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(RESEARCH ARTICLE)

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Impact of chelator treatment on post-transfusion hemochromatosis in thalassemic patients under Deferasirox

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Abstract

The management of beta thalassemia may require periodic blood transfusions, iron chelation therapy, and bone marrow or stem cell transplantation. This study is a descriptive retrospective analysis of clinical, biological, and therapeutic parameters to evaluate the impact and effectiveness of chelation therapy in managing post-transfusional hemochromatosis in 26 β-thalassemia patients treated at the Hussein Dey University Hospital Center in Algiers, Algeria. The results of this study show a certain correlation between the doses of iron chelators taken and the improvement in ferritin levels and creatinine clearance, which is indicative of a reduction in renal function impairment. Five profiles were identified based on this relationship. The study also found that all patients had normal kidney function, but there was a tendency towards a decrease in creatinine clearance, necessitating continuous monitoring. It is important to note that even with careful monitoring, complications of thalassemia may occur gradually and at a late onset. This study highlights the need to integrate pharmaceutical practices and introduce the concept of clinical pharmacy to improve adherence to long-term chelation therapy and ultimately enhance survival in children with major thalassemia.

Keywords: β-thalassemia; Hemochromatosis; Iron chelation; Ferritin levels; Creatinine clearance

1. Introduction

Thalassemia is a hereditary hematologic condition that impairs the synthesis of hemoglobin, the globular protein responsible for carrying oxygen in erythrocytes throughout the body [1]. Individuals with thalassemia exhibit diminished or absent hemoglobin production, which can result in anemia, fatigue, and other adverse health outcomes [2].

Management of beta thalassemia may entail periodic blood transfusions, iron chelation therapy to alleviate the toxic effects of iron overload, and bone marrow or stem cell transplantation [3].

Objectives

Conduct a study that analyzes clinical, biological, and therapeutic parameters to evaluate the evolution of β-thalassemic patients receiving treatment at Chu d'Hussein Dey. The study will focus on assessing the impact and effectiveness of chelation therapy in managing post-transfusional hemochromatosis [4,5].

Contribute to the implementation of a patient-centred pharmaceutical act which results in the integration of scientific and technical skills with the concept of responsibility towards the patient [5].

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2. Methods

2.1. Type of study [4,6]

- Descriptive retrospective study with analysis of clinical, biological and therapeutic parameters; of the (26) β-thalassemia patients treated in the Hussein Dey University Hospital Center (Algiers, Algeria), by evaluating the impact and monitoring of chelation therapy on post-transfusion hemochromatosis
- Period: (01) year (december2014 to december 2015).

2.2. Inclusion criteria [4,6]

- Any child with a confirmed diagnosis of β-thalassemia (homozygous form).
- Age under 16 plus (03) patients aged 17 to 21.
- Patients followed regularly in the pediatric hematology unit.

2.3. Support and tool [4,6]

- Patient records : paper and digital.
- Short interviews : patients (parents) and general practitioners.
- Data collected is recorded on the exploitation sheet + statistical analysis (Excel®).

3. Results

3.1. Pharmacoeconomic, epidemiological, clinical and paraclinical data

Epidemiological data are summarized in Table 1 :

Table 1 Epidemiological data of current study

Number of patients	**26**	**100%**
Ratio M/F (male/female)	F (12) M (14)	1.16
Age of patients (year)	07 to 11 (8)	30.77%
	12 to 16 (15)	57.69%
	Over 17 (3)	11.54%

The largest age range of patients is between 12 and 16 years old (pediatric department) and the ratio M/F=1.16 this means that the disease affects both men and women ; in fact the disease is carried by autosomal chromosomes [6].

