The Impact of Patient and Parents' Education by Nurses on Serum Ferritin Levels in Children with Beta-Thalassemia Major

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Abstract: *Background:* Through education and information, nurses can help patients learn more about their health status and can contribute to improvement in patient drug adherence, clinical and laboratory outcomes. The aim of this study was to assess the impact of patient and their family education by nurses on serum ferritin levels.

Methods: The study included 85 children with transfusion-dependent beta-thalassemia aged between 2.4 to 17 (mean 7.6 ± 3.3) years, 44 (52%) of whom were male. All patients received deferasirox doses ranged from 12 to 40 mg/kg/day. Patients and their families were requested for education intervention provided by nurses. Seventeen patients (group 1) (11 male, 6 female) refused to receive education or not compliant with the study protocol. Sixty-eight (33 male, 35 female) patients (group 2) and their parents educated by nurses, including drug instructions, telephone interviews and home visits for 12 months.

Results: Mean deferasirox dose at the 24th and 36th months of the study were 31.6 ± 7 and 32 ± 8 mg/kg/day in group 1, and were 32.7 ± 8 and 33.6 ± mg/kg/day in group 2, respectively. Mean serum ferritin levels at the 24th and 36th months of the study were reduced from 4424 ± 2305 ng/mL to 3425 ± 1661 ng/mL (the mean difference was 662 ng/mL) (P =0.044) in group 1, and were reduced from 3177 ± 1645 to 2748 ± 1343 ng/mL (the mean difference was 274 ng/mL) (P = 0.033) in group 2, respectively

Conclusion: Our study's results suggested that patient and parents' education by nurses have no significant impact in reducing ferritin levels in children with beta-thalassemia major. Deferasirox dose was the only significant predictor that contributed to reduction in ferritin levels.

Keywords: Beta-thalassemia major, Deferasirox, Ferritin; nurses, Patient education.

INTRODUCTION

Iron chelation therapy in patients with beta thalassemia major has led to the prevention of iron accumulation in addition to treating iron overload and iron-induced end-organ complications, which provided to achieve a normal pattern of complication-free survival and of quality of life [1].

Deferasirox is a once-daily oral iron chelator that has proven to be effective in reducing liver and serum ferritin levels over 1 year in patients with various transfusion-dependent anemias [2-4]. We previously reported about the safety, tolerability and efficacy of deferasirox use in children, who received deferasirox for 3 years, with transfusion dependent beta-thalassemia at Sanliurfa province located in the southeast region of Turkey [4]. The superiority of deferasirox over deferoxamine for treatment of iron burden lies in its oral preparation and its long half-life that provides once a day dosage, which may contribute to reducing substantial long-term compliance problems [5]. Medication adherence is increasingly recognized as an important issue that has significant impact on the clinical course of disease and patient quality of life, Further, patients' adherence with their medication is poor especially in chronic diseases, including diabetes, coronary heart diseases, cancer and chronic hematological diseases such as beta-thalassemia major [5]. Because patients with chronic diseases are prone to develop serious complications associated with their illness, efforts must be focused on developing effective and efficient intervention strategies for early detection and prevention of these complications. One of the approaches to overcome this problem is patient education by nurses. As a healthcare provider, nurses may play a unique and important role in assisting patients to carry out healthy behaviour in the context of treatment adherence and achieving better clinical outcomes. In the current study, we aimed to highlight the importance of patient education by nurses and to establish whether it will provide a beneficial effect on ferritin levels in the context of adherence to chelation therapy in patients with beta thalassemia major.

