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UNRAVELING HUNTINGTON'S DISEASE: CONCEPTS, TREATMENTS AND HEALTH POLICY CHALLENGES

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ABSTRACT: Huntington's disease (HD) is an inherited, rare neurodegenerative disorder caused by repeated mutations in the huntingtin gene. In Brazil, there are estimated to be 13,000 to 19,000 carriers. A literature review highlighted specific challenges in Brazil, including the absence of curative treatments, the demand for a specialized and sensitive approach for HD patients in the Unified Health System (SUS), and the scarcity of epidemiological studies. The 2014 National Policy for Comprehensive Care of People with Rare Diseases (PNAIDR) endeavors to provide access to diagnosis, treatment, rehabilitation, and palliative care for individuals with HD. However, meeting these patients' specific needs poses significant challenges. Effective implementation of strategies to improve early diagnosis, patient support, and quality of life necessitates close collaboration between health professionals, researchers, and policymakers.

Keywords: Epidemiological monitoring. Health professionals. Dementia, neuronal death.

RESUMO: A doença de Huntington (HD) é um distúrbio neurodegenerativo raro e hereditário causado por mutações repetidas no gene huntingtina. No Brasil, estima-se que haja de 13.000 a 19.000 portadores. Uma revisão da literatura destacou desafios específicos no Brasil, incluindo a ausência de tratamentos curativos, a necessidade de uma abordagem especializada e sensível para pacientes com HD no Sistema Único de Saúde (SUS) e a escassez de estudos epidemiológicos. A Política Nacional de Atenção Integral às Pessoas com Doenças Raras (PNAIDR) de 2014 busca oferecer acesso a diagnóstico, tratamento, reabilitação e cuidados paliativos para indivíduos com HD. No entanto, atender às necessidades específicas desses pacientes apresenta desafios significativos. A implementação eficaz de estratégias para melhorar o diagnóstico precoce, o suporte ao paciente e a qualidade de vida requerem uma colaboração estreita entre profissionais de saúde, pesquisadores e formuladores de políticas.

Palavras-chave: Monitoramento epidemiológico. Profissionais de saúde. Demência. Morte neuronal.

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INTRODUCTION

The prevalence of dementia has doubled in the last two decades, affecting thousands of individuals worldwide. These conditions belong to a group of pathologies called neurodegenerative diseases, which are characterized by the dysfunction and progressive death of neurons in both the central and peripheral nervous systems. Among the most common neurodegenerative diseases are amyotrophic lateral sclerosis (ALS), Parkinson's disease, Alzheimer's disease, and Huntington's disease. In many cases, dementia is the first identifiable symptom. (MACEDO et al., 2019)

The global recurrence of these conditions emphasizes the critical importance of studying, mapping, and categorizing neurodegenerative diseases. This effort not only aids in planning more effective care but also in evaluating the associated public health costs, implementing specific policies, and comprehending their impact on an aging society. (MACEDO et al., 2019)

In the Brazilian context, there is a significant lack of studies on the prevalence and importance of dementias, resulting in limited availability of reliable information on this topic. This knowledge gap highlights the need to invest in research and initiatives to promote a more comprehensive and grounded understanding of the dementia landscape in the country. (SILVA et al., 2021)

Rare diseases, such as Huntington's, have become a complex issue in global health. Patients dealing with these conditions face challenges such as limited therapeutic options, high treatment costs, medical underreporting, and psychological stress. Currently, there is no international consensus on the precise definition of rare diseases. The average threshold is between 40 and 50 cases per 100,000 people, representing approximately 3.5-5.9% of the global population. In the Brazilian context, the Ministry of Health considers a rare disease to affect up to 65 people per 100,000 individuals. (CARDOSO JÚNIOR et al., 2023; ZHANG et al.,2023)

