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Application of the WHOQOL-100 for the assessment of quality of life of adult patients with inherited metabolic diseases

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ABSTRACT

Background: As advances in neonatal and pediatric care for patients affected by inherited metabolic diseases (IMD) improve their outcome and allow for better survival rates, there is a growing interest in the quality of life (QoL) of patients reaching adulthood. In order to address this subject we designed a study to evaluate the QoL of a group of adult IMD patients who are receiving various treatments, in a comprehensive manner.
Methods: A mixed-method study was conducted to assess the QoL in adult IMD patients. The multidimensional World Health Organization Quality of Life questionnaire (WHOQOL-100) was applied for quantitative evaluations, and an additional semi-standardized interview, was conducted for qualitative measurement of patients' perceptions of the impact of illness on their daily life, and the perceived adherence to their treatment recommendations. A total of 82 patients affected by IMD were enrolled. The inherited metabolic disorders included principally amino acids disorders, urea cycle defects, organic acidurias, carbohydrates disorders, and lysosomal disorders. The WHOQOL-100 and the semi-standardized interview were administered in a clinical setting to adult patients with IMD.
Results: The mean for the whole group indicates that adult patients with IMD can have a normal value of General QoL. Despite this value, the results of each domain show lower scores in the domains of perception of independence and quality of social relationships. We made a further analysis to compare the patients with dietary treatment with the patients with pharmacological treatment, and we observed a statistically significant difference in General QoL, in the Physical, Independence, Spiritual domains and in the facet of Medication.
These results suggest that Global QoL measures might not be sufficient to assess the QoL for adult patients with IMD. Furthermore, the implementation of a qualitative semi-standardized interview, especially suitable for adult patients, added important features on illness perception and on perceived adherence to the treatment by adult IMD patients.
Conclusion: In this study we underlined the importance of applying multidimensional instruments, like WHOQOL-100, to evaluate the quality of life of adult patients with IMD. The WHOQOL-100 has been demonstrated to be a valid instrument to measure the QoL of IMD patients.
Moreover, the administration of a tailored psychometric instrument in combination with a qualitative interview may help us to better characterize special issues related to IMD. Indeed, other factors beyond the physical manifestations of the disease, such as psychological wellbeing, social behavior, illness perception and adherence to the treatment, strongly influence QoL and may serve as valid targets for intervention to improve patients' care. We believe this kind of approach is especially useful for adult patients with inherited metabolic diseases.

1. Introduction

Inherited metabolic diseases (IMD) are rare genetic diseases generally due to inherited point mutations in genes coding for metabolic enzymes. Nowadays more than 500 diseases have been reported, and an increasing number of patients are reaching adulthood in improved condition due to advances in neonatal and pediatric care. These improvements are mainly due to early diagnosis and therapeutic interventions, which lead to prolonged and better survival rates for patients with IMD [1].

Abbreviations: IMD, Inherited metabolic diseases; PKU, Phenylketonuria; Phe, Phenylalanine; Tyr, Tyrosine; QoL, Quality of Life; WHOQOL-100, World Health Organization Quality of Life −100; CADASIL, Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy; ERT, Enzyme replacement therapy; IQ, Intelligence Quotient; WAIS-R, Wechsler Adult Intelligence Scale-Revised.

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In the near future early diagnosis, facilitated by expanded neonatal screening programs, will increase the number of patients with IMD, and likely improve their clinical outcome. Successful treatments, including nutrition therapy, enzyme replacement therapy (ERT), and organ transplants, have led to many of these patients surviving into adolescence and adulthood. However, the patient's burden of having a genetic metabolic illness cannot be solely assessed by objective parameters of the disease but also requires measuring personal perceptions.

To facilitate better patient care and compliance, there is a growing interest in evaluating the psychological and physical impact of a disease on a patient's everyday life. One possibility to measure these factors is by administering health-related quality of life (QoL) questionnaires to patients. Impairment of QoL has been described in children and adults with inborn errors of metabolism, particularly in phenylketonuria (PKU) [2,3]. Regarding the burden of dietary treatment for PKU patients, different studies have led to different conclusions. The study of Gassiò et al. [4] on the QoL of adult PKU patients seems to conclude that there is an improvement on QoL after resuming a strict low-Phe diet. Patients expressed they did not feel socially limited by their dietary regimen, but only 3 out of 15 participants had good treatment adherence. The instrument used in the study of Gassiò et al. had only 24 items, which in our opinion were not sufficient to deeply investigate QoL in such complicated circumstances as PKU, even if the items used were adapted by the authors according to issues considered of particular importance to PKU patients.