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MATERIALS AND METHODS

The study included 85 children with transfusion-dependent beta-thalassemia at Harran University Research Hospital Pediatric Hematology Department aged between 2.4 to 17 (mean 7.6 ± 3.3) years, 44 (52%) of whom were male. All patients received deferasirox (Exjade®, Novartis). The assigned dose of deferasirox was administered as a suspension in water half an hour prior to breakfast 7 days a week. Children with beta-thalassemia major, aged ≥2 years, with serum ferritin levels greater than 1000 ng/mL and using deferasirox were eligible for inclusion in the study regardless of prior type of chelation treatment. Patients were excluded from this trial if they had one of the following conditions: undergone bone marrow transplantation, no regular follow-up visits, noncompliance with prescribed therapy, gastrointestinal conditions preventing absorption of an oral medication or concomitant conditions preventing therapy with deferasirox. Patients and their families were informed about beta thalassemia major and chelation therapy by pediatric physician assistant and pediatric hematologist at our Pediatric Hematology outpatient clinic. Blood transfusions were regularly administered during the study period according to the patients' requirements. Laboratory analysis, carried out at Harran University Research Hospital Biochemistry Department, including complete blood count, electrolytes, liver function tests, serum creatinine and serum ferritin levels were performed at monthly intervals to assess safety and efficacy of chelation treatment. In addition to regular information given at Pediatric Hematology outpatient clinic, all patients and their families were requested for education intervention provided by certified and registered nurses, however, 17 patients (11 male, 6 female) (group 1) refused to receive education or not compliant with the study protocol. Sixty-eight (33 male, 35 female) patients and their parents (group 2) received education provided by nurses at outpatient transfusion center during regular blood transfusion of every 3-4 weeks, and followed by home visits and telephone contact for 12 months.

Education intervention, based on prescribing information of Exjade®, the main points were as follows:

1. Take the drug once daily on an empty stomach at least 30 minutes prior to food, preferably at the same time every day.

2. Completely disperse the tablets in water, orange juice, or apple juice, and drink the resulting suspension immediately. After the suspension has been swallowed, resuspend any residue in a small volume of the liquid and swallow.

3. Do not chew or swallow tablets whole.

4. Do not take aluminum-containing antacids and Exjade simultaneously.

5. There may have the risk of fatal and nonfatal gastrointestinal bleeding, ulceration, and irritation more frequently if Exjade is being taken by combination with drugs that have known ulcerogenic or hemorrhagic potential, such as NSAIDs, corticosteroids, oral bisphosphonates, or anticoagulants.

6. Be cautious if Exjade is being taken by concomitantly with drugs that are potent UGT inducers (*e.g.*, rifampicin, phenytoin, phenobarbital), drugs metabolized by CYP3A4 (*e.g.*, cyclosporine, simvastatin, hormonal contraceptive agents), which may potentially cause loss of effectiveness of Exjade and necessities to increase the dose of Exjade.

7. Be cautious about the most frequently occurring (>5%) adverse reactions associated with Exjade use, which are diarrhea, vomiting, nausea, abdominal pain, skin rashes, and increases in serum creatinine, and if occured, contact doctor immediately.

8. Be cautious about severe skin rashes that may occur during Exjade treatment, and if occurred, stop taking Exjade and contact doctor immediately.

9. Store Exjade tablets at 25°C (room temperature), at 15°C-30°C while on excursion and protect from light and moisture.

10. If a dose is missed, take it as soon as remember. If it is near the time of the next dose, skip the missed dose and resume usual dosing schedule. Do not double the dose to catch up.

Upon conclusion of the sessions, the educator provides written curriculum reflecting current evidence and evaluating outcomes. There have not been any reports on patient compliance with an education prescription in real clinical practice.

The study was approved by the local scientific ethics committee, and informed consent was obtained from the parents of the patients.

STATISTICAL METHODS

The data were expressed as number (%), mean ± SD, median and range. The paired samples *t*-test was used to compare mean serum ferritin levels [95% confidence interval]. All statistical tests were two-sided and the level of statistical significance was set at P< 0.05. Statistical analyses were performed using SPSS for Windows Release 11.5 (SPSS, Chicago, IL, USA).)

