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TRIMETHYLAMINURIA AND COGNITIVE BEHAVIORAL THERAPY AS AN INTERVENTION OPTION

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ABSTRACT

Trimethylaminuria (TMAU), known as fish odor syndrome, is a rare metabolic condition that prevents trimethylamine from metabolizing, resulting in intense and unpleasant body odor. This condition significantly impacts the quality of life of individuals, leading to social isolation, difficulties in work and school environments, and negatively affecting self-esteem. People with TMAU often face social stigmas, which can culminate in serious mental health problems such as anxiety, depression, and suicidal ideation. Although there is no cure for TMAU, symptoms can be managed through dietary interventions, pharmacology, and strict hygiene practices. In this context, psychotherapy, especially Cognitive-Behavioral Therapy (CBT), emerges as an essential tool. CBT offers a structured and evidence-based treatment, promoting not only emotional relief, but also autonomy and empowerment, which contributes to greater satisfaction with life, even in the face of the challenges imposed by the chronic condition. This therapeutic approach is constantly evolving, incorporating new practices that broaden the understanding of treatment. Techniques such as acceptance and mindfulness have become key, helping patients to embrace their internal experiences without judgment, which favors well-being. In addition, behavioral activation stimulates engagement in activities that provide pleasure and meaning, which are essential for emotional recovery. The evolution of CBT, which integrates methods from different disciplines, results in a more flexible approach that is adaptable to the needs of each individual. In this way, it seeks not only to treat the symptoms, but also to promote a significant transformation in the way patients deal with their emotions and relationships, favoring a more dignified and fulfilling life. Finally, it is crucial to invest in research in psychosocial areas to avoid biological reductionism in the treatment of TMAU. It is necessary to expand management and psychological support resources, with a deeper understanding of the condition and its impacts, especially in the training of health professionals. Thus, we will be able to offer more effective support, allowing patients to overcome their difficulties and achieve a life of greater quality and dignity.

Keywords: Trimethylaminuria (TMAU). Metabolic disorders. Psychological support. Cognitive-Behavioral Therapy (CBT). Psychological intervention. Mental health and rare diseases.

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INTRODUCTION

Trimethylaminuria (TMAU), also known as fish odor syndrome, is a rare metabolic condition in which the body cannot metabolize trimethylamine, a foul-smelling substance similar to rotting fish, feces, or garbage. This condition can have serious implications on the social and mental health of affected individuals (Wise et al., 2011).

Historically, there have been records of people with body odors similar to that of rotting fish. William Shakespeare, in his play "The Tempest" (1611), mentions a character, Caliban, who exudes such an odor (Mackay et al., 2011). Furthermore, Flaherty et al. (2024) indicate that the earliest account of symptoms compatible with TMAU can be found in the Indian epic "Mahabharata", where a young girl, Satyavati, is rejected by society due to her odor. These reports reflect a persistent social stigma, although they do not establish a direct correlation with the pathology.

The first scientific report on the condition was made by John Arbuthnot (1667-1735) in "An Essay Concerning the Nature of Aliments" (1727), as well as articles in the journal "The Lancet" (Cashman et al., 2003). In 1970, Humbert et al. reported a clinical case of a six-year-old girl with a fishy odor, whose mother also had similar symptoms (Humbert et al., 1970). The authors found that trimethylamine was not metabolized and accumulated in body secretions, confirming this through urine tests and liver biopsies.

Research on TMAU has evolved, revealing both primary and secondary genetic causes (Yamazaki et al., 2004; Awosika & Anastasopoulou, 2023). The condition affects individuals of all ages, and hormonal fluctuations during the menstrual cycle, pregnancy, and puberty can exacerbate symptoms, especially in women and adolescents (Awosika & Anastasopoulou, 2023). The global prevalence of TMAU is estimated to be between one in 200,000 and one in a million, but the actual number is thought to be higher due to underreporting and low diagnostic rate (Wise et al., 2011).

Li et al. (2011) indicate that the prevalence of TMAU is significantly higher than previously thought. In specific populations, the prevalence of heterozygous carriers of the allele related to TMAU is about 1% in the British white population, and may reach 3% in Ecuador and 11% in Papua New Guinea. These carriers often experience mild symptoms or transient episodes of fish odor syndrome.

