ORIGINAL ARTICLE

QUALITY OF LIFE OF PATIENTS WITH GAUCHER DISEASE

QUALIDADE DE VIDA DE PACIENTES COM DOENÇA DE GAUCHER

CALIDAD DE VIDA DE PACIENTES CON ENFERMEDAD DE GAUCHER

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ABSTRACT

Objective: to evaluate the quality of life of patients with Gaucher disease. Method: this is a quantitative, descriptive study, based on case studies, performed in 17 patients with Gaucher disease. Patients older than 12 years old were excluded, and those with associated diseases that affect cognition, severe motor impairment, and those who did not adhere to Enzyme Replacement Therapy were excluded. Questionnaires for socio-demographic evaluation and the SF-36 to evaluate the quality of life were used. Data were analyzed by Microsoft Office Excel®-2013 Software and the results were presented in tabular format. Results: It was observed that the dimensions with lower averages were general health status (57.6) and vitality (64.3) and the ones with higher averages were limitations due to emotional aspects (98.1) and limitations due to physical aspects (88.2). Conclusion: patients with enzyme replacement therapy presented above-average quality of life. Descriptors: Gaucher Disease; Metabolism Inborn Errors; Quality of Life.

RESUMO

Objetivo: avaliar a qualidade de vida de pacientes com doença de Gaucher. Método: estudo quantitativo, descritivo, a partir de análises de casos, realizado em 17 pacientes com doença de Gaucher. Foram selecionados pacientes com faixa etária acima dos 12 anos de idade e excluídos aqueles com doenças associadas que afetasssem a cognição, acometimento motor severo e os que não aderiram à Terapia de Reposição Enzimática. Utilizou-se questionários para avaliação sociodemográfica e o SF-36 para avaliar a qualidade de vida. Os dados foram analisados pelo Software Microsoft Office Excel®-2013 e os resultados foram apresentados em formato de tabelas. Resultados: observou-se que as dimensões com menores médias foram de estado geral de saúde (57.6) e vitalidade (64.3), e as com maiores médias foram limitações por aspectos emocionais (98.1) e limitações por aspectos físicos (88.2). Conclusão: apresentaram qualidade de vida acima da média os pacientes que realizam terapia de reposição enzimática. Descritores: Doença de Gaucher; Erros Inatos do Metabolismo; Qualidade de Vida.

RESUMEN

Objetivo: evaluar la calidad de vida de pacientes con enfermedad de Gaucher. Método: estudio cuantitativo, descriptivo, a partir de análisis de casos, realizado en 17 pacientes con enfermedad de Gaucher. Fueron seleccionados pacientes con edad mayor que los 12 años, y excluidos aquellos con enfermedades asociadas que afectasen la cognición, acometimiento motor severo y los que no se adherieron a Terapia de Reposición Enzimática. Se utilizaron cuestionarios para evaluación sociodemográfica y el SF-36 para evaluar la calidad de vida. Los datos fueron analizados por el Software Microsoft Office Excel®-2013 y los resultados fueron presentados en formato de cuadros. Resultados: se observó que las dimensiones con menores medias fueron de estado general de salud (57.6) y vitalidad (64.3) y las con mayores medias fueron limitaciones por aspectos emocionales (98.1) y limitaciones por aspectos físicos (88.2). Conclusión: presentaron calidad de vida arriba de la media los pacientes que realizan terapia de reposición enzimática. Descriptores: Enfermedad de Gaucher; Erros Innatos del Metabolismo; Calidad de Vida.

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INTRODUCTION

Gaucher disease (GD) is a lysosomal reservoir disease with an autosomal recessive inheritance characterized by a deficiency in the activity of acid beta-glucosidase or beta-glucocerebrosidase, which causes the accumulation of glycolipids in macrophages, also called Gaucher cells, especially in spleen, liver, bone marrow and lung. GD may also present in the central nervous system by accumulation of endogenous glycosphingolipid metabolites in brain tissue.1

GD is a pan-ethnic disease and it has a global incidence estimated at 1:40,000-60,000 entering the rare diseases group because of this ratio. However, among the Ashkenazi Jews, the estimate ranges from 1:500-800 individuals.1 After the United States and Israel, Brazil is the third country in the world with the highest number of patients diagnosed with GD. According to the International Collaborative Gaucher Group (ICGG Gaucher Registry) of April 2010, there were more than 550 cases diagnosed in the country.2