- The circumstances of thalassemia discovery in the patients of the study are represented in figure 1 :

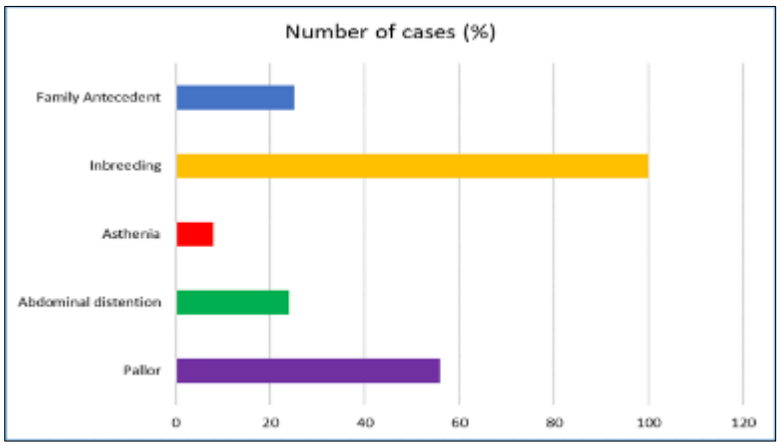

Figure 1 Discovery circumstances of thalassemia in the patients of the study

From the diagram we conclude that most cases of beta thalassemia are due to inbreeding because it is an inherited disease [7].

The symptoms caused by thalassemia and reported among the patients of this study are presented in figure 2 :

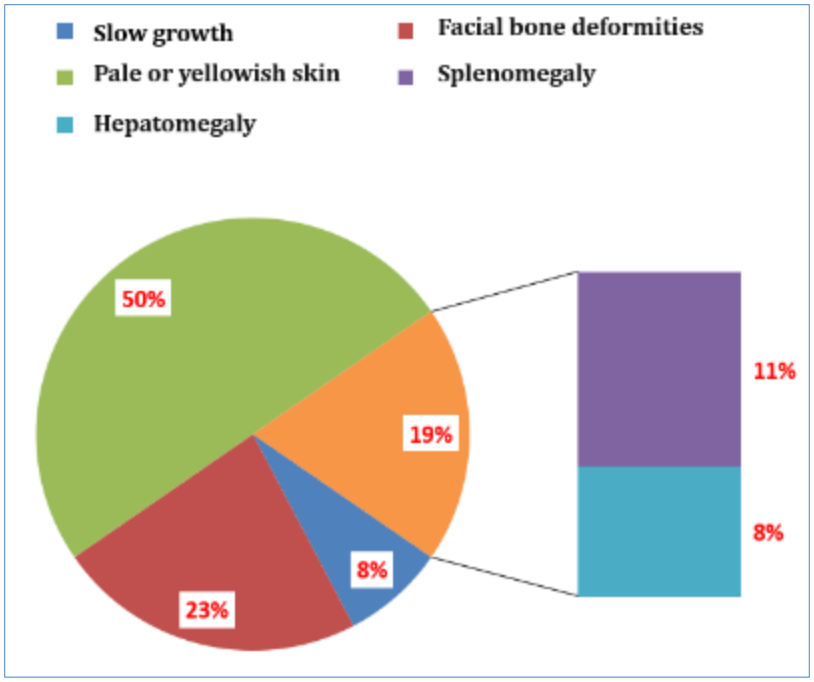

Figure 2 Distribution of symptoms related to thalassemia among patients

- According to the diagram the main symptom is the mucous skin pallor which is due to the anemia that this disease causes [7].
- we also have orofacial symptoms of thalassemia (Asian facies)that are due to bone changes associated with ineffective erythropoiesis. The symptom of spleomegaly is due to the high rate of hemolysis [7].
- Pharmacoeconomic data are summarized in Table 2

Table 2 Cost of iron chelator consumption per patient and per dosage.of current study

Tablet Dosage	Cost Per Dosage (USD)	Cost Per Patient/ Per Dsage (USD)
500 mg	231 572,72	8 906,64
250 mg	88 743,04	3 413,19
125 mg	33 846,13	1 301,77
Total (USD)	354 161,89	13 621,61

- We observe that the 500 mg tablets are the most dispensed dosage (maintenance therapy) compared to other dosages, especially the 125 mg, which allows for more dose adjustment [8,9].