In the Brazilian and Latin American context, the lack of accurate data on TMAU is remarkable, mainly due to the rarity and underdiagnosis of the condition. In São Paulo, the Support Service for Patients with Idiopathic Systemic Odor (SEAPOSI) offers

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multidisciplinary support to patients with body odor syndromes, including TMAU. This group is composed of professionals from different areas, such as doctors, geneticists, psychologists, nutritionists and lawyers, and integrates care with teleconsultations for patients registered with MEBO-Brasil, a philanthropic organization linked to international metabolic body odor associations.

A study conducted at the American University of Pennsylvania, which looked at 353 patients with unexplained bad odor, revealed that 30% of cases were diagnosed with TMAU, highlighting the need for more research and clinical support for affected individuals. This theoretical essay, therefore, seeks to explore the biochemical and genetic bases of trimethylaminuria, in addition to discussing therapeutic approaches and the reception of the psychosocial repercussions faced by those living with this condition.

DEVELOPMENT

GENETIC AND BIOCHEMICAL BASES

Trimethylaminuria, or TMAU, is a genetic condition usually passed down in an autosomal recessive manner. This means that an individual needs to inherit two copies of the defective gene, one from each parent, to develop the condition. TMAU results from the reduced activity of the enzyme flavin monooxygenase 3 (FMO3), responsible for the oxidation of trimethylamine (TMA) into trimethylamine N-oxide (TMAO), an odorless substance (Alibrandi, 2023).

TMA is produced from compounds such as choline, carnitine, and lecithin, which are present in foods such as fish, eggs, soybeans, and some plants. In individuals with normal FMO3 function, TMA is rapidly converted to TMAO in the liver and excreted in the urine. However, in people with TMAU, TMA accumulates and is excreted in body fluids such as sweat, urine, and breath, resulting in a distinctive and disturbing odor (Veyrat-Durebex et al., 2021).

TMAU is classified into two categories:

1. Primary: Results from genetic mutations that affect FMO3, preventing the oxidation of TMA into TMAO. More than forty genetic variants have been identified as related to the disease (Rutkowski et al., 2019).
2. Secondary or acquired: This form can be caused by hormone regulation problems, liver disease, kidney disease, or viral infections. In these cases, TMA production is

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increased due to excess dietary precursors, overloading the enzyme responsible for oxidation (Rutkowski et al., 2019).

PSYCHOSOCIAL ASPECTS OF TRIMETHYLAMINURIA (TMAU)

TMAU significantly impacts the quality of life of affected individuals. Persistent body odor can lead to social isolation, difficulties in the work and school environment, in addition to damaging self-esteem (Wise et al., 2011; Alibrandi, 2023; Todd, 1979; Mayatepek & Kohlmüller, 1998). Feelings of shame and stigma associated with odor often result in mental health problems such as anxiety, depression, and even suicidal ideation (Wise et al., 2011; Veyrat-Durebex et al., 2021; Lateef & Marshall-Lucette, 2017; Flaherty et al., 2024).

TMAU is not just a physical condition; It is an experience that permeates the daily life of the individual, affecting dynamics in marital, family, professional and social relationships, as well as religious experiences and employment issues. These factors highlight the interconnection between the condition and the individual's emotional and social life.

Therefore, it is crucial that health professionals serve this population in a sensitive and comprehensive way. Researchers such as Ezeakor et al. (2020) and Paulides et al. (2021) emphasize that, in addition to psychological support, people with TMAU need the understanding and support of friends, family, and health professionals. This holistic approach is key to improving quality of life and facilitating social reintegration.

MANAGEMENT AND TREATMENT OF TRIMETHYLAMINURIA (TMAU)

Although there is no cure for TMAU, symptoms can be managed through several therapeutic approaches:

1. Diet: TMA production can be reduced by decreasing consumption of foods rich in TMA precursors, such as fish, eggs, and certain vegetables (Li et al., 2011).
2. Supplements and Medications: The absorption of TMA in the gut can be decreased with the use of supplements, such as activated charcoal and copper. Antibiotics can also be used to reduce the gut bacteria responsible for TMA production (Arseculeratne et al., 2007).
3. Personal Hygiene: The use of acidic soaps and body washes can help decrease the odor associated with TMAU (Arseculeratne et al., 2007).
4. Multidisciplinary Team Support: Consultations with professionals from different areas, such as nutritionists, geneticists, dermatologists, psychiatrists, and

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psychologists, are essential for effective management of the condition (Flaherty et al., 2024).

