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Full Length Research Paper

Beta thalassemia major: The Moroccan experience

M. Agouzal[1]*, A. Arfaoui[1], A. Quyou[1] and M. Khattab[2]

[1]Biological Assays Laboratory, Ibn Tofail University, Morocco.
[2]Hemato-oncology Service, Ibn Sina hospital, Rabat, Morocco.

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Thalassemia has been described originally around the Mediterranean Sea. The main objective of this study is to find out how Morocco deals with it. It is a retrospective study which has been done in the hemato-oncology service that treats patients with beta thalassemia major who are registered for receiving blood transfusions. With sample size of 78, demographics, clinical and family data were collected and descriptive statistics were done in the Biological Assays Laboratory in Kenitra, which lasted for three months. Age ranges from 5 to 10 years. 20 and 30 kg is the most common weight of patients with thalassemia. 61% are issued from consanguineous marriages. All patients are transfused but only 14% are not chelated as they have a ferritinnemia rate < 1000 ng/ml. Among these patients 74% are low-income earners. These results confirm that thalassemia is a reality in our country. A public health policy towards this disease is highly recommended.

Key words: Beta thalassemia major, complications, treatments, consanguinity, Morocco.

INTRODUCTION

There is no national registration for thalassemias, the only reference centre is the Hemato-Oncology Service in the Avicennes Hospital in Rabat. Other treatment centres are paediatrics, internal medicine and transfusion centres. This service is for certain number of patients with β-thalassemia major treated in Rabat but it also recruits thalassemia patients from the north of Morocco.

The objective addressed by this work is to describe patients with b-thalassemia major living in Morocco. It is very interesting to understand the difficulties encountered by clinicians who follow patients with b-thalassemia major, as well as those encountered by the patients themselves. Using this information, one can define the healthcare program needed in a particular context.

INCIDENCE OF B-THALASSEMIA MAJOR IN THE WORLD AND IN MOROCCO

Beta-thalassemias in Morocco are classified as the tenth in regard to annual conceptions in the eastern Mediterranean region (Modell and Darlison, 2008).

*Corresponding author. E-mail: agouzal.mouna@yahoo.fr.

Morocco is classified as the 28th country in regard to the percentage of carriers of beta thalassemia (3%), and the number of carriers of beta-thalassemia (445 thousands) and also for annual pregnant carriers (12000s) (Modell and Darlison, 2008).

In Morocco, thalassemias are spread in small towns. Its prevalence in the north of Morocco is 3.8* 10 - 3%. Towns like Aouamra and Mnasra have high beta-thalassemia major cases (Agouzal et al., 2009).

CLINICAL MANIFESTATION OF B-THALASSEMIA

Clinical sequelae of thalassemia includes: delay in growth and development, deformity of bones due to ectopic marrow expansion, osteopenia and most important iron overload.

It is iron overload in tissues that is eventually fatal in patients with or without transfusion dependency if not adequately treated with iron chelating therapy. In absence of chelating therapy, iron accumulates in and damages heart, liver, endocrine glands and reproductive organs. Onset of puberty is delayed and growth stunted. Deferoxamine has been the mainstay of iron chelation since its introduction in the 1980s (Smiers et al., 2009). However, patient acceptability and compliance were severely limited by the discomfort caused by the need of

Table 1. Descriptive study of the sample

Variables	Percentage (%)
Age (n = 76)	
(0 - 15)	73
(15 - 50)	27
Sex (n = 76)	
Female	44
Male	56
Weight (n = 40)	
(10 - 15)	15
(15 - 30)	45
(30 - 55)	40
Consanguinity (n = 63)	
Absent	39
Present	61
Socio-economic level(n = 65)	
Low-income	74
Assured	26

daily subcutaneous infusion of the drug. The introduction of oral iron chelator Deferasirox has dramatically improved the patient acceptability of chelation. It remains to be seen whether this will consistently translate into improved compliance and optimal iron chelation.

Research is ongoing on the potential role of deferiprone, an oral iron chelator, which may be more effective in reversing cardiac iron overload. Efficacy was shown, but side effects like agranulocytosis are sometimes serious and affect widespread introduction. In combination with other chelators, synergistic chelation can sometimes be achieved. Currently iron overload induced cardiac death still is the main cause of death in transfused thalassemia patients.