Currently, there is no curative treatment available for these diseases. One of their primary features is their progressive nature, which results in intellectual and physical limitations that affect the lives of those affected and their families. Huntington's Syndrome, also known as Huntington's Chorea, is a neurodegenerative pathology caused by the expansion of repeats of three cytosine-adenine-guanine nucleotides (triple CAG) of the huntingtin gene on chromosome 4. It is characterized by being autosomal dominant and has a central hereditary character. The disease affects the GABA neurotransmitters. (MACEDO et al., 2019; PINHEIRO et al., 2020)

Huntington's Disease (HD) is a rare condition that affects approximately three (3) out of every 100,000 people worldwide. While the prevalence of HD is lower in Asians and Blacks, it is more common in Caucasians. The syndrome affects both men and women and is characterized by a triad of symptoms: psychiatric problems, cognitive deficits, and involuntary movements (including decreased grip strength and altered gait), which is commonly referred to as chorea. (DE OLIVEIRA et al., 2018; MINISTERIO DE SALUD, 2017)

Symptoms typically appear between the ages of 40 and 50 in the majority of cases, with cytosine-adenine-guanine (CAG) nucleotides playing a crucial role in determining their onset. It has been observed that the earlier the symptoms manifest, the greater the expansion of the CAG repeats. There are reports of patients experiencing the triad of

symptoms as early as 5 years of age, characterizing the condition known as juvenile Huntington's, whose average survival is 15 to 20 years. (DE OLIVEIRA et al., 2018; MINISTERIO DE SALUD, 2017)

Conducting epidemiological research on rare diseases requires significant time and resources. Additionally, the non-uniform distribution of information poses a challenge. Obtaining case reports, conducting epidemiological studies, and gathering expert opinions are all time-consuming tasks. Socio-economic factors in each country further complicate data acquisition. The constant updating of databases is a crucial factor in collecting information and developing effective public policies to address these pathologies. (KARIAMPUZHA et al., 2023; ZHANG et al., 2023)

Verifying these reports poses significant challenges due to the complexity of the required tests, such as metabolite analysis, pathological examinations, and genetic testing. Consequently, databases often have information gaps and delays. Epidemiological studies face an additional challenge due to the diversity of characteristics and peculiarities of each rare disease. Therefore, it is imperative to classify these conditions to guide targeted and more effective research. (KARIAMPUZHA et al., 2023; ZHANG et al., 2023)

Epidemiological monitoring is essential to evaluate the effectiveness of pharmacological, physiotherapeutic, speech therapy, and psychiatric treatments for Huntington's Disease. It can be challenging to implement, but it is necessary. (PINHEIRO et al., 2020)

The purpose of this study is to outline how public policies and current treatments are impacting the quality of life of patients diagnosed with Huntington's Syndrome.

METHODS

Study design

This scientific article utilizes a narrative literature review approach, which involves a descriptive and interpretive synthesis of information from previous studies on a specific topic. (GREEN, JOHNSON, & ADAMS, 2006) The review's central question was formulated based on the PVO model, which stands for population (Huntington's Syndrome patients), variables (public policies and treatment), and outcomes (impacts on patients' lives). "How are current public policies and treatments impacting on the quality of life of patients diagnosed with Huntington's Syndrome?"

Search Strategy

Thorough searches were conducted in electronic databases, namely PubMed, BIREME, SCIELO, and LILACS, from September 1, 2022, to November 14, 2023. The following descriptors were used: 'Huntington's disease', 'Public policies', 'Epidemiological surveys', 'Epidemiological monitoring', 'Health profile', 'SUS', and 'Rare diseases', combined using the Boolean operators AND and OR (Table 1).

Additionally, we performed a manual citation tracking search and reviewed the reference lists of the chosen articles to identify any other pertinent sources. To expand the search, we looked for information in English, Portuguese, and Spanish, utilizing a comprehensive strategy that included all variations of the cited terms. To optimize the search, we focused on articles published between 2016 and 2023.