It is important to note that the treatment of TMAU may be limited and may not be effective for all patients. Dietary and pharmacological strategies, along with rigorous personal hygiene practices, are essential, but there is still an urgent need for research to enhance treatment options and offer more comprehensive support to patients.

IMPORTANCE OF PSYCHOTHERAPY

Psychotherapy is essential to promote the emotional well-being of individuals living with TMAU. This intervention provides the necessary support for a dignified and satisfying life, especially in severe conditions, where the emotional impact can be devastating.

The main contributions of psychotherapy include:

1. Emotional Support: TMAU can generate intense emotions, such as fear and sadness. Psychotherapy allows patients to express and manage these emotions in a healthy way, developing resilience and adaptation mechanisms, which can improve treatment adherence (Ezeakor et al., 2020).
2. Stress Reduction: Stress management techniques such as relaxation and mindfulness are taught in psychotherapy and are especially helpful for those facing ongoing stress related to the illness (Paulides et al., 2021).
3. Quality of Life: Patients in psychotherapy often report improvements in quality of life, discovering a new sense of purpose and peace, which are essential for overall well-being (Ezeakor et al., 2020).

Psychotherapy provides a safe environment for patients to explore their emotions and develop skills to cope with their difficulties. According to Strijbos and Jongepier (2018), therapy seeks to increase patients' understanding of their mental states, especially those that influence their emotional and behavioral reactions.

Another crucial aspect is the psychotherapist's ability to create a welcoming space, promoting a therapeutic alliance. This alliance allows for a deeper reflection on the challenges faced, essential for the self-knowledge necessary for mental health recovery (Ramos, 2024).

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2.5 COPING AND SELF-KNOWLEDGE

Living with TMAU requires significant adaptation. Studies indicate the psychosocial challenges faced by these individuals (Todd, 1979; Alibrandi, 2023; Flaherty et al., 2024). Psychotherapy helps patients develop coping strategies, such as illness acceptance and stress management, which are key to maintaining mental health.

The management of expectations in relation to cure and treatment is another relevant point in psychotherapy. Bukowski (2020) states that therapy can help patients balance hope and acceptance of the limitations imposed by the condition. As highlighted by Bukowski (2020), apud Snyder (2002), hope is a central component of the human psyche, encouraging actions and helping individuals find alternative ways to face their circumstances.

During the therapeutic process, patients have the opportunity for deeper self-knowledge, identifying negative thought patterns and understanding the influence of their emotions on their behaviors (Leontopoulou, 2020). This allows for a healthier approach to stressful situations.

COMBATING ISOLATION AND STIGMA

Patients with TMAU often face the desire to isolate themselves due to the stigma associated with the condition (Alibrandi, 2023; Flaherty et al., 2024). Psychotherapy offers an empathetic space, allowing them to find new ways to connect and confront prejudice. A study in the United Kingdom of adults with TMAU revealed that 100% of participants wanted more mental health support, highlighting the relevance of psychotherapy (Flaherty et al., 2024).

Therapy not only relieves emotional distress but also promotes autonomy and empowerment. Patients who have access to psychotherapy often report greater satisfaction with life, even in the face of the adversities imposed by the disease.

MAIN THERAPEUTIC LINES

Several therapeutic approaches stand out in psychology, offering valuable tools for the management of conditions such as TMAU. Among the main lines, the following stand out:

1. Cognitive-Behavioral Therapy (CBT): Focused on identifying and restructuring dysfunctional thought patterns (Beck, 1976; Ellis, 1962).

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2. Psychoanalysis: Explores deep emotional dynamics from the unconscious (Freud, 1900).
3. Humanistic Therapy: Values empathy and authenticity, promoting a safe environment for self-exploration (Rogers, 1961; Maslow, 1954).
4. Behavioral Therapy: It is based on principles of observable behavior, with a focus on practice and results (Skinner, 1953; Watson, 1913).
5. Systemic Therapy: Considers the individual in the context of his or her family and social relationships (Bowen; Minuchin, 1974).
6. Gestalt Therapy: Emphasizes the experience of the "here and now" and self-awareness (Perls, 1951).
7. Existential Therapy: Examines questions of meaning and freedom, helping patients find purpose (Frankl, 1946; May, 1953).
8. Acceptance and Commitment Therapy (ACT): Integrates acceptance and mindfulness with behavioral change strategies (Hayes, 1999).
9. Emotion-Focused Therapy: Helps patients regulate their emotions in a healthy way (Greenberg, 2002).