The GD is classified into three types, according to the presence or absence of progression of neurological manifestations. In more than 90% of the cases, the GD is present in a neuropathic form or Type 1. It has a varied phenotype, with manifestations that can appear in childhood or in adult life. The most frequent findings are hepatosplenomegaly, hematological anomalies (anemia and thrombocytopenia) secondary to hypersplenism and hematopoiesis, as well as skeletal disease, secondary to the infiltration of Gaucher cells into the bone marrow, promoting bone pain and osteonecrosis.1 Neuropathic presentations, Type 2 and 3, are characterized by the primary involvement of the central nervous system, and even the visceral frame, leading to early death.1 Clinical diagnosis is given through morphological findings such as anemia with hemoglobin and platelets below the recommended parameters, enzymatic and molecular analyses.3 The gold standard for clinical diagnosis is the demonstration of the low activity of acid β-glycosidase in peripheral blood leukocytes.1,3

Delayed diagnosis and lack of appropriate treatment can lead to severe complications and permanent sequels.4 However, the scientific literature is unanimous in recognizing the benefits of Enzyme Replacement Therapy (ERT) in patients with GD, a treatment that consists of the replacement of the deficient enzyme.4 This has been shown to be safe and effective in preventing, reducing and/or reversing some aspects of bone diseases, hematological and visceral manifestations, bringing a better quality of life.4,5

According to the World Health Organization (WHO), quality of life is defined as the individual's perception of their position in life, in the context of culture, value systems in which they live in relation to their goals, expectations, standards, and concerns.6 Thus, the presence of the disease results in damages to the individual, since they add physical, emotional and social difficulties in their daily lives.7

In the context of chronic diseases, the evaluation of quality of life has been a focus of important studies, since the emergence of different treatments for these diseases favors the control of symptoms and delays its evolution.8

OBJECTIVE

- To analyze the quality of life of patients with Gaucher disease who undergo enzyme replacement therapy at a Center for Inborn Errors of Metabolism.

METHOD

This is a quantitative, descriptive study, based on character case analyses, in which patients participated in the Center for the Treatment of Inborn Errors of Metabolism (CETREIM) of the Integral Medicine Institute Prof. Fernando Figueira (IMIP), reference hospital in the Northeast Region of Brazil.

The sample was selected by the non-probabilistic technique for convenience9, in the period between September and November 2014. The inclusion criteria used for the evaluation of socio-demographic characteristics and quality of life were patients with Gaucher’s disease and age above 12 years old. As exclusion criteria, the presence of associated diseases that could lead to cognitive sequels and severe motor impairment that would prevent the patient from responding to the questions asked and patients who did not join the Enzyme Replacement Therapy was used.

The data collections were performed at CETREIM - IMIP, daily during the data collection period, by two previously trained examiners. Initially, the participants were identified through a socio-demographic data sheet, with clinical and personal data. The SF-36 Quality of Life questionnaire was then applied.

The SF-36 (Medical Outcomes Study 36) is a generic instrument composed of 36 items organized in eight subscales. Four of them
assess physical health status (PHS): functional capacity (FC), physical aspects (FA), emotional aspects (EA) and pain. The rest deal with the state of mental health (MHS): general health (GH), vitality (VT), social aspects (SA) and mental health (MH). Higher scores are associated with better QOL, and may range from 0 to 100.

The data were tabulated and analyzed using the Microsoft Office Excel®-2013 Software, where data were tabulated in a database and presented in tables and charts to characterize the investigated sample by medians, standard errors, absolute and relative frequencies and maximum and minimum values of the variables classes.

The study was approved by the Research Ethics Committee of the Integral Medicine Institute Prof Fernando Figueira - IMIP, under CAAE: 32134314.2.0000.5201.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N = 17</th>
<th>%</th>
<th>Standard Error (±)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset of clinical manifestations (years)</td>
<td>Median = 9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 - 11</td>
<td>11</td>
<td>64.7</td>
<td>±0.85</td>
</tr>
<tr>
<td>12 - 59</td>
<td>5</td>
<td>29.4</td>
<td>±3.7</td>
</tr>
<tr>
<td>≥60</td>
<td>1</td>
<td>5.9</td>
<td>0</td>
</tr>
<tr>
<td>Age at diagnosis (years)</td>
<td>Median = 14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 - 11</td>
<td>6</td>
<td>35.3</td>
<td>±0.6</td>
</tr>
<tr>
<td>12 - 59</td>
<td>9</td>
<td>52.9</td>
<td>±3.7</td>
</tr>
<tr>
<td>≥60</td>
<td>2</td>
<td>11.8</td>
<td>±1.6</td>
</tr>
<tr>
<td>Age of onset of TER</td>
<td>Median = 14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 - 11</td>
<td>4</td>
<td>23.5</td>
<td>±0.6</td>
</tr>
<tr>
<td>12 - 59</td>
<td>11</td>
<td>64.7</td>
<td>±3.6</td>
</tr>
<tr>
<td>≥60</td>
<td>2</td>
<td>11.8</td>
<td>±1.7</td>
</tr>
<tr>
<td>Presenting adverse reaction to ERT</td>
<td>Yes</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>17</td>
<td>100</td>
</tr>
</tbody>
</table>