3.2. Therapeutic data and patient evolution

- The changes in serum ferritin levels at the beginning and end of the study are represented by Figure 3 :

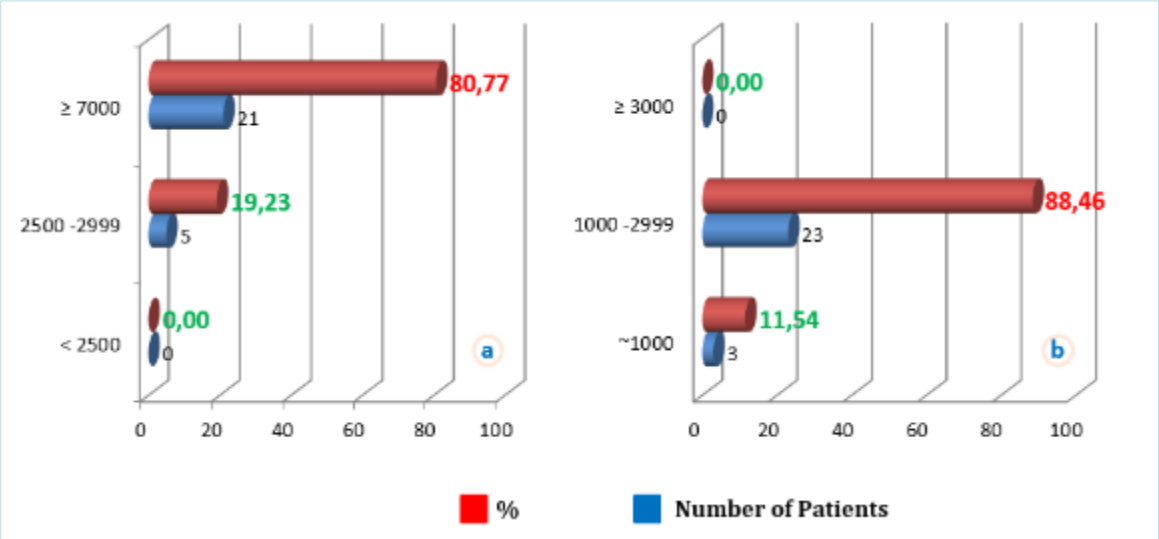

Figure 3 Evolution of iron overload under the influence of deferasirox [(a) and (b) beginning and end of the study period]

- Serum ferritin level decreased at the end of the study due to compliance and the follow-up treatment of patients. After one (01) year of treatment, the peak of ferritinemia moved from levels around 7000 ng/ml to levels below 3000 ng/ml, which means that the patients responded well to deferasirox chelation therapy [10,11].
- The treatment history of iron chelators alone or in combination with other adjuvant therapies shows a certain correlation between the doses taken and the improvement in ferritin levels and creatinine clearance, which is synonymous with a reduction in renal function impairment. This relationship allows us to distinguish five profiles [10,11], which are represented by the graphs below (Figure 4, 5, 6, 7, 8) :

3.2.1. Profile (1)

- The patients (2.3, 4, 5, 7, 9, 10, 11, 14,15, 16, 17, 18, 19, 20, 21, 23, 24 and 26): All saw a constant and significant decrease in their ferritin levels, thus reflecting the effectiveness of chelation (figure 4) .