Table 1- Search strategy

DATABASES	SEARCH STRATEGY
SCIELO	(Huntington's disease AND SUS) (Huntington's disease OR Health profile) (Huntington's disease OR Epidemiological surveys) (Huntington's disease OR SUS)
PubMed	(Huntington's disease OR Health profile) (Huntington's disease OR Epidemiological monitoring) (Huntington's disease OR SUS) (Huntington's disease OR Public policies)
LILACS	(Huntington's disease OR Health profile) (Huntington's disease OR Epidemiological surveys)
BIREME	(Huntington's disease AND SUS) (Huntington's disease OR SUS) (Huntington's disease OR Health profile) (Huntington's disease AND Health profile) (Rare diseases AND epidemiology)

RESULTS AND DISCUSSION

Thirteen references were cataloged from 2016 to 2023 and categorized into specific themes for clarity (Table 1). Five of these references discuss the concept and treatments for Huntington's Disease, providing a contextualization of the disease's pathophysiology and presenting the latest therapeutic approaches for the syndrome. Four papers focus on the impacts of Huntington's Disease on patients and their families, while two articles discuss related health policies in Brazil. This provides valuable insight into the government's approach to this specific population.

Table 1. Summary of articles selected by thematic considerations

Related Subject	Article title	Author	Thematic considerations
Contextualizing pathophysiology	Use of non-invasive stimulation in movement disorders: A critical review.	Godeiro et al.	The critical review addresses the question of the scientific basis for the use of non-invasive stimulation in movement disorders, analyzing and discussing the main clinical trials conducted on the subject.
	Apenas mais um acidente de trabalho? Relato de um caso clínico de coreia de Huntington.	Cunha and Lopes	Case report of a 41-year-old unemployed man who came to the Family and Community Medicine clinic with symptoms suggestive of Huntington's disease.

	Acut cerebellar ataxia: Differential diagnosis and clinical approach	Pedroso et al.	This study addresses cerebellar ataxia, a frequent finding in neurological practice, with a wide variety of causes, ranging from chronic cerebellar degeneration to acute lesions in the cerebellum, as well as hemorrhage and/or edema.
	New avenues for the treatment of Huntington's disease.	Kim et al.	The study looks at the historical treatments for involuntary movements, as well as the new drugs being studied for Huntington's Disease.
	Tratamento da demência: recomendações do Departamento Científico de Neurologia Cognitiva e do Envelhecimento da Academia Brasileira de Neurologia	Caramelli et al.	This study aimed to characterize pharmacological and non-pharmacological therapies for neurodegenerative diseases.
Impacts on patients' and their families' Activities of Daily Living (ADLs)	Avaliação funcional em indivíduos com doença de Huntington: uma série de caso.	Oliveira et al.	This cross-sectional study aimed to catalog, evaluate and explain the measures taken by six patients with Huntington's disease to improve their Activities of Daily Living (ADLs).
	Doença de Huntington	Gonzalez-Usugli	This manual explains the pathophysiology of the disease and how it affects contacts or people close to the affected individual.
	Potential disease modifying therapies for Huntington's disease, lessons learned and future opportunities.	Tabriz et al.	This study aims to highlight new therapies for Huntington's disease, including intervention in the huntingtin DNA and RNA gene, huntingtin protein clearance, DNA repair pathways, and other treatment strategies aimed at reducing inflammation and cell replacement.

