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CONSTRUCTION OF AN EDUCATIONAL BOOKLET ON FRAGILE X SYNDROME FOR HEALTHCARE PROFESSIONALS

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Abstract: Introduction: Fragile X syndrome (FXS) occurs due to a mutation in the FMR1 gene — located on the long arm of the X chromosome —, preventing the production of FMRP, a protein that regulates protein synthesis and other signaling pathways in neuronal dendrites. The most frequent symptoms are difficulties with communication, learning and intellect, physical abnormalities, among others. About SFX, symptoms, associated disorders, diagnosis, treatments and discussions about: the importance of the dentistry professional, the value of family and school support with the patient and Fragile X Syndrome in Brazil. Objective: To carry out a literature review with an emphasis on Brazil to create a multidisciplinary booklet on fragile X syndrome for health professionals. Methodology: Search for literary basis in various databases to create the booklet. The inclusion criteria established were qualitative or quantitative articles and books in English or Portuguese between the period 2019 and 2024. The established inclusion criteria were theses, dissertations, response letters and editorials. Results: After the review, a booklet in 2-fold folder format was created using CANVA containing the topics: What causes SFX; the symptoms; associated disorders; the diagnosis; treatment; dental perspective; considerations about family and school support; fragile X syndrome in Brazil. Conclusion: The multidisciplinary educational booklet project on Fragile X Syndrome can promote professional training, enabling greater learning among health professionals, allowing for application and dissemination. Subsequently, such work in health education can add value to the diagnosis of FXS, an underreported disease mainly because it is rare and often unknown.
Keywords: Fragile X Syndrome; Reading Phase Mutation; Genetics.

INTRODUCTION

Fragile X syndrome (FXS) is a genetic condition that causes intellectual disability, behavioral and learning challenges, and various physical characteristics. Although it occurs in both sexes, men are affected more frequently than women and generally with greater severity. (WHITING, 2017). According to the systematic review by Hunter et al. (2014), it is estimated that FXS affects approximately 1 in 11,000 women and 1 in 7,000 men.

It is caused by a mutation in the Fragile X Messenger Ribonucleoprotein 1 (FMR1) gene, present on the X chromosome, which produces a protein called FMRP, necessary for brain development. In the 5' untranslated region of this gene, the CGG DNA pattern is repeated continuously. Most people have fewer than 45 reps. People who have 55 to 200 repetitions have a "pre-mutation", not having FXS and being able to later develop other associated fragile disorders. People with a complete mutation (more than 200 CGG repeats) have the syndrome. (CENTERS FOR DISEASE CONTROL AND PREVENTION, 2018)

Individuals affected by FXS may have intellectual disabilities, Autism Spectrum Disorder (ASD) and Anxiety Deficit Hyperactivity Disorder (ADHD). Although there are many medications to manage comorbidities, there are no specific treatments. The goal of treatment as early as possible is to improve the intellectual disability, communication difficulties and social interaction characteristic of FXS. Furthermore, despite the recommendation to carry out genetic testing in children with intellectual disabilities or global developmental delays, this is not carried out in many Latin American countries. (SALCEDO-ARELLANO et al., 2019)

The oral characteristics frequently found in patients with FXS are: narrow and deep palate, characteristic of high palate, mandibular prognathism, malocclusion, macroglossia and enamel hypoplasia. Due to behavioral characteristics, poor hygiene, presence of biofilm and/or cavities, calculus and gingivitis are also described — which can occur due to both anatomical causes and the presence of intellectual disability. There is also a description in the literature of incisal wear due to tooth attrition. (MARTINS et al., 2020)

The study by Nash et al. (2019) concluded that children of both genders with fragile X syndrome (FXS) have intellectual and behavioral abilities that affect daily life, although the focus of research on FXS is often on men. Women with FXS need support and consideration of their specific needs, particularly in an academic setting.