MATERIALS AND METHODS

Population

Sample size is 78. The study was done during three months in 2009.

Inclusion criteria

The samples were all β thalassemia major patients who undergo monthly transfusion and are also perfused by deferoxamine if it is available by the service. The sign of chelation treatment is hemo-chromatosis. In general, patients should start iron chelation after receiving 10 to 20 transfusions, or when their ferritin level exceeds 1000 mg/l.

Treatments prescribed are deferoxamine and deferiprone:

a) Deferoxamine is monitored by a pump specially designed to slowly infuse the drug under the skin for 8 - 12 h, at least 6 days (a week). The exact dose of each patient is calculated on the basis of age, body iron load, and clinical conditions. In the hemato-oncology service, desferal powder is freely soluble in salted serum.

b) Deferiprone is an oral chelating agent. Each capsule has a dose of 250 or 500 mg. For adults and children, the minimal dose of kelfer to achieve a negative balance is 75 mg/kg/day divided into 2 to 4 doses.

Exclusion criteria

Patients with b-thalassemia intermediate. There is a genotype for 60 from the patients included.

Data collection

Data collection on patients with thalassemia was done by visiting transfusion rooms in the service of the hospital. The coordinator of the study was the chief of the service.

We used a data collection sheet that was filled using the computerized register of the service. This sheet was also filled using patients' medical files which contain medical information (Demographics, family survey, treatment received, electrophoretic analysis and evolution).In some cases, we referred to the personal monitoring notebook of the patient. We also interviewed parents of the patients to complete information.

Variables analyzed

To achieve the objectives, the data collected was described clearly: age, weight, clinical complications, treatments and consanguinity as shown in table 1. The statistical analysis was done in the laboratory of biological assays in the Ibn Tofail University in Kenitra.

Data was recorded on MS Excel spreadsheet program. We used SPSS for the descriptive statistics. SPSS's version is 11:5:1 and it is manufactured by IBM compagny.

RESULTS

The distribution of the number of patients shows that age groups between 5 and 10 years old are mostly affected by this disease. The mean age is 10 ± 5 years. Beyond 15 years, the number of cases decreases (Figure 1).

The distribution of thalassemia patients according to sex shows male predominance with a sex ratio of 1:3. However, there is no significant difference between male and female regarding the occurrence of the disease ($p = 0.2$). 20 and 30 kg is the most common weight of patients with thalassemia because mostly affected patients were aged between 0 and 15 years. The average weight is 27 ± 11 kg.

The patients issued from consanguineous marriages are affected by the disease with a rate of 57 and 43% are issued from non-consanguineous marriage.

A study done recently in the same service among 193 thalassemia patients and that includes the 78 beta-thalassemia patients studied (Khattab, 2008), showed

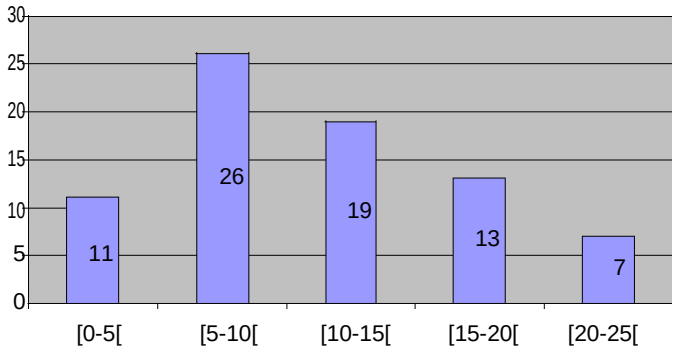

Figure 1. Age brackets of patients (by frequency).

that complications of thalassemia (Table 2) are: delay of puberty (63%), hypoparathyroidism (4.6%), diabetes(7%), deformity of bones(4.6%) and hearth complications (6%). Among these patients, six deaths were registered:

Two deaths were due to diabetes, two deaths were due to heart failure and to splenic sequestration and recently a patient died from an alloimmunisation.