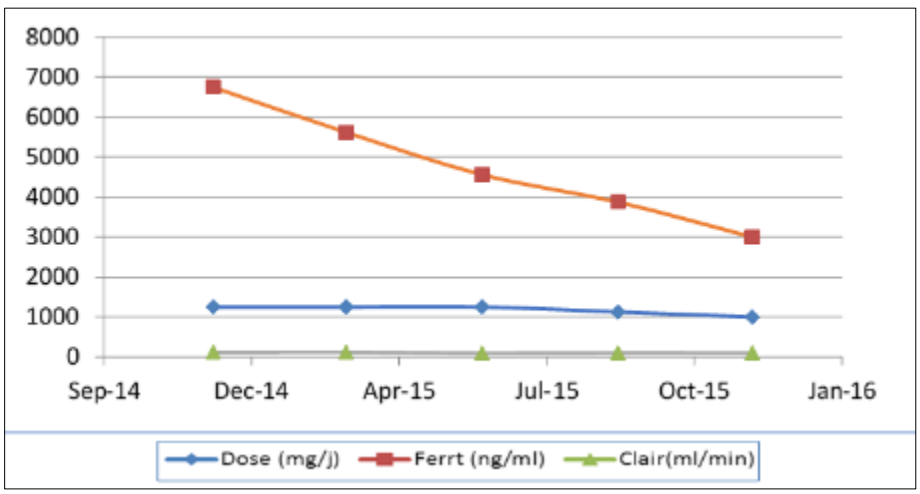

Figure 4 Correlation between the doses of deferasirox taken and the improvement of both ferritin levels and creatinine clearance (profile 1)

3.2.2. Profile (2)

- Patients (1,8,13 and 22) Their respective ferritin levels experienced a slight increase in the first trimester and then a constant decrease. In fact, the chelation stimulated the release of iron from the cells to the external environment (figure 5).

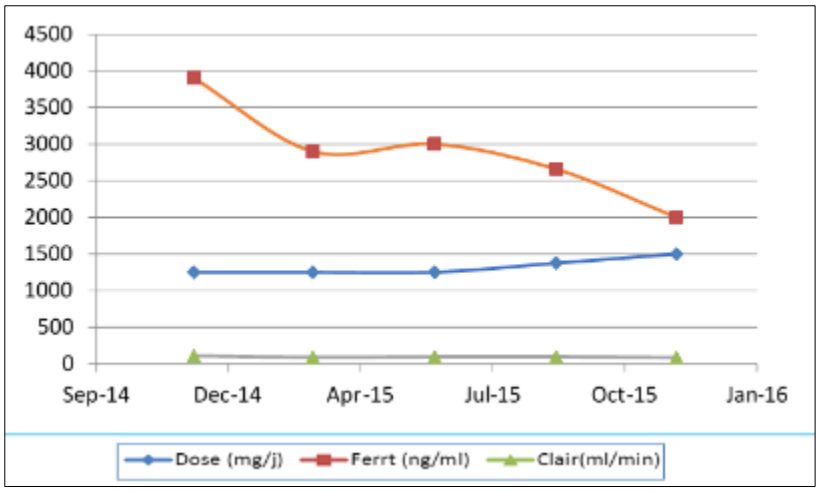

Figure 5 Correlation between the doses of deferasirox taken and the improvement of both ferritin levels and creatinine clearance (profile 2)

3.2.3. Profile (3)

Patients (6, 20 and 25) The chelation treatment resulted in a slight decrease in serum ferritin during the second semester (2000 ng/ml) but we observed a slight rise in the latter to stabilize around (2000 to 2400 ng/ml). This explains the prescription of a deferasirox (DFX)- deferoxamine (DFO) (figure 6) [10,11].

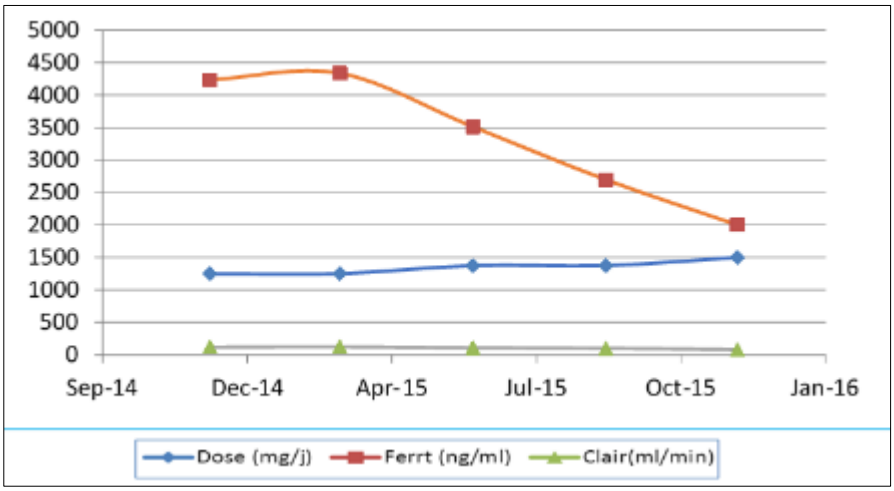

Figure 6 Correlation between the doses of deferasirox taken and the improvement of both ferritin levels and creatinine clearance (profile 3).