Despite the recommendation to perform genetic testing in children with intellectual disabilities or global developmental delay and in those families whose families are affected, these tests are not performed in several Hispanic countries. Diagnostic genetic surveys are available and several Latin American countries have been reported in FXS prevalence studies, however, determining the true prevalence of genetic disorders is difficult due to the fact that in many Hispanic nations there is no official national registry. Countries such as Chile, Brazil, Colombia, Argentina, Peru and Spain have already seen the need to program better screening and diagnosis processes for prevalent genetic diseases, including FXS. Furthermore, there are economic, political, and social barriers facing the neurogenetics field, particularly in developing countries. (SALCEDO-ARELLANO et al., 2019)

According to PINHO et al. (2023), it is important to disseminate information about Fragile X Syndrome, raise awareness among families and the medical field about FXS, as it is an unknown pathology for most health professionals. Referral for diagnosis and immediate treatment is essential, as it is little known and as it presents varied signs, it can be confused with ADHD, ASD, Tourette Syndrome, Sotos Syndrome, among others.

The more Fragile X syndrome becomes known in Brazil and around the world, the faster and easier people will identify this syndrome in those who present it; thus, affected individuals will be able to obtain the appropriate diagnosis and begin treatment correctly so that interventions can be carried out. (SILVA; COLELLA, 2021)

GOAL

The main objective of this work is, after reviewing the literature with an emphasis on Brazil, to build a multidisciplinary booklet on fragile X syndrome for health professionals. Furthermore, the design produced must consider accessibility for people with color blindness.

METHODOLOGY

This is a methodological study conducted between August and October 2023, whose development involved the construction and validation by the audience of the VIII North-Northeast Congress of Medical Genetics (VIII CONNEGEM), held from November 30 to December 2, 2023. The focus of the research is fragile X syndrome, aimed at health professionals, and resulted in the creation of an educational booklet. The process of preparing the booklet followed the following steps: 1 - integrative review on the topic; 2 - preparation of a storyboard for the development of educational technology; 3 - validation of the material by the organization of VIII CONNEGEM, through the acceptance of the simple summary and the subsequent indication for presentation in e-poster format

of the booklet, evaluated by a panel, in addition to approval by the target audience of the congress who attended the presentation.

BIBLIOGRAPHIC SURVEY

Data were collected in September 2023 to select articles related to fragile X syndrome. Several databases were consulted, including Virtual Health Library (VHL), Latin American Literature in Health Sciences (LILACS), Scientific Electronic Library Online (SciELO), National Center for Biotechnology Information (NCBI), Medical Literature Analyzes and Retrieval System Online (MEDLINE), Google Scholar, Directory of Open Access Journals (DOAJ), Scopus and the Web of Science (WoS), in addition to PubMed. The terms used for the search were: "Fragile X Syndrome", "FXS", "FMR1", "School Fragile X Syndrome" and "Fragile X Mental Retardation Protein". The search strategy combined these terms using the logical AND operator. The established inclusion criteria were qualitative or quantitative articles and books in English, Spanish and Portuguese, published between 2019 and 2024. Editorials, theses, dissertations, response letters and other materials that were not directly related to the research topic were excluded.

A total of 38 relevant publications were identified, of which 14 were selected after careful analysis of the abstracts and full content of the articles. These 14 articles were subjected to a reflective reading, where the most important points that served as the basis for creating the content of the educational booklet were summarized. During this process, essential information was collected, such as title, year of publication, country, language, objective, method, results, conclusions and level of evidence. In addition, information was integrated from fall prevention protocols available on reliable websites, such as the MSD Manual (POWELL-HAMILTON, 2023), the Centers for Disease Control and Prevention (CDC, 2024) and the National Fragile X Foundation (NFXF, 2024).

CONSTRUCTION OF EDUCATIONAL MATERIAL

After selecting the relevant content for the booklet, an outline was created containing essential information, scenarios and texts for the material. Next, there was an adaptation of the scientific language, making it more accessible to the target audience. The design of the booklet was then carried out, opting for the color blue as the main color in reference to World Fragile X Syndrome Awareness Day, with secondary colors in shades of purple and lilac. The language used is clear and objective. The choice of the responsible professional was based on his vast experience in creating educational materials aimed at health professionals, contributing to the construction of comprehensive educational resources about the disease, in addition to serving as a source of consultation for dissertations, theses and expansion of knowledge about the syndrome to the general public. The layout and structure of the text followed recommendations for educational materials (INMAN; ROSE, 2023; O'CATHAIN et al., 2019; ROONEY et al., 2021), while the colored illustrations were developed using the CANVA program. The booklet was formatted in a 2-fold folder model, covering topics such as causes of SFX, symptoms, associated disorders, diagnosis, treatment, dental perspectives and considerations on family and school monitoring, in addition to a specific section on fragile X syndrome in the Brazilian context.

