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NOTE PREVIEW ARTICLE

EPIDEMIOLOGICAL AND CLINICAL PROFILE OF PATIENTS WITH FABRY DISEASE

PERFIL EPIDEMIOLÓGICO E CLÍNICO DE PACIENTES COM DOENÇA DE FABRY

PERFIL EPIDEMIOLÓGICO Y CLÍNICO DE PACIENTES CON ENFERMEDAD DE FABRY

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ABSTRACT

Objective: to analyze the epidemiological, clinical and therapeutic profile of patients with Fabry disease, with emphasis on family care. ***Method:*** this is a quantitative, epidemiological, cross-sectional study. A large mining town and a university hospital will be listed as scenarios. The study will be based in phases and, at the first moment, will be analyzed the patients who follow the outpatient clinic. In a second moment, using a database and the application of questionnaires, a comparative study with two groups, one with manifestations of symptoms and in treatment of the disease and another group asymptomatic and without treatment will be carried out. Questions about family history, feeding and hydration, sleep / rest, eliminations (urinary and intestinal), medical history of the consultation, presence of signs and symptoms, date of diagnosis, allergies, regimen of treatment, complaints, among other variables present. ***Expected results:*** the results of the research should contribute to the identification of fragilities, difficulties and possible solutions, allowing the dissemination of data and findings in scientific compliance, besides revealing the prevalence of the cases, making them statistically visible. ***Descriptors***: Rare Diseases; Fabry Disease; Clinical Evolution; Kidney; Family; Kidney Diseases.

RESUMO

Objetivo: analisar o perfil epidemiológico, clínico e terapêutico de pacientes com Doença de Fabry, com ênfase na atenção à família. ***Método*:** trata-se de um estudo quantitativo, epidemiológico, tipo transversal. Elencar-se-ão, como cenários, uma cidade mineira de grande porte e um hospital universitário. Fundamentar-se-á o estudo em fases e, no primeiro momento, serão analisados os pacientes que fazem acompanhamento ambulatorial. Realizar-se-á, em um segundo momento, utilizando um banco de dados e a aplicação de questionários, um estudo comparativo com dois grupos, um com manifestações de sintomas e em tratamento da doença e outro grupo assintomático e sem tratamento. Levantar-se-ão, nas partes clínica e terapêutica, questões dos antecedentes familiares, alimentação e hidratação, sono/repouso, eliminações (urinária e intestinal), histórico médico da consulta, presença de sinais e sintomas, data do diagnóstico, alergias, regime de tratamento, queixas, dentre outras variáveis presentes. ***Resultados esperados*:** deve-se contribuir, pelos resultados da pesquisa, para a identificação de fragilidades, dificuldades e possíveis soluções, possibilitando a divulgação dos dados e achados em conformidade científica, além de permitir revelar a prevalência dos casos, tornando-os visíveis, estatisticamente. ***Descritores*:** Doenças Raras**;** Doença de Fabry; Evolução Clínica; Rim; Família; Doença Renal.

RESUMEN

Objetivo: analizar el perfil epidemiológico, clínico y terapéutico de pacientes con enfermedad de Fabry, con énfasis en la atención a la familia. ***Método:*** se trata de un estudio cuantitativo, epidemiológico, tipo transversal. Se enumerarán, como escenarios, una ciudad minera de gran porte y un hospital universitario. Se fundamentará el estudio en fases y, en el primer momento, serán analizados los pacientes que realizan seguimiento ambulatorio. Se realizará en un segundo momento utilizando un banco de datos y la aplicación de cuestionarios, un estudio comparativo con dos grupos, uno con manifestaciones de síntomas y en tratamiento de la enfermedad y otro grupo asintomático y sin tratamiento. En las partes clínicas y terapéuticas, se plantean, en las partes clínica y terapéutica, cuestiones de antecedentes familiares, alimentación e hidratación, sueño/reposo, eliminaciones (urinaria e intestinal), historial médico de la consulta, presencia de signos y síntomas, fecha del diagnóstico, alergias, régimen de tratamiento, quejas, entre otras variables presentes. ***Resultados esperados:*** se deben contribuir, por los resultados de la investigación, para la identificación de fragilidades, dificultades y posibles soluciones, posibilitando la divulgación de los datos y hallazgos en conformidad científica, además de permitir revelar la prevalencia de los casos, haciéndolos visibles, estadísticamente. ***Descriptores***: Enfermedades Raras; Enfermedad de Fabry; Evolución Clínica; Riñón; Familia; Enfermedades Renales

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INTRODUCTION

The concept of rare diseases of difficult understanding and unanimity is presented, not only from a conceptual point of view, but also from its epidemiological profile and public policies. Rare diseases are generally characterized by the involvement of a disease affecting a small part of the population, and it is estimated that there are around 7000 rare diseases worldwide and that around 80% of them are of genetic origin.[1-2]

According to the World Health Organization (WHO), for a disease to be considered rare, it is necessary to have an incidence of 65 cases per 100 thousand inhabitants.[2] One asks, in this context, how to quantify and categorize a disease, if there are no national epidemiological studies to know the reality of these cases?