3.2.4. Profile (4)

Patient (12) This patient required a higher dose of DFX, this is due to inter-individual variability His serum ferritin fluctuated a lot, a decrease during the first trimester and then an increase during the second and third trimester, then a decrease again. This explains the increased doses of DFX (figure 7) [10,11].

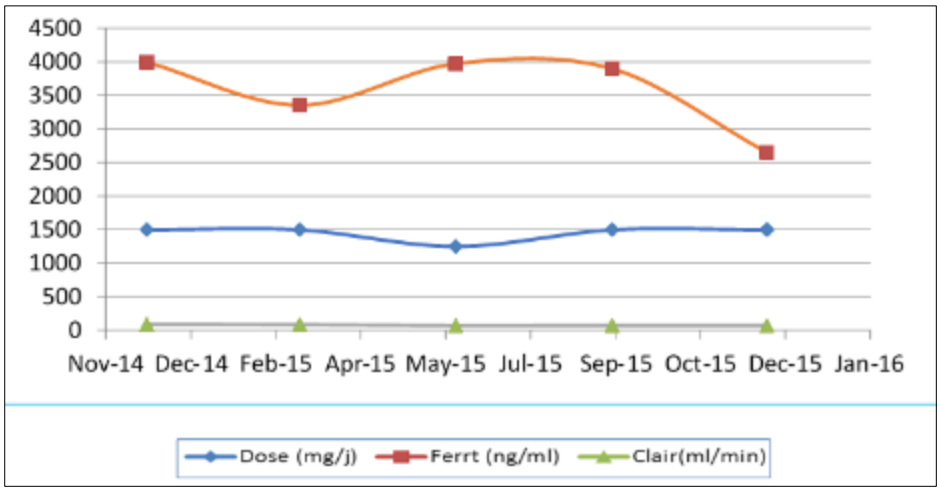

Figure 7 Correlation between the doses of deferasirox taken and the improvement of both ferritin levels and creatinine clearance (profile 4).

3.2.5. Profile (5)

Patients (8, 21 and 23) At the end of the study, their respective ferritin levels stabilized around 1000 ng/ml (figure 8).

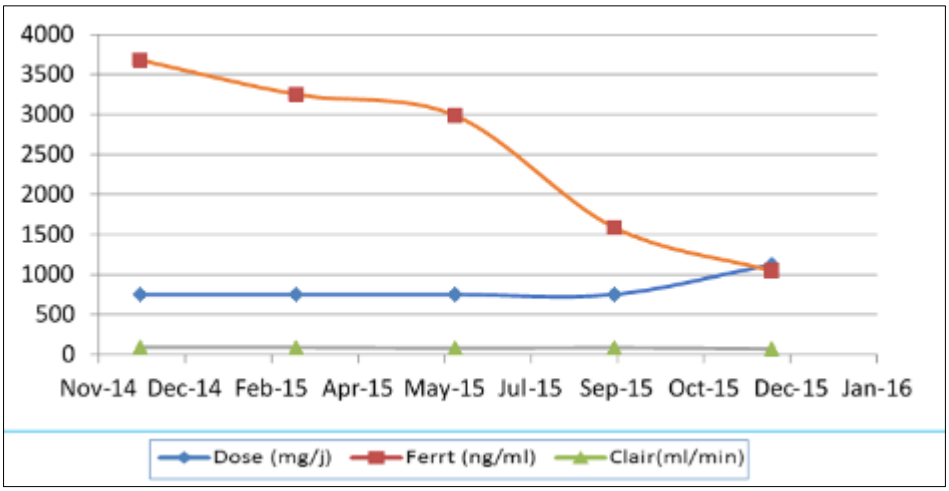

Figure 8 Correlation between the doses of deferasirox taken and the improvement of both ferritin levels and creatinine clearance (profile 5)