Evaluation and Approval by the VIII CONNEGEM panel and by the judge, judging member of the presentation and by the listeners and participants of the congress

This study was initially presented as a simple summary and selected to be displayed

as an e-poster at the VIII North-Northeast Congress of Medical Genetics (VIII CONNEGEM), which implied its approval by the congress organizing committee for publication. In addition, there was an evaluation by an expert appointed to judge the e-poster presentation, who had experience in the congress theme, which covers a variety of professional disciplines related to genetic health. The main objective of the event was to exchange knowledge between professionals, promote scientific research and debate on the diagnosis and treatment of genetic conditions. The judge was nominated by the VIII CONNEGEM organizing team due to his expertise in Medical Genetics. During the congress, the presentation was attended by the evaluating judge, as well as other participants, many of whom were health professionals. At the end, suggestions for improvements were requested to make the material more understandable or illustrative. After the presentation, revisions were made to the sentences to facilitate understanding by the target audience, and the illustrations were improved, including more vibrant colors and images representing recommended practices in the text.

After approval of the content as mentioned previously, the educational material was submitted for evaluation by VIII CONNEGEM participants. This choice is justified by the booklet's objective of providing a multidisciplinary view of fragile X syndrome, aimed at health professionals. During the congress, a presentation was made in the presence of the evaluating judge, as well as the participants, many of whom were health professionals. At the end, suggestions were requested to improve understanding or illustration of the material. Subsequently, the printed booklet was distributed to everyone present along with an evaluation form. Each participant was instructed to read the booklet, analyze the content and images, and then indicate whether the material was approved, approved with modifications, or failed in terms of quality.

ETHICAL ASPECTS

This study did not require approval by the Research Ethics Committee. The reason for this exemption lies in the fact that the work consisted exclusively of a bibliographical review of subjects available on the internet. We emphasize that all resources used were properly referenced and did not involve the collection of primary data or experiments with humans, animals or biological materials. The bibliographic review was carried out in accordance with the ethical principles of scientific research and respect for copyright.

RESULTS

A multidisciplinary educational booklet was created, which aims to provide information about Fragile X Syndrome. The booklet has updated data, providing reliability of information to health professionals. The pamphlet has simple language, but is technical enough for the target audience in question to understand, learn and pass on information about Fragile X Syndrome.

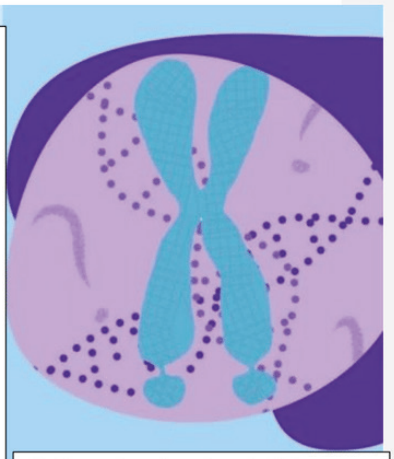
FXS: Fragile X syndrome.

What causes?
The syndrome occurs due to a mutation in the FMR1 gene, located on the long arm of the X chromosome, preventing the production of FMRP, a protein that regulates protein synthesis and other signaling pathways in neuronal dendrites.
It is more common in men, affecting 1 in 7,000 men and 1 in 11,000 women.

Fragile X syndrome in Brazil

Fragile X syndrome is the most common hereditary intellectual disability in the world population, however, there is not a large number of diagnoses in Brazil. The program: ``I SAY X`` estimates that there are 52,750 people with FXS, of which 34,633 are men.
The greatest surveillance occurs in the south and southeast region, with the north and northeast regions being the least supported areas. This makes it difficult to obtain enough data to know the picture of FXS.