All patients are transfused monthly. For transfusional safety, patients are vaccinated by engerix B (it is a vaccine developed for the prevention of hepatitis B virus infection). 80% of patients are chelated. 7% of patients combine deferiprone and deferoxamine. Only one patient takes deferoxamine alone. Two patients take deferasirox. Of these patients 66% take deferiprone alone. 41% of patients with thalassemia are splenectomised (mean age is 12.34 year). When thalassemia patients are splenectomised, they develop infections, so physicians prescript antibiotics: Oracilline is taken every day while Extencilline is taken every 15 days by low-income patients. Oracilline and extencilline are princeps molecules.

Other treatment options are corticotherapy and allograft. Corticotherapy was performed among 9 patients and only one thalassemia patient received an allograft abroad. One patient is candidate for allograft and will do it abroad.

Genotypes of 60 patients

In beta-thalassemia major patients issued from different regions in Morocco, 24 mutations were identified (Modell and Darlison, 2008; Agouzal et al., 2009):

1) 16 mutations.
2) VSII-729 (A → G) reported for the first time.
3) Seven mutations (identified among 65% of the 120 chromosomes):

i) Codon 39 (C →T).
ii) Frame shift codon 8 (-AA)
iii) IVSII-745 (C→G).
iv) Frame shift codon 6 (-A).
v) 29 (A→G).
vi) IVSI-1 (G→A).
vii) IVSI-110 (G→A) : It is a mutation very frequent in the Mediteranean sea (Perrin P. Les thalassémies, témoins des migrations préhistoriques dans le bassin méditerranéen : Projet mené par le centre de Génétique Moléculaire et Cellulaire).

DISCUSSION

The fact that the number of patients with thalassemia decreases beyond 15 years could be explained by death mostly among children older than 15 years. This can be explained by the fact that if children are not transfused, they die before the age of 6 years and if they are transfused and non-chelated, they die before the age of 20.

According to a study done about consanguineous marriages in Morocco, the overall prevalence of diseases issued from consanguineous marriages reached 66.22 and 47% among non-consanguineous ones (Danilo, 2009). The prevalence of b-thalassemia major is especially high in countries where there are close family marriages (Ghosh et al., 2008).

Comparison of the prevalence of complications with other reports shows that delay of puberty is higher in Morocco than in the other countries.The prevalence of diabetes, hearth complications and hypoparathyroidy varies among countries (FIT study, Cyprus and Iran) but it is higher in Italy. Presented percent for heart complications (6%) is very lower than other reports and in the study done in Italy (69%) (Gamberini et al., 2004). Deaths investigations show that a patient died because of diabetes and another by heart failure. Death by heart failure was noted in a thalassemia patient during a study done in Casablanca. Diabetes and heart failure are serious complications due to iron overload.

The analysis of survival rates according to the age shows that patients that are daily perfused with deferoxamine have a survival rate of 100%. Patients who are perfused three times a week die at the age of 32 years, unlike people who can die at the age of 22 years when they are not perfused. Therefore, the chelating treatment improves the survival rate of patients with thalassemia. The traditional chelator is deferoxamine. The new compounds deferiprone and deferasirox are currently the mostly used (Ronson and Hershko, 2008). When deferoxamine is available in the service, 27% do not take deferoxamine regularly because of long parenteral administration. In France as well, it appeared that 20 to 40% of patients were not compliant with deferoxamine because it is chro-nic, repetitive, and administered every day (Girot et al., 2006). Only 9 patients received corticosteroids because they are administered due to auto-immune complication (Michallet and Coiffier, 2006).

Table 2. Prevalence of complications among countries

Complications	Prevalence % (children hospital) (El Khattab, 2008)	Prevalence % (De Sanctis et al., 2004)	Prevalence % (Gamberini et al., 2004)	Prevalence % (Toumba et al., 2007)	Prevalence % (Karamifar et al., 2003)
Delay of puberty	63	40.5	-	35	-
Diabetes	9.2	3.2	15	9.4	7.3
Hearth complications	6		69		
Hypoparathyroidy	4.6	6.9	21	1.2	7.3

The allograft treatment is based on a transplantation of a donor to a receptor issued from the same biological species, but being two distinct individuals. The donor and receptor complexes have different major histocompatibility complex.