It is certainly understood that, in fact, there are no estimates, since these diseases are not notified and diagnosed, much less the mapping of their carriers is made, often making them invisible and neglected those with a rare disease. It becomes the exact prevalence of each rare disease difficult because of the low level of consistency between the studies, and estimates of indication of prevalence are presumed and can not be accurate in the Brazilian reality.

It is questioned, in front of this: but, in Brazil, there is no specific policy and patients do not receive care and treatment? It is known that, even though it does not have a specific policy, the treatments and medicines occur through the judicial process, and the Unified Health System (UHS), in one way or another, serves the users, however, in a fragmented way, without planning , generating costs and great waste of public resources due to lack of planning and specific public policies.

It is thus caused by the identification of the demographic, epidemiological and clinical profile of a disease, a substantial impact in the costing of the operation of the health sector, in the rare diseases scenario, in particular, FD, considered as one of the "orphan diseases" , in which epidemiological surveillance is not only focused on patients' morbidity and mortality outcomes, since it also focuses on modifying risk factors with the main causes of death.

Population-based studies and surveys are also very important for monitoring disease risks and their implications, which allows the identification and categorization of population subgroups at greater risk and help in the development of more efficient interventions.

In this sense, the FD is chosen, among thousands of other rare diseases, due to the free admission demand of some index cases and their relatives, already with serious commitments, that have raised some concerns: FD is not a rare disease?; from an epidemiological point of view, the incidence and prevalence are very small, but since each week a new patient or relative is admitted to treat some complication or symptomatology?; if it is rare, why so much demand and search for treatment ?; will chronic kidney disease patients be at risk? It is pointed out that many questions mark this theme and context and such developments, in themselves, justify the study of this group.

In this context, the Fabry Disease (FD) is rare and genetic. This disease is defined as an inborn error of X-linked inheritance pattern and secondary to mutations in the lysosomal α-galactosidase A (α-GAL).[3-5]

The phenotypic result in the total or partial inability to catabolize lipids with terminal residues of α-galactosyl, mainly globotriaosylceramide (Gb-3), which progressively accumulate in lysosomes in the endothelium, podocytes, tubular epithelial cells, cells myocardial, valvular fibroblasts, dorsal ganglia root neurons and autonomic nervous system, which can lead to renal, cardiac and cerebrovascular complications.[5-7]

The prevalence of Fabry disease among 1: 17,000 to 1: 117,000 males in Caucasian populations is further estimated. One sees, however, the disease in all ethnic and racial groups. The prevalence of Fabry disease is probably underestimated because of the lack of studies, since the manifestations of the disease are nonspecific and the diagnosis is often not considered by clinicians, given the rarity of the disease.[6-8]

On the other hand, life expectancy is reduced because of impairment, which may be cardiovascular, neurological and renal, since in most diagnoses, these are usually late. However, its important detection for the early diagnosis and the beginning of the correct treatment, in order to avoid late complications, reducing the morbidity and mortality of the pathology.[9-10]

OBJECTIVE

- To analyze the epidemiological, clinical and therapeutic profile of patients with Fabry disease, with an emphasis on family care.

METHOD

This is a quantitative, epidemiological, cross-sectional study. As scenario of the development of the study, a large mining town and a university hospital will be listed. As users of the UHS, they will be raised as users of the UHS, and may also be by "free demand", through an agreement or private consultation, due to the rarity of the diagnosis and treatment, regardless of the mutation or symptoms.

All patients who undergo outpatient follow-up will be analyzed at the first moment. In a second moment, using a database and the questionnaires,

a comparative study with two groups, one with manifestations of symptoms and in treatment of the disease and another asymptomatic and without treatment will be carried out. As criteria for inclusion of the study, patients with a diagnosis of FD, regardless of whether they were index cases or family members, of both sexes, were enrolled and attended at the outpatient clinic and who underwent follow-up / treatment at the outpatient clinic; and, as exclusion criteria, the cases of deaths and patients who refuse to participate in the study.