RESULTS

Mean deferasirox dose at the 0th, 12th, 24th and 36th of the study was 20 ± 9 mg/kg/day, 24 ± 9 mg/kg/day, 31 ± 8 mg/kg/day and 32 ± 8 mg/kg/day, respectively. Mean serum ferritin levels decreased slightly between 12th to14th months of the study, while progressive decrease in ferritin levels were achieved when the average actual dose of deferasirox increased to >30 mg/kg/day after 22th months of the study in all patients. Mean serum ferritin levels increased progressively during the first 22 months of treatment, from 3.152 ± 1.650 ng/mL to 3.373 ± 1.1818 ng/mL (*P* = 0.227), and then decreased gradually to 2.868 ± 1.414 ng/mL (*P* = 0.004) at 36 months of the study for all studied patients (Figure **1**). The mean age of the patients at the start of the study was 8.7 ± 4.2 years (range, 12–17 years; 11 male and 6 female) in group 1, and was 7.5 ± 4.2 years (range, 2–17 years; 33 male and 35 female) in group 2 (Table **1**) (*P* > 0.05). Mean serum ferritin levels reduced from 3.130 ± 1.477 to 2.749 ± 1.343 ng/mL (*P* = 0.044) (mean difference: 315 ± 751 ng/mL) in group 2 after education program and reduced from 4.221 ± 2.167 ng/mL to 3.425 ± 1.661 ng/mL (*P* =0.033) (mean difference: 785 ± 826) in group 1 (Figure **2**), despite the fact that they were not educated at the same period (Figure **3**). At the end of the study, the rate of patients receiving deferasirox at a dose of ≤25 mg/kg/day showed a marked decrease; and the mean final dose of deferasirox was ~32 mg/kg/day in most of the patients (Table **1**). There was a significant decrease in ferritin level in patients with ferritin level >4.000 ng/mL in both groups. Forty-two percent of patients in group 1 and 45% of patients in group 2 maintained serum ferritin levels ≤2500 ng/mL at the end of treatment, respectively.

Table 1: Demographics and Patient Characteristics of Deferasirox Treatment in the Groups

	Group 1 (*n* = 17)		Group 2 (*n* = 68)	
Characteristic	**Start of Education**	**End of Education**	**Start of Education**	**End of Education**
Age, y				
Mean ± SD	8.7 ± 4.2‡	11.8 ± 4.3	7.5 ± 4.2‡	11.9 ± 4.2
Sex (%)				
Male	11^	11	33^	33
Female	6	6	35	35
Serum Ferritin, ng/mL				
Mean ± SD	4221 ± 2.167	3.425 ± 1.661 †**	3.130± 1.477	2.749 ± 1343†*
Median (range)	3.334 (1.730-8.212)	3.141 (1.501 -6.428)	2.648 (1.284-7.827)	2.494 (470 -6.879)
Mean difference, ng/mL	-	785 ± 826	-	315 ± 751
Serum Ferritin Category, %				
<1000 ng/mL	0	0	0	5
1000-2500 ng/mL	25	42	48	45
2501-4000 ng/mL	31	33	32	38
>4000 ng/mL	44	25	20	12
Deferasirox dosing, mg/kg/day	32.7	33.6	31.6	31.9

‡ Student t-test (*P* = 0.310)
†Paired sample *t*-test (**P* = 0.033, ***P* = 0.044)
^Chi-square test (*P* = 0.232)

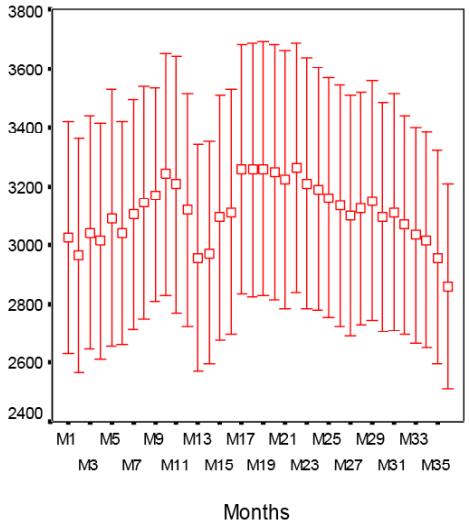

Figure 1: Changes in serum ferritin levels in all children with beta-thalassemia.

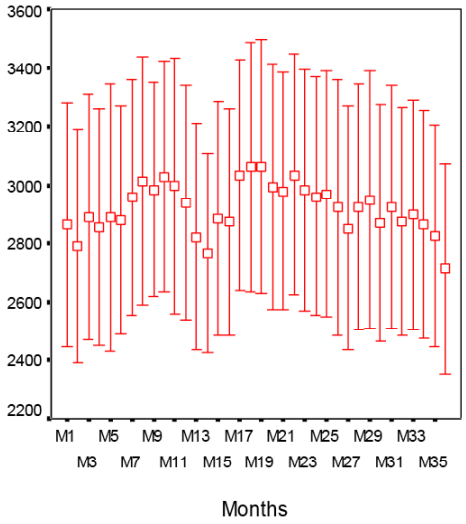

Figure 2: Changes in serum ferritin levels and deferasirox dose in group 1.