The data presented in Table 1 present clinical data regarding the patients evaluated. The median age of onset of clinical manifestations was 9 years old, presenting a higher percentage between 1-11 years old (64.7%). When referring to the median age of diagnosis, it was noticed an increase of 5 years, the highest percentage being between the range of 12-59 years old (52.9%). The median age at the beginning of ERT was 14 years old, maintaining the same range as the diagnosis, from 12-59, increasing its percentage of patients to 64.7%. And another aspect observed is that 100% of the patients never presented adverse reactions to the treatment.

**RESULTS**

Twenty-two patients with Gaucher Disease were evaluated in this study and 17 of them were included. The others were excluded because they did not meet the inclusion criteria.

Of the subjects evaluated, it was observed that most of them were female (64.7%), adults, aged between 19 and 59 years old (64.7%), with a median of 26 years old. Patients to be evaluated, ranging from 14 to 78 years old, single marital status (52.9%), brown (70.6%), participants of the Catholic religion (52.9%) with an average of education level of 10.6 years, where most of them studied between 9-11 years (58.8%) were excluded. As for the work situation, 76.5% received some type of income, ranging from 1 to 6 minimum wages (64%).
The values of the domains evaluated by the SF-36 are shown in Table 2. Among the patients with GD in ERT in the evaluated dimensions, the ones with the lowest average were the general health status domains (57.59 ± 15.9) and vitality (64.29 ± 17.3). The highest average was limited by emotional aspects (98.05 ± 8) and limitations due to physical aspects (88.23 ± 26.7). However, when the minimum values are observed, it is noted that some patients scored 0 in the domains of limitations due to physical aspects and pain and in the other domains, the scores were below 67. No patient had the maximum value of 100 in the general state of health (82) and mental health (92).

### DISCUSSION

This study identified that the patients had an average education level of 10.9 years studied and that most of them did not attend educational institutions. In general, people with GD have normal intelligence, but cognitive acquisitions can be affected by deficits in social context, as well as by other physical limitations that they may present due to illness.

It was observed in this study that 23.5% of the participants were unemployed and 23.5% received the Continuous Social Assistance Benefit (BPC), which is a benefit of the social assistance policy where it integrates the basic social protection in the scope of the System Social Assistance (SUAS). It is a singular, non-lifelong and inalienable benefit that guarantees a monthly minimum wage for the elderly, sixty-five years old or older, and the disabled person of any age, with long-term difficulties, in the physical, mental, intellectual or sensory. In both cases, they prove ways of not guaranteeing their own livelihood, nor offered it by their families, for which the per capita family monthly income must be less than a quarter of the minimum wage in force.

According to data from the 2010 Brazilian Institute of Geography and Statistics (IBGE), the North and Northeast regions showed that the highest percentages of families survive that they earn up to a minimum wage as monthly labor remuneration. In this study, considering the value of the minimum wage of the year of data collection, it was observed that a large part of the patients (64.7%) live with family income above the IBGE statistics, this can impact in a way quality of life.

According to this study, the mean age at the onset of clinical manifestations is 17.7 years old. However, most patients presented characteristics in the first 11 years (64.7%). In another study carried out in Porto Alegre-RS, the mean age of the manifestations of the symptoms is varied, mainly affecting children and adults. The mean age of the diagnosis of the GD was 24.2 years old, corroborating with the literature that most diagnoses are confirmed in adolescence or adult life.

It can be inferred that the difficulty of recognizing the picture by the doctor is leading to an underreporting of the disease. Another factor that could contribute to the low prevalence of the GD would be its heterogeneity since the manifestations cover a wide clinical picture in the children's age group.

Although the study shows that most of the reported symptoms begin in childhood, ERT was started in the adult phase of these patients, with a mean age of 25.29 years old, about one year after the mean age of diagnosis. Early diagnosis and correct therapy are indispensable for a better quality of life for these patients. Since January 30, 2014, the Ministry of Health has presented Portaria 199, Establishing the National Policy for Integral Care to People with Illness, promotion, prevention, early detection, timely treatment, disability reduction and palliative care, contribute to the reduction of morbidity and mortality and secondary manifestations and to the improvement of the quality of life of the individuals.