Regarding the ethical and legal procedures, in the development of the research, Resolution 466/2012 of the National Commission of Ethics in Research (CONEP) will be considered, and the research will be submitted to an Ethics Committee, through Plataforma Brasil, waiting to appear. It is intended to contact the potential research subjects to invite them to participate after an explanation of the objectives, the proposed method and the implications of their participation, as well as the signing of the Informed Consent Term).

It will be defined, for those who accept to participate in the research, schedules and dates for the application of the questionnaires by the researchers, without compromising the service and routine of their services. It is emphasized that the moment of the routine outpatient routine follow-up of these patients will be used to carry out the data collection of the study. It is expected that this collection will be performed in a place that guarantees the privacy of the subjects in a private room.

However, primary, secondary and source data will be used to reach the proposed objectives: in the first stage, variables from the research database, which is under construction, will be used with sociodemographic, epidemiological, clinical and therapeutic, via chart analysis; the sociodemographic variables used will be sex, age, marital status, religion, naturalness, occupation, schooling, income, occupation, characteristics of domicile, sanitation conditions and means of transportation used; As for epidemiological variables, risk factors can be enumerated (smoker, alcoholic, physical activity, presence of preexisting diseases, questions about deaths, at home, in the last 12 months, etc.).

In the clinical and therapeutic parts, there will be: family history questions; nutrition and hydration; sleep / rest; eliminations (urinary and intestinal); medical history of the consultation; presence of signs and symptoms; date of diagnosis; allergies and treatment regimen; complaints, among other variables present.

In the second step, a survey-type evaluation of grouped data, especially the variables domicile, place of birth and place of treatment, will be used using ArcGis software to map the locations of each index case and its relatives, georeferencing, on the map, the locations and their displacements for treatment. The technique of analysis based on the spatial location of each patient (case) and their relatives will be used, crossing the demographic variables of the household x cases and domicile x treatment site. We find, therefore, mappings to locate and define patterns of analysis.

Patients with FD will be interviewed in the third stage, but beforehand, the Free and Informed Consent Term will be read. The respondent is expected to spend, on average, 30 minutes to respond to the questionnaire in a privacy situation. The instrument will be applied by a trained interviewer. In this stage, an exploratory analysis of the clinical part applied directly to the patients of the FD will be carried out, using questionnaires on the perception of the disease (Brienf Disease Perception Questionnaire IPQ), the Summary Inventory of Pain and classification of the impact of pain in their daily life by applying the Pain-Related Disability Index. The SF-36 questionnaire will be used to measure the quality of life and, initially, everyone will respond to it. One will then compare the results of 50 patients who present with symptoms and are on treatment with 50 others who do not present symptoms and do not use treatment.

Participants will be selected for convenience because it is a rare disease. After the previous steps, the data will be collected and tabulated, another comparative, now, according to the types of mutations of the index cases, correlating with the heredograms in front of the family genetic counseling.

The data will be analyzed initially by means of descriptive statistics, which will allow the classification of patients regarding epidemiological and clinical aspects, with emphasis on the characteristics, stage and symptoms of the disease. They will be tabulated in electronic spreadsheets, summarizing them and presenting them in tables and figures, in the form of mean ± standard deviation (quantitative data) or absolute frequency and percentage for categorical variables. The questionnaires, as well as the database, will be used in the preparation of the same specific programs as Epi Info and Survey Monkey software, specific for the treatment of questionnaire data and epidemiological variables. Statistical analysis will also be done through the statistical package Statistical Package for Social Science (SPSS), version 23.0.

EXPECTED RESULTS

It will contribute, through the study, to epidemiological data and the profile of patients with FD, and the results will serve to analyze and plan strategies on the issue of reception and attendance in the UHS and review of public health policies and, also , in the review of the judicial

process for patients and their families. It is mentioned that 100% of these patients use their rights to require treatment because of the high cost of it.

However, in recent studies, the importance of diagnosis, early treatment and family counseling in an attempt to avoid the occurrence of irreversible late damage or complications, whether in the kidneys or in other organs, is reduced in order to reduce morbidity, mortality and increase the quality and life expectancy of patients affected.

Therefore, the results of the research should contribute to the identification of weaknesses, difficulties and possible solutions, enabling the dissemination of data and findings in scientific compliance, besides revealing the prevalence of cases, making them statistically visible, since they are missing estimates and national epidemiological studies to demonstrate the reality that patients and family members experience every day.

Finally, knowledge about the subject will be produced, which may generate direct benefits for a large number of UHS users who need specific care, both in primary care and in other levels of health care.

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