gender are the important parameters of poor adherence to the medication. In our study, patients are not stick to their therapy, buy the drugs or had problem to remember to take their medication. Iron chelation therapy significantly decrease iron load, hence can provide better clinical outcomes among thalassaemia patients in the future. By improving adherence among thalassasemic patients, we can decrease the morbidities and mortality associated with non-adherence.

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Table 1 Demographic characteristics

	Frequency (Percentage)
Age-groups	
≤ 4	9 (16.4%)
5-8	14 (25.5%)

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9-12	16 (29.1%)
13-16	12 (21.8%)
> 16	4 (7.3%)
Mean±SD (years)	
Gender	
Male	33 (60%)
Female	22 (40%)
Region	
Urban	49 (89.1%)
Rural	6 (10.9%)
Socio-economic status	
Upper	4 (7.3%)
Upper Middle	10 (18.2%)
Lower Middle	30 (54.5%)
Upper Lower	6 (10.9%)
Lower	5 (9.1%)

Table 2 Correlation of demographic factors with compliance

	Compliance		
	≤90%	>90%	p-value
Age-groups			
≤ 4	6 (18.8)	3 (13.0)	0.325
5-8	6 (18.8)	8 (34.8)	
9-12	10 (31.3)	6 (26.1)	

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13-16	9 (28.1)	3 (13.0)	
> 16	1 (3.1)	3 (13.0)	
Gender			
Male	18 (56.3)	15 (65.2)	0.503
Female	14 (43.8)	8 (34.8)	
Region			
Urban	27 (84.4)	22 995.7)	0.383
Rural	5 (15.6)	1 (4.3)	
Socio-economic status			
Upper	1 (3.1)	3 (13.0)	0.447
Upper Middle	5 (15.6)	5 (21.7)	
Lower Middle	20 (62.5)	10 (43.5)	
Upper Lower	4 (12.5)	2 (8.7)	
Lower	2 (6.3)	3 (13.0)	

Table 3 Correlation of demographic factors with MMAS-8 score

	MMAS-8 score			
	<6	6-8	>8	p-value
Age-groups				
≤ 4	4 (22.2)	2 (14.3)	3 (13.0)	0.689
5-8	3 (16.7)	3 (21.4)	8 (34.8)	
9-12	6 (33.3)	4 (28.6)	6 (26.1)	
13-16	4 (22.2)	5 (35.7)	3 (13.0)	
> 16	1 (5.6)	0 (0)	3 (13.0)	

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Gender				
Male	9 (50.0)	9 (64.3)	15 (65.2)	0.572
Female	9 (50.0)	5 (35.7)	8 (34.8)	
Region				
Urban	15 (83.3)	12 (85.7)	22 (95.7)	0.471
Rural	3 (16.7)	2 (14.3)	1 (4.3)	
Socio-economic status				
Upper	0 (0)	1 (7.1)	3 (13.0)	0.659
Upper Middle	3 (16.7)	2 (14.3)	5 (21.7)	
Lower Middle	10 (55.6)	10 (71.4)	10 (43.5)	
Upper Lower	3 (16.7)	1 (7.1)	2 (8.7)	
Lower	2 (11.1)	0 (0)	3 (13.0)	

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