Revista Brasileira de Hematologia e Hemoterapia
Brazilian Journal of Hematology and Hemotherapy
www.rbhh.org

Original article

Study of enzyme replacement therapy for Gaucher Disease: comparative analysis of clinical and laboratory parameters at diagnosis and after two, five and ten years of treatment

*Ana Maria Almeida Souza**, *Thiago Pimentel Muniz*, *Rafael Maciel Brito*

Universidade Federal do Pará (UFPA), Belém, PA, Brazil

ARTICLE INFO

Article history:
Received 7 September 2013
Accepted 17 March 2014
Available online 28 May 2014

Keywords:
Gaucher disease
Enzyme replacement therapy
Anemia
Splenomegaly

ABSTRACT

Objective: To evaluate the impact of enzyme replacement therapy for Gaucher Disease on clinical and laboratory parameters after two, five and ten years of treatment.
Methods: Data were collected from patient records and analyzed using BioEstat software (version 5.0). Student's t-test, Analysis of Variance (ANOVA), Wilcoxon test and Kruskal–Wallis test were used for statistical analysis. Hepatomegaly and splenomegaly were analyzed using the Kappa test.
Results: There was a significant increase in hemoglobin levels (p-value <0.01) and platelet counts (p-value = 0.01) within two years of therapy. At the same time, the frequencies of splenomegaly (p-value <0.01) and hepatomegaly (p-value <0.05) reduced. These results were similar at five and ten years of enzyme replacement therapy.
Conclusions: There are substantial and quick (within two years) laboratory and clinical responses to enzyme replacement therapy. These improvements continue as long as enzyme replacement therapy is administered every two weeks, as recommended by the literature.

© 2014 Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular. Published by Elsevier Editora Ltda. All rights reserved.

Introduction

Gaucher Disease (GD) is a recessive autosomal hereditary disorder classified as an inborn error of the metabolism. It is the commonest lysosomal storage disease and was the first one for which a specific treatment was developed. It occurs due to a deficiency in the activity of the enzyme β-glucosidase and is characterized by the intra-lysosomal accumulation of glucocerebroside in reticuloendothelial system cells.[1] The enzyme deficiency is caused by a mutation in the β-glucosidase gene, located on chromosome 1 (GBA1).[2] GD is a rare pan-ethnic disorder, but it presents a high incidence among Ashkenazi Jews. The worldwide incidence is estimated at from 1:50,000

* *Corresponding author at*: Instituto de Ciências da Saúde, Faculdade de Medicina da Universidade Federal do Pará, Praça Camilo Salgado, 1, Umarizal, 66050-060 Belém, PA, Brazil.
E-mail address: anamas@oi.com.br (A.M.A. Souza).
http://dx.doi.org/10.1016/j.bjhh.2014.05.005
1516-8484/© 2014 Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular. Published by Elsevier Editora Ltda. All rights reserved.

to 1:100,000 live newborns,[3] whereas the incidence in the Jewish population ranges from 1:400 to 1000 live newborns in the USA.[4]

Clinically, GD presents a wide variety of signs and symptoms and is classified as non-neuronopathic (Type 1) or neuronopathic (Types 2 and 3). Type 1 GD (95% of cases) usually manifests with splenomegaly, hepatomegaly, anemia, thrombocytopenia, bone disease and delayed growth.[5] Type 2 is characterized by a precocious and fast brainstem degeneration;[3] these patients do not respond to treatment and death occurs within the first two years of life.[6] Type 3 GD patients have a slow evolving neurologic disease and usually present with seizures, eye movement abnormalities and mild systemic involvement with mean survival being to the third decade of life.[7] The treatment of GD is based on enzyme replacement therapy (ERT), initially by alglucerase,[8] but this was widely substituted by its therapeutic equivalent, imiglucerase.[9] Accordingly to Brazilian Ministry of Health, there were 610 ERT-dependent patients in the country in 2010. There are no data concerning the national incidence of the disease.[10]

The objective of this study was to evaluate the impact of ERT on clinical and laboratory parameters of GD through a comparative analysis of data at diagnosis and after two, five and ten years of treatment in a population from Pará State, Brazil.