In the study of Bosch et al. [5] adult PKU patients had a normal QoL; however, this result might have been influenced by a bias regarding the administration of the questionnaire. Indeed, the authors sent the questionnaires by mail to all eligible patients and enrolled only patients who returned the filled-out form. In contrast, PKU patients (adolescents and adults) investigated by Simon et al. [2] reported lower or delayed autonomy. Also in this study, the instrument includes 40 items which measured physical, psychological and social capacity of performance and wellbeing, without considering other important aspects like the perception of independence, the subjective perception of dependence on a specific medical treatment, the perception of belonging to a safety contest, the perception of social care, and the patient's spiritual support. Moreover this study, as stated by the authors, had an important bias on patient selection [2]. Based on these considerations we can argue the importance of using a qualitative-interpretative methodology like semi-standardized interview for the evaluation of quality of life of IMD patients, as recently stated by MacLaughlin et al. and Vegni et al. [6,7].

The aims of our study were: 1) to apply a more detailed QoL questionnaire (the WHOQOL-100), different from traditional QoL questionnaires, which include a limited number of domains (e.g. SF-36), to adult patients with IMD; 2) the development of a qualitative semi-standardized interview, which is suitable especially for adult patients, to further understand which issues specifically affect the quality of life of IMD patients. By means of the open interview we focused on specific issues which appear fundamental for the evaluations of QoL in adult patients with IMD: the perceived impact of their illness and therapy on the QoL, and the perceived adherence to the treatment; 3) the investigation of the burden of dietary treatment in adult IMD patients, based on the results of the WHOQOL-100 and the semi-standardized interview.

Despite the clinical and genetic differences, adult IMD patients share many problems and challenges: 1) the complexity of the clinical picture; 2) the early and recurrent hospitalization; 3) the difficulty to be diagnosed in adulthood, and when it happens it requires many years; 4) the limited number of specific drugs; 5) the lack of a dedicated medical figure in the adult clinical setting. All these features have a great impact on QoL, therefore we decided to study adult IMD patients as a single group.

Our results show that the WHOQOL-100 is a suitable tool for the investigation of the quality of life of adult IMD patients. The analysis of the numerous domains and facets allows us to better understand different aspects of the daily life of adult patients with inherited metabolic diseases. The adjunctive semi-standardized interview can help us to focus on patients needs and their perceptions of the treatment of chronic illness.

2. Methods

2.1. Patients' enrollment

Inclusion criteria for patients' enrollment were: 1) age ≥ 16 years; 2) a confirmed diagnosis of an inherited metabolic disease; 3) patient IQ > 70; the Wechsler Adult Intelligence Scale-Revised (WAIS-R) [8] was administered to all patients; 4) the patient should have been in treatment; 5) the patient should have completed the WHOQOL-100 questionnaire and the semi-standardized interview. Informed written consent was obtained from each participant.

Participants were enrolled from January 2008 to March 2010. A total number of 97 patients with IMD were studied, but 82 patients (76 with IMD, 6 with CADASIL) were enrolled (Table 1). We also included a group of patients with Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL), a chronic genetic non-metabolic adulthood onset disease with neurological complications. This condition is caused by a mutation in the *NOTCH3* gene, and is characterized by migraine, recurrent strokes, and subcortical dementia. CADASIL is a cerebrovascular disorder without any specific therapy; indeed, only supportive therapy exists (including antiplatelet drugs and analgesics) [9].

Fifteen patients were excluded: 2 were waiting for molecular confirmation, 2 were waiting to start treatment, and 11 had an IQ < 70. Table 2 shows the classification of patients according to disease groups and treatment.

Regarding the group of PKU patients (the most representative group of patients according to the number), 15 patients were enrolled: 11 affected by the classical form (Phe tolerance up to 600 mg/day), and 4 affected by the moderate form (Phe tolerance more than 600 mg/day). Both groups of patients were supplemented with Phe-free amino acid mixtures.

Table 1
Demographic characteristics of all patients.

	All patients (including 6 patients with CADASIL) (n = 82)
Sex	
Male	43
Female	39
IQ [a]	
Mean	91.82
SD	12.28
Range	70–121
Marital status	
Married	28
Unmarried	52
Divorced	2
Widowed	0
Education	
Primary school	10
Middle school	18
High school	48
University	6
Professional status	
Students	20
Employed	41
Unemployed	21

[a] Mean of reference populations for the IQ is 100 (SD 15).