	Perfil e capacidade funcional em sujeitos com Doença de Huntington.	Pinheiro et al.	This cross-sectional study aims to identify, through a questionnaire, the functional capacity of individuals with Huntington's Disease (HD) who receive care at a physiotherapy outpatient clinic in the Federal District.
Health policies for Huntington's disease	Módulo de princípios de epidemiologia para o controle de enfermidades (mopece) módulo 4: vigilância em saúde pública	Suarez	Public document drawn up to identify public surveillance and epidemiological principles.
	Formação de um residente de Medicina de Família e Comunidade no contexto da Política Nacional de Atenção Integral às Pessoas com Doenças Raras	Júnior et al.	This study is a case report of a medical professional who is studying changes in the mortality profile of genetic diseases, epidemiological data being scarce, and also deals with the National Policy for Comprehensive Care for People with Rare Diseases, which aims to promote comprehensive care for these patients in the Unified Health System (SUS).
	Política Nacional de Atenção Integral às Pessoas com Doenças Raras	Brazil	The National Policy for Comprehensive Care for People with Rare Diseases (PNAIDR), established by Ordinance No. 199 of January 30, 2014, aims to guarantee access to diagnosis, treatment, rehabilitation and palliative care, as well as promoting social inclusion and quality of life for people with rare diseases.
	Estratégia Global para Doenças Raras 2013-2020	World Health Organization	The Global Strategy for Rare Diseases 2013-2020 was launched by the World Health Organization (WHO) in 2013. The strategy aims to improve the lives of people living with rare diseases, which are defined as diseases that occur in fewer than 1 in 2,000 people.

DISCUSSION

Contextualizing the pathophysiology of the syndrome

Pathologies related to abnormal involuntary movements are clinically and pathologically heterogeneous. They initially manifest as movement disorders, resulting in involuntary, uncoordinated, or imperfect movements. The execution of normal, fluid movement depends on two neurological components: the primary motor pathway and the modulatory systems, which include the cerebellum, basal nuclei, and sensory functions. (GODEIRO et al., 2021)

The investigation of movement-related disorders typically falls under the purview of neurology and may necessitate specific diagnostic tools. Patients with uncoordinated movements often retain normal muscle strength and motor pathways, suggesting a pathological process in the modulatory system. (CUNHA & LOPES, 2016)

This study focuses on Huntington's chorea, a type of dystonia, along with other relevant types of pathological movement such as tremors, Parkinson's disease and parkinsonism, drug-induced movement disorders, hemiballismus, tics, myoclonus, cerebellar ataxia, sensory ataxia, and choreoathetosis. (PEDROSO et al., 2019)

One group of diseases that stands out is Chorea, a term derived from Latin meaning 'dance'. Clinically, it is characterized by spontaneous, rapid, and abrupt uncoordinated movements, lacking a predictable pattern in time and bilateral body distribution. Movement disorders are often classified as those with decreased or slow movements (hypokinetic disorders), seen in Parkinson's disease, or increased movements (hyperkinetic disorders), as in chorea (CUNHA & LOPES, 2016)

Movement disorders are often classified as those with decreased or slow movements (hypokinetic disorders), as seen in Parkinson's disease, or increased movements (hyperkinetic disorders), as in chorea Hyperkinetic disorders give the observer a "restless" appearance, and the inability to maintain a motor act (motor impersistence) are typical findings during the neurological physical examination of the syndrome. (CUNHA & LOPES, 2016)

Pharmacological interventions for Huntington's Disease (HD) that have received approval from both the FDA and ANVISA include tetrabenazine (TBZ) and deutetrabenazine. Deutetrabenazine has an improved risk-benefit profile compared to TBZ and both drugs are approved for treating chorea associated with HD in adults. However, these treatments are associated with high costs and are currently in phase 3 studies. It is important to note that although these drugs are effective, they have a concerning adverse effect: an increased risk of suicide. (KIM et al., 2021)

Other non-specific drugs for Huntington's Disease (HD) include neuroleptics that act as dopamine antagonists, such as olanzapine and haloperidol. Additionally, anti-glutamatergic drugs, such as amantadine and riluzole, act as antagonists to excessive glutamate neurotransmission in the basal ganglia. (KIM et al., 2021)

Memantine is beneficial in treating cognitive impairment in HD due to its moderate affinity that stabilizes glutamatergic tone. Although there is insufficient evidence to guide the pharmacotherapy of depression in HD, selective serotonin reuptake inhibitors (SSRIs) have yielded positive results. Additionally, antipsychotics like risperidone have been used to treat HD-associated symptoms. (KIM et al., 2021)

Non-pharmacological interventions are essential in alleviating symptoms, slowing the progression of Huntington's Disease (HD), and enhancing the quality of life, including the Activities of Daily Living (ADLs) of patients. (CARAMELLI et al., 2022).