IMPORTANCE OF COGNITIVE BEHAVIORAL THERAPY (CBT)

CBT was chosen as the primary approach of this study due to its evidence-based framework and proven efficacy in several areas of psychology, including clinical, educational, and organizational (Pineda et al., 2020). Recognized for its ability to address a wide range of psychological difficulties, CBT uses specific techniques to deal with cognitive, behavioral, and emotional issues.

The flexibility of CBT allows methods from various disciplines to be incorporated, making it suitable for the individual needs of patients. New approaches within CBT emphasize the relationship between therapist and client, recognizing the importance of this interaction in the therapeutic process.

EFFICACY AND RESEARCH

CBT has a solid research base that confirms its effectiveness. Meta-analyses demonstrate that CBT is especially effective in the treatment of anxiety disorders, depression, and bulimia, with significant results ranging from medium to large (Butler et al.,

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2006; Hofmann et al., 2012). In addition, CBT shows more promising long-term results compared to pharmacotherapy, with significantly lower relapse rates (Newman et al., 2017).

Based on the available evidence, it is expected that patients with TMAU can benefit from Cognitive Behavioral Therapy, as well as those facing other serious conditions. CBT not only provides immediate relief but also promotes lasting learning, empowering patients to face emotional challenges more effectively.

DISCUSSION

Body image plays a crucial role in the formation of the individual's identity, constituting an essential subjective component (Bonfim, 2015). According to Finato et al. (2013), body image encompasses the perception that individuals have of themselves, encompassing both internal and external aspects, and influences their physical, mental and emotional attitudes, contributing to the construction of self-image. Patients with trimethylaminuria (TMAU) face significant challenges related to this aspect, as the emission of unpleasant odors can result in deep emotional discomfort. This suffering is exacerbated by the messages and body representations conveyed in the media, which intensify the discomfort experienced by patients. In this context, the support of health professionals, such as nutritionists, geneticists, dermatologists, psychiatrists, and psychologists, is essential to provide more effective management (Cuipers et al., 2020).

Psychological intervention, especially cognitive behavioral psychotherapy (CBT), is a widely recognized approach to treating conditions such as depression and anxiety, and is recommended by several clinical guidelines. Studies, such as those by Ebrahimi et al. (2024), Eziakor (2020), and Paulides et al. (2021), demonstrate the effectiveness of CBT in improving the quality of life and understanding of the disease by affected individuals. Although CBT does not directly reduce the physical symptoms of TMAU, it has been shown to be effective in decreasing the psychoemotional symptoms associated with the condition.

Regarding the management of TMAU, dietary approaches, such as reducing the consumption of foods rich in trimethylamine precursors (TMA), such as fish, eggs, and certain vegetables, can help (Li, 2011). In addition, the use of supplements and medications, such as activated charcoal and copper, can reduce the absorption of TMA in the gut, while antibiotics can limit the production of TMA by gut bacteria (Arseculeratne et al., 2007). Personal hygiene measures, such as the use of acidic soaps, are also recommended to minimize body odor (Arseculeratne et al., 2007).

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Currently, TMAU is classified into two categories:

1. Primary: It results from a deficiency in the enzyme flavin monooxygenase 3 (FMO3), which prevents the conversion of TMA into trimethylamine N-oxide (TMAO), an odorless substance. This condition is caused by genetic mutations, with more than forty variants identified (Schmidt & Leroux, 2020; Rutkowski et al., 2019).
2. Secondary or acquired: It can be triggered by hormonal problems, liver disease, kidney disease, or viral infections, increasing the production of TMA due to excess dietary precursors, which overloads the body's ability to metabolize it (Rutkowski et al., 2019).

TMAU, known as fish odor syndrome, is a rare metabolic condition that results in a characteristic body odor, causing profound psychosocial impacts on the lives of affected individuals (Wise et al., 2011).

In view of this scenario, it is essential to carry out more research in the psychosocial areas, avoiding biologist reductionism in the treatment of AMTM. There is a need to expand management and psychological support resources, promoting a deeper understanding of the impacts of the condition. This is especially relevant in the training of health professionals, so that they can offer more effective support and resources, allowing patients to overcome their difficulties and live with a higher quality of life and dignity.

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