As it is a rare condition, the diagnosis is often not considered because it is unknown to both the population and healthcare professionals.



What are the main symptoms?

The most frequent symptoms are difficulty with communication, learning and intellect. FXS is the main monogenic cause for the development of autism spectrum disorder. Symptoms are generally more pronounced in men.
And 60 percent of people with SFX also have a diagnosis of autism.

In July, Fragile X Syndrome Awareness Month is celebrated. Information is essential for early diagnosis.

I would like to know about a project about fragile X syndrome, from the Buko Kaesemodel institute.
Access the website: eudigox.com.br and find out about the project: ``I SAY X``.

Fragile x syndrome: do you know what it is?

Health professional handbook

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Other Symptoms?
Prominent jaw and/or elongated face
Big ears
Excavated chest
Hyperflexibility
Echolalia (repetition of other people's speech)
Attention deficit and/or hyperactivity

Early diagnosis and treatment are of great benefit to the patient and can guide them to a better quality of life, whether social, academic or professional. In women, symptoms tend to be milder.

How is the diagnosis made?
After evaluating the Symptoms, the chromosomal alteration can be confirmed by DNA analysis, looking for an increase in CGG repeats, which may be a pre-mutation or total mutation.

CGG repetitions

Person without SXF	Person with pre-mutation	Person with SXF
Up to 46 repetitions	From 55 to 200 repetitions	Over 200 repetitions

A dental vision

The oral characteristics frequently found in patients with FXS are:
Deep narrow palate
Mandibular prognathism
Malocclusion
Macroglossia
Enamel hypoplasia

Due to the behavioral characteristics of SFX, there is generally poor hygiene, leading to more frequent cavities and tooth wear due to tooth attrition.

Associated Disorders

Fragile X-associated tremor/ataxia syndrome.

It causes tremor, ataxia and major neurocognitive disorder. It is more common in men.

Primary ovarian failure
Primary alteration of the ovary that generates reproductive and endocrine dysfunction in women under 40 years of age, causing infertility.
It is a rare and normally idiopathic disorder; however, 2 percent of cases are associated with SFX.

Tremor syndrome and primary ovarian insufficiency are associated with premutation

What is the treatment?

As it is a genetic disease, there is no cure.
However, there are multidisciplinary treatment options to improve the patient's quality of life.
Among the options, the following can be highlighted:

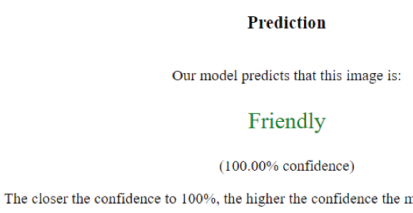
Medication to treat anxiety, depression and aggression
Psychological, physiotherapeutic, speech therapy, pedagogical and dental support

Family and school support

In addition to medical monitoring and other healthcare professionals. It is important that the patient has family, school and professional support.

Inclusion is a human right. And as a healthcare professional, it is important to disseminate information to the patient's family and society, to create a support network.
A life with quality and inclusion is not only possible, it is necessary!

For certification that the flyer design is accessible to colorblind people the "Colorblind Image Tester" tool, by Stevens et al., 2023, was used. 100% reliability was received, a positive result, on both sides of the pamphlet.



CONCLUSION

The project of the multidisciplinary educational booklet on Fragile X Syndrome can promote professional training, enabling greater learning among health professionals. Health education must be continuous and constantly updated. At undergraduate level, topics relating to FXS are little debated, making it necessary to produce materials that encourage curiosity and discussion among students and health professionals.

Subsequently, such work in health education can add value to the diagnosis of FXS, an underreported disease mainly because it is rare and usually unknown. By seeking support from bodies and places specializing in rare diseases, the pamphlet can be distributed and used or even improved to reach more and more healthcare professionals who have direct contact with patients and who can help identify the syndrome and subsequently treat it. for a better quality of life for people affected by fragile X syndrome.

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