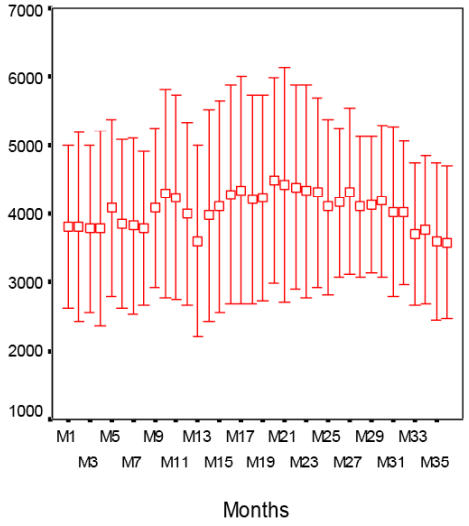

Figure 3: Changes in serum ferritin levels and deferasirox dose in group 2.

DISCUSSION

The oral iron chelator deferasirox was approved in the USA in 2005, in Europe in 2006, and in Turkey in 2007 for clinical use as a first-line therapy for blood-transfusion-related iron overload, respectively. It is an orally ingested, highly bioavailable chelator that is absorbed in the gastrointestinal tract, and its dose-dependent half life of 12 to 18 hours provides once a day dosage [6]. It is reported that daily use of a single oral dose of 20-30 mg/kg per day results in dose-dependent decrease in serum ferritin [7, 9]. Cappelini *et al*. reported that a dose of 20 mg/kg was predicted to be able to maintain stable iron balance in regularly transfused patients [7]. However, in our previous study, deferasirox treatment at a mean dose of 24 ± 8 mg/kg/day did not create a stable iron balance during the first year of the study, where as negative iron balance was achieved at a dose of ≥ 30 mg/kg/day during the third year of the study [4]. Taher *et al*. also reported that deferasirox doses ≥ 30 mg/kg/day were generally required because of high transfusional iron intake and high baseline serum ferritin levels, highlighting the importance of administering an adequate dose to achieve net negative iron balance [10]. However, a proportion of patients do not achieve net negative iron balance, even at a dose of 40 mg/kg/day [11, 12] The efficacy of deferasirox was dependent on transfusional intake and optimal dose, highlighting the importance of timely dose adjustment in order to achieve clinical goals [13].

Because a growing number of patients prefer oral chelation therapy rather than intravenous administration, the issue of adherence is becoming increasingly important in patients with beta-thalassemia major as in other chronic disease treatment. Oral chemotherapy is cost effective, if it is taken as prescribed. However, if patients are non-adherent to medication, the cost burden of unused medicines is substantial [14]. In general, patients are considered to be adherent if the ≥80% of prescribed medication is taken timely and at an appropriate dose without missing dose or extra dose [15]. A number of factors are associated with medication adherence. There are three levels of barriers to adherence: patient, healthcare provider, and healthcare system levels [16]. The patient-related factors include health beliefs and socioeconomic factors, while communication and the complexity of the regimen are regarded as healthcare-provider factors [15]. One of the approaches for

overcoming the problem of patient-related factors is patient education provided by nurses. There are barriers to effective patient education for nurses especially in crowded outpatient clinical setting [17]. Limited time for teaching, patients and their parents' physical or psychological condition are important challenge for nurses that can limit the effectiveness of patient education in such crowded outpatient departments [18]. In this context, overuse of hospital outpatient departments in urban areas of developing countries, like our Pediatric Hematology Center in Turkey, is still perceived as a problem by many health planners. However, despite these challenges, our results showed that the current study's patients and their parents, in both groups, were adherent to medications regardless of patient education interventions provided by nurse [19]. This is the first report evaluating the impact of patient education by nurses on drug adherence and ferritin levels in patients with beta thalassemia major receiving oral chelator. The major limitations of the current study were that patients number and mean ferritin levels were not similar for both groups.

IN CONCLUSION

Our results suggested that patients and their parents' education by nurses did not provide a contribution in reducing serum ferritin level, deferasirox dose was the only significant predictor.

DECLARATION OF COMPETING INTERESTS

We declare that we have no competing interest that influences the results and discussion of this article.

INSTITUTIONAL COMPETING INTERESTS

Our academic institution has no competing financial interests that influence the results and discussion of this article.

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