These results show that all patients have normal kidney function and no cases of renal insufficiency or toxicity have been observed. However, a certain tendency towards a decrease in creatinine clearance is observed, hence the need for continuous monitoring [10,11]. It should be noted that even if the patients are well monitored, complications of thalassemia will gradually but late onset [5,6]

4. Conclusion

Enhancing adherence to long-term chelation therapy is likely the primary route to improving survival in children with major thalassemia. This can be achieved by consolidating the pharmacist-patient relationship through the integration of pharmaceutical practices. Additionally, the concept of clinical pharmacy should be introduced and widely adopted. This includes interactions with caregivers and patients, as well as monitoring and supervising responses to drug treatments.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors and all co-authors declare that they have no conflicts of interest in connection with this document, and the material described is not in the process of being published nor is it intended for publication elsewhere.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Cao, A., & Galanello, R. (2010). Bêta-thalassemia. Genetics in medicine, 12(2), 61-76.

[2] Borgna-Pignatti, C., Rugolotto, S., De Stefano, P., Piga, A., Di Gregorio, F., Gamberini, MR., ... & Cappellini, MD. (2004). Survival and complications in patients with thalassemia major treated with transfusion and deferoxamine. Haematologica, 89(10), 1187-1193.

[3] Farmaki, K., Tzoumari, I., Pappa, C., Chouliaras, G., Berdousi, H., & Perifanis, V. (2011). Deferasirox: a new hope for the treatment of iron overload in patients with β-thalassemia. European Journal of Haematology, 86(1), 1-9.

[4] Cappellini MD, Cohen A, Porter J, Taher A, Viprakasit V. Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT). 3rd ed. Nicosia, Cyprus: Thalassaemia International Federation; 2014.

[5] Li, A., Li, X., Li, H., Ma, Q., & Xu, Y. (2021). The application of clinical pharmacy in the management of β-thalassemia patients with deferasirox treatment. Journal of Clinical Pharmacy and Therapeutics, 46(5), 1198-1204.

[6] Ladis V, Chouliaras G, Berdousi H, Kanavakis E, Kattamis C. Longitudinal study of survival and causes of death in patients with thalassemia major in Greece. Ann N Y Acad Sci. 2005 ;1054 :445-450. Doi : 10.1196/annals.1345.062.

[7] Musallam, KM., Cappellini, MD., Wood, JC., Motta, I., Graziadei, G., Tamim, H., & Taher, AT. (2012). Elevated liver iron concentration is a marker of increased morbidity in patients with β thalassemia intermedia. Haematologica, 97(11), 1605-1612.

[8] Porter J, Garbowski M. The Cost-Effectiveness of Iron Chelation Therapy for Patients with Beta-Thalassemia Major. PharmacoEconomics. 2017 ;35(3) :333-349. doi : 10.1007/s40273-016-0483-y.

[9] Amirkhosravi A, Mousa SA, Amaya M, Blaydes S, Desai H, Meyer T. The pharmacoeconomics of iron chelation therapy in transfusion-dependent thalassemia patients: a US perspective. J Med Econ. 2011 ;14(4) :427-435. Doi : 10.3111/13696998.2011.582980.

[10] Davis BA, Porter JB. Long-term outcome of continuous 24-hour deferoxamine infusion via indwelling intravenous catheters in high-risk bêta-thalassemia. Blood. 2000 ;95(4) :1229-1236.

[11] Taher, AT., Saliba, AN., & Kattamis, A. (2018). Deferasirox: challenging the role of deferoxamine as a standard of care in transfusion-dependent thalassemia. European Journal of Haematology, 100(6), 535-545.