The occasional infusion reactions are quite particular for each patient, so the need for pre-medication and its intensity must be assessed for each case. It was verified in this study that only 11.8% of the patients had any

<table>
<thead>
<tr>
<th>Domains</th>
<th>Mean (±)</th>
<th>Minimum</th>
<th>Maximum</th>
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<tbody>
<tr>
<td>Physical component</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional capacity</td>
<td>83.23 ±18.3</td>
<td>40</td>
<td>100</td>
</tr>
<tr>
<td>Physical aspects</td>
<td>88.23 ±26.7</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Ache</td>
<td>70.73 ±27.9</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>General Health Status</td>
<td>57.59 ±15.9</td>
<td>27</td>
<td>82</td>
</tr>
<tr>
<td>Mental component</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitality</td>
<td>64.29 ±17.3</td>
<td>20</td>
<td>100</td>
</tr>
<tr>
<td>Social aspects</td>
<td>87.53 ±17.1</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Emotional Aspects</td>
<td>98.05 ±8</td>
<td>67</td>
<td>100</td>
</tr>
<tr>
<td>Mental health</td>
<td>77.41 ±14.3</td>
<td>40</td>
<td>96</td>
</tr>
</tbody>
</table>
reaction the ERT, such as hypertension and hyperthermia. The SF-36 used in this study is an internationally recognized quality of life instrument.\textsuperscript{15} It is easy to understand, so there were no difficulties by the patients about its understanding.

Faced with the physical component and in relation to the functional capacity, which represents the independence to perform basic daily activities that require motor and cognitive abilities, the SF-36 evaluates both the presence and extent of limitations related to physical capacity.\textsuperscript{16} In this study, there was a mean score of 83.23 with a standard deviation of (±) 18.3. According to the literature the clinical manifestations of the GD are characterized by clinical heterogeneity, with visceral, hematological and musculoskeletal involvement, which may generate limitations in activities of daily life, and they may promote functional disability and impairment of quality of life.\textsuperscript{16,17}

The evaluation of physical and emotional aspects not only addresses the limitations in the type and quantity of work but also the extent to which these limitations hinder the patients to perform their work and daily life activities.\textsuperscript{15} Regarding physical aspects, it was observed that the mean was high, being 88.23 and in relation to the emotional aspects, the patients presented an average of 98.05, being this domain that presented a better average between the other scores of the evaluation of the quality of life, reflecting that there are no difficulties in their physical independence and the absence of anxiety or sadness, seemingly satisfied with these aspects. It is noteworthy that studies show characteristics that may be limiting individuals, such as skeletal manifestations that are associated with a high degree of morbidity, impact on daily, leisure and work activities.\textsuperscript{16,18}

Because they present clinical manifestations such as skeletal and visceral alterations, it is quite common for these individuals to present pain.\textsuperscript{5} The average pain that the patients with GD presented was 70.73, some scored 0 in this regard. In the same way as described in the literature, the treatment managed to minimize, but not completely abolish, the complaint of pain in some patients, but in fact, ERT has a beneficial effect to reduce pain in these patients, being an important factor for a good quality of life.\textsuperscript{16-18}

Under the item social aspects, mental health and vitality, participants were above average, 87.53, 77.41 and 64.29, respectively, indicating that they perform their social activities adequately and with little interference from physical or emotional problems.\textsuperscript{19,20}

The general state of health presented an average of 57.59, which evaluates the concept of general health perception, including not only current health but also disease resistance and healthy appearance. The literature justifies this finding, related to the domains in which the ERT did not extinguish symptoms. However, the average found corroborates findings found in studies comparing the QOL of patients with Brazilian and American GD.\textsuperscript{19,20}

**CONCLUSION**

The SF-36 questionnaire proved to be a significant instrument for the evaluation of the quality of life in patients with GD since it allowed to detect that the individuals who perform the ERT, have a perception of above average quality of life, and may suppose that some basic functions are not changed.

Regarding quality of life, the lowest score is related to the General State of Health, but it is above average and the highest scores observed were the Physical Aspects, Emotional Aspects, and Social Aspects, considering that quality of life is designated by the perception of the subject and depends on multiple factors, this data suggests that these individuals have a global perception of satisfactory quality of life.

It was also observed that the quality of life in patients with GD is still an unexplored topic since the disease is considered as rare and also due to the scarcity of studies published on this subject. Therefore, we reinforce the need to develop rigorous studies to evaluate the quality of life in this population.

**REFERENCES**


Freitas SEO, Ferreira TTC, Costa BGS et al.


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