Several approaches are available to address cognitive symptoms, including Cognitive Stimulation Therapy (CST), psychosocial/psychoeducational interventions, acupuncture, and light therapy. Light therapy has the potential to improve functional performance and long-term cognition, as well as benefit blood flow, hippocampus volume, and neurogenesis, providing relief from neuropsychiatric symptoms. The Multicomponent/Multidisciplinary Cognitive Rehabilitation (MCRP) program includes computer-assisted stimulation and therapy, physical training, physiotherapy, reading, crossword puzzles, and board games. (CARAMELLI et al., 2022).

Impacts On Patients' And Their Families' Activities Of Daily Living (Adls)

Huntington's disease is an autosomal dominant hereditary trait caused by a mutation in the huntingtin protein gene (HTT). Affected individuals possess at least one defective allele of this gene, which contains 36 or more repeats of cytosine-adenine-guanine (CAG) trinucleotide sequences on the short arm of chromosome 4. Penetrance is complete for the disease in carriers with 40 or more repeats, while those with 36 to 39 CAG repeats have incomplete penetrance. (DE OLIVEIRA et al., 2018; TABRIZI et al., 2022)

The number of CAG repeats is a determining factor for the age of onset and severity of symptoms in individuals with the syndrome. A higher number of CAG repeats leads to earlier manifestation of the disease and faster clinical progression in carriers of the mutation. (DE OLIVEIRA et al., 2018; TABRIZI et al., 2022)

Symptoms of the disease typically manifest in the fourth decade of life, with the exact age of onset dependent on the number of CAG repeats. The disease is hereditary and results in a reduction of life expectancy to 15-20 years after the onset of clinical signs. Motor deterioration is a central component of the disease's progression, characterized by a slow and continuous worsening of the hyperkinetic disorder. According to De Oliveira et al. (2018), the result is a total loss of mobility and weakening of the muscles responsible for swallowing and breathing. (DE OLIVEIRA et al., 2018)

The onset of chorea is typically accompanied by various clinical symptoms and can occur during childhood or, in some cases, in later stages from the age of 63. Initially, mild personality and behavioral disorders may arise, which can progress to schizophreniform psychosis. This is characterized by a gradual deterioration that affects speech and gait. Symptoms such as cognitive deterioration, dementia, mood swings, depression, agitation, and aggression are included in this triad. As the condition progresses, the characteristic triad of the disease becomes evident, consisting of psychiatric problems, cognitive impairment, and dyskinesias. (CUNHA & LOPES, 2016)

Huntington's chorea is characterized by brain loss and a marked decrease in small neurons in the putamen. This is caused by intranuclear degeneration of the huntingtin protein and atrophy in the caudate nucleus. The diagnosis of Huntington's disease is based on clinical assessment, confirmed by genetic analysis to measure the number of CAG repeats, and neuroimaging. (GONZALEZ-USUGLI, 2022)

The diagnosis of this condition is typically based on observable signs and symptoms, as well as a positive family history. Imaging studies are often used to identify caudate atrophy, which is frequently accompanied by predominant frontal cortical atrophy. (GONZALEZ-USUGLI, 2022)

Individuals with Huntington's Disease (HD) face challenges with executive functions, such as attention, judgment, and perception, from the earliest stages of the condition. Personality changes are a significant harbinger that compromises the individual's adaptation to the environment. (GONZALEZ-USUGLI, 2022)

Providing clarification and guidance on Huntington's disease (HD) is crucial, particularly for offspring and caregivers. However, this task is challenging due to the apparent scarcity of guidance available in health services and the lack of support to deal with the dilemmas present in dialogues between the children and caregivers of carriers. This lack of support directly impacts the quality of life. (PINHEIRO et al., 2020).