Methods

This was an analytical observational longitudinal retrospective study (historical cohort) of patients at the Fundação Centro de Hemoterapia e Hematologia do Pará (HEMOPA), Belém, Pará State. The patients were diagnosed with non-neuronopathic (Type 1) and neuronopathic (Type 3) GD and were treated and followed-up at HEMOPA between 2000 and 2011.

The inclusion criteria for the study were to have a confirmed diagnosis of GD and to be treated and followed-up at HEMOPA for at least 24 months. Clinical records prior to treatment were also necessary.

Data were collected from patient records using a questionnaire designed for this study. This questionnaire included the following items: demographic characteristics, genetic profile, ERT dose, hematological aspects (hemoglobin levels, white cell count and platelet count) and clinical manifestations (splenomegaly, hepatomegaly and neurological symptoms). Data were collected at four different time points: at diagnosis and after two, five and ten years of ERT. Diagnosis was defined as the time when Gaucher's cells and/or the β-glucosidase deficiency were identified. Data concerning the two-, five- and ten-year time points were collected based on the first administration of ERT. This study was approved by the Ethics Committee of HEMOPA (register # 0016.0.324.324-11).

Statistical analysis

Data were placed in tables and graphs drawn using the Microsoft Excel 2010 software. ERT doses, hemoglobin levels, white cell count and platelet count over time were analyzed using Student's *t*-test, Analysis of Variance (ANOVA), Wilcoxon and Kruskal–Wallis tests, as applicable. Splenomegaly and hepatomegaly were analyzed using the Kappa test. All results with p-values <0.05 were considered significant and tests were carried out using the BioEstat (version 5.0) software.

Results

Demographic characteristics

Records of 24 patients diagnosed with GD were found and of these, 13 met the inclusion criteria. Eight were female (61.50%) and five were male patients (38.50%). Ages ranged from four to 43 years (mean: 24.53 years). Thirteen patients (100%) were on ERT for two years; nine (69.23%) had completed five years of treatment and six patients (46.15%) had been treated for ten years. In order to preserve patients' identity, they are numbered 1 through 13.

At diagnosis, the mean age of patients was 13.49 years old (±30.10 years). Eight patients (61.53%) were under 12 years old at diagnosis (patients 1, 3, 4, 5, 8, 11, 12 and 13), three (23.07%) were women over 12 years (patients 6, 9 and 10) and two (15.4%) were men over 12 years (patients 2 and 7). Only one patient (7.7%) was diagnosed with Type 3 GD; this patient died at age 22 after ten years of treatment. All other patients were diagnosed as Type 1.

Genetic profile

Ten patients (76.92%) were submitted to GBA1 mutation analysis with the frequencies of the mutations listed in Fig. 1.

ERT dose

ERT was administered every two weeks. Table 1 shows the amount of enzyme (IU/kg) given to each patient during the study intervals.

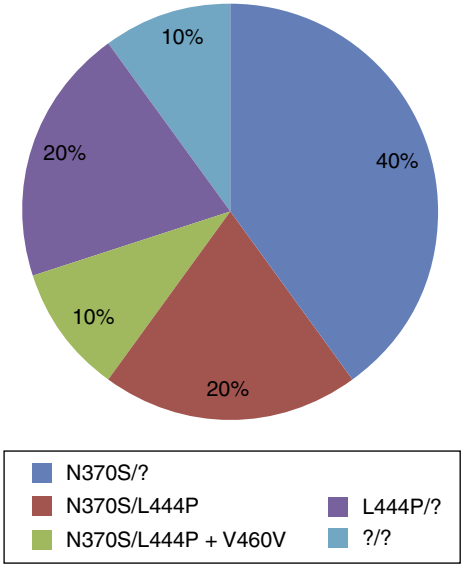

Figure 1 – Frequency of mutations in patients with GD submitted to GBA1 analysis at HEMOPA.

Download English Version:

https://daneshyari.com/en/article/3333081

Download Persian Version:

https://daneshyari.com/article/3333081

Daneshyari.com