The following information must be involved in selecting a donor:

a) The donor must have an HLA compatible (Girot, 2003).

b) The best results are observed in patients whose ferritin is lower than 3 000 ng/ ml, and who have received regular chelation by deferoxamine (Girot, 2003).

c) Patients who have a ferritin greater than 3 000 ng/ ml and were not subject to regular chelation by deferoxamine are not the best candidates for transplantation because the risk of complications in the short and medium term is high (Girot, 2003).Thus, only two patients were candidates for an allograft that has been successful because they met the requirements.

Morocco is part of the Mediterranean countries mostly affected by thalassemia which is highly concentrated in small towns. We are facing too many problems like poor management, as the disease is not taken as a high priority for authorities, also the lack of awareness of people as most of them do not know how to deal with symptoms of the disease; finally the lack of chelating treatments in hospitals (Except donations and some parents able to pay their treatments or are insured).

To come up with these problems, a project named 3H#59779 made in collaboration between the service, the association of thalassemia and hemoglobinopathies and Rotary international. The project will take place from 2007 to 2011. Its objective is to assure a free screening to stop spreading of the disease. Up till now, 4000 cases were analyzed. Also the project aims to inform students in the high schools of the severity of the disease. Sensibilization invites them to do the screening so as to diagnose carriers of the disease. Sensibilization aims also to increase awareness of people about the symptoms of the disease and incite them to consult the physicians, once they notice symptoms to avoid serious complications of the disease.

Finally, the project receives donations especially from Italy to overcome the problem of lack of chelator drugs.

Conclusion

Thalassemia represents a reality in our country. It must be taken as a public health problem and a long term policy will allow competent volunteers to reach objectives assigned by the project.

REFERENCES

Agouzal M, Quyou A, Khattab M (2009). Prévalence de la thalassémie dans la région Nord-Ouest du Maroc. Revue Marocaine des Maladies de L'Enfant (In press).

Danilo C. Mariage : ces marocains consanguins. La gazette du Maroc [En ligne]. 2009 ; n°611[13/05/2009] disponible au site web : http://www.lagazettedumaroc.com/articles.php?r=7&n=611.

De Sanctis V, Eleftheriou A, Malaventura C (2004). Prevalence of endocrine complications and short stature in patients with thalassaemia major: a multicenter study by the Thalassaemia International Federation (TIF).Pediatr Endocrinol Rev. 2:249-55.

Gamberini MR, Fortini M, De Sanctis V, Gilli G, Testa MR (2004). Diabetes mellitus and impaired glucose tolerance in thalassaemia major: incidence, prevalence, risk factors and survival in patients followed in the Ferrara Center. Pediatr Endocrinol Rev., 2:285-291.

Ghosh S, Bandyopadhyay SK, Bandyopadhyay R, Roy D, Maisnam I, Ghosh MK (2008). A study on endocrine dysfunction in thalassaemia. J Indian Med. Assoc., 106 (10):655-656, 658-659.

Girot R (2003). La bêta-thalassémie. Enc. Orphanet. p 9, 10 available on line on http://www.orpha.net/data/patho/FR/fr-betatha.pdf.

Girot R, Hagège I, Jean-François Deux, Lionnet F (2006). Traitement de la surcharge en fer dans les maladies hématologiques (Hémochromatoses héréditaires exclues). Hématologie.12: 181-193.

Karamifar H, Shahriari M, Sadjadian N (2003).Prevalence of endocrine complications in beta-thalassaemia major in the Islamic Republic of Iran. East Mediterr. Health J. 9 (1-2):55-60.

Michallet A, Coiffier B (2006). Anémie et hémopathies lymphoïdes chroniques. Hématologie.12: 3-9.

Modell B, Darlison M (2008). Global epidemiology of haemoglobin disorders and derived service indicators.Bulletin of the World Health Organization. 86:480-487.

Ronson A, Hershko C (2008). Progress in the treatment of iron chelator. Hematology.14 : 378-85.

Smiers FJ, Krishnamurti L , Lucarelli G (2009). Hematopoietic Stem Cell Transplantation for Hemoglobinopathies: current practice and emerging trends. Pediatric Clinic of North America. 57(1): 181-205.

Toumba M, Sergis A, Kanaris C, Skordis N (2007). Endocrine complications in patients with Thalassaemia Major. Pediatr. Endocrinol. Rev. 5(2):642-8.