Health policies for Huntington's disease

Epidemiological surveys are used worldwide to highlight situations of all pathologies, including HD, in populations. Such surveys are important for monitoring disease and health processes, and for health systems to recognize the need to establish epidemiological surveillance of the population. (SUAREZ, 2017; CARDOSO JÚNIOR, 2023)

In 2014, Brazil introduced the National Policy for Comprehensive Care for People with Rare Diseases (PNAIDR) to address rare genetic diseases. PNAIDR aims to provide comprehensive care in the SUS for individuals with rare diseases, 80% of which have a genetic etiology and 20% of which are caused by immunological and infectious diseases. (SUAREZ, 2017; CARDOSO JÚNIOR, 2023)

The PNAIDR is a significant achievement in Brazilian healthcare, as it represents the first public policy specifically designed for rare diseases. The policy aims to ensure access to diagnosis, treatment, rehabilitation, and palliative care, while also promoting social inclusion and improving the quality of life for patients with rare diseases. (SUAREZ, 2017; CARDOSO JÚNIOR, 2023)

The policy consists of four main components (BRASIL, 2014; OMS, 2013). The first component is access to diagnosis and treatment, which includes the establishment of a referral and counter-referral network for rare disease diagnosis and treatment. The network will consist of reference centers, primary health care centers (CAPS), and state reference units, as outlined by BRASIL (2014) and OMS (2013).

The policy includes rehabilitation services for patients with rare diseases. Specialized professionals must provide rehabilitation services that meet the specific needs of each person. (BRASIL, 2014; OMS, 2013)

The policy also promotes the social inclusion of patients with rare diseases. Actions that facilitate access to education, work, and culture must be taken to promote social inclusion. (BRASIL, 2014; OMS, 2013)

The policy also aims to promote the quality of life for patients with rare diseases. Actions that meet people's physical, emotional, and social needs must be taken to promote quality of life. (BRASIL, 2014; OMS, 2013)

The PNAIDR is a crucial policy for ensuring the rights of patients with rare diseases. The policy is currently being implemented, and it has already helped to improve access to diagnosis, treatment, and care for patients with rare diseases in Brazil (BRASIL, 2014; OMS, 2013).

CONCLUSION

The final section of this article discusses the need for specialized care that is sensitive to the needs of patients with Huntington's disease (HD) within the context of the Brazilian Unified Health System (SUS).

The analysis covers cruciais aspects, from the pathophysiology of HD to current health policies and available treatments. The literature review revealed the various challenges encountered by patients, families, and healthcare professionals when dealing with this neurodegenerative disease.

A comprehensive comprehension of HD's pathophysiology, symptoms, and progression is crucial in developing effective public policies. The analysis within SUS indicated the necessity for a more focused and tailored approach to address the distinctive needs of individuals with HD.

The presence of health policies aimed at rare diseases, such as HD, is a crucial step. However, it is imperative to improve and adjust these policies to ensure a comprehensive and accessible approach. Current treatments, both pharmacological and non-pharmacological, offer promising prospects. Nevertheless, issues of cost and adverse effects require continued attention.

The study emphasizes the significance of a comprehensive approach to managing HD by incorporating non-pharmacological interventions, such as cognitive therapies and multidisciplinary rehabilitation programs. It also highlights the pressing need for specialized care that is sensitive to the needs of HD patients within the context of the SUS.

Collaboration among health professionals, researchers, and policymakers is essential for developing effective strategies to improve early diagnosis, patient support, and the quality of life for their families. Continued dedication to research and the ongoing adaptation of health policies are necessary to meet the complex challenges presented by HD.

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