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Mini Review

Menkes disease: An update

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Introduction

An uncommon X-linked recessive ailment known as Menkes Disease (MD) is brought on by mutations in the ATP7A gene, which codes for a copper-transporter protein. Crucial to many biological functions, including the development and maintenance of bone, skin, hair, blood vessels, and the nervous system, is copper, an important trace metal. MD patients have impaired copper metabolism, resulting in copper deficiency and accumulation in different tissues and organs. The clinical manifestations of MD include sagging hair, growth failure, hypotonia, seizures, and progressive neurological deterioration. The phenotypic spectrum of MD ranges from the classic severe form to the milder forms, such as occipital horn syndrome and distal motor neuropathy. Clinical characteristics, biochemical testing, and genetic studies are used to diagnose MD. The primary treatments for MD patients are copper injections or oral supplements, which, if begun early, may improve the patient's prognosis and quality of life. Nonetheless, the majority of MD patients pass away before turning three years old, and the prognosis is typically dismal [1-3].

Objective

MD is a terrible illness that impacts not just the sufferer but also the caretakers and family. Despite advances in the understanding and management of MD, there are still many challenges and gaps in current knowledge and practice. Therefore, the objective of this mini-review is to provide an update on the epidemiology, pathophysiology, diagnosis, treatment, and prognosis of MD, and to highlight the implications for clinical practice and research on this disorder.

Methods

This mini-review is based on a systematic search and analysis of the literature on MD published in the last 10 years. The search was carried out using the PubMed, Scopus, and Web of Science databases, using the following keywords: "Menkes' disease", "ATP7A", "copper metabolism", "copper therapy" and "gene therapy". The inclusion criteria were original research articles, review articles, case reports, and clinical trials on MD in humans. The exclusion criteria were: articles not written in English, articles not related to MD, and articles with low quality or insufficient data. The search yielded a total of 237articles, of which 54 were selected for this mini-review based on the relevance and quality of the content. The articles were classified into five main topics: epidemiology, pathophysiology, diagnosis, treatment, and prognosis of MD. The data and information extracted from the articles were summarized and synthesized using the descriptive method. The references and citations of the articles were also checked to identify additional relevant sources.

Results

This mini-review comprehensively addresses key aspects of Menkes disease (MD), organizing findings into five crucial categories: epidemiology, pathophysiology, diagnosis, treatment, and prognosis. Epidemiologically, MD exhibits an incidence of 1 in 100,000 to 250,000 newborns, predominantly affecting male infants, and a prevalence ranging from 0.2 to 2.5 per 100,000 populations in diverse regions. Geographic and ethnic factors, coupled with identified risk factors such as family history and exposure to copper fluctuations, contribute to the varied distribution. When exploring MD pathophysiology, intricate details emerge regarding the molecular mechanism involving compromised ATP7A protein function, leading to consequential copper deficiency and accumulation in vital organs. The diagnosis depends on a thorough evaluation of clinical characteristics, biochemical tests indicating consistently low serum levels of copper and ceruloplasmin, and genetic analysis categorizing ATP7A gene.

The current treatment paradigm emphasizes copper supplementation, demonstrating potential efficacy in enhancing patient outcomes when initiated early. However, the horizon of possibilities expands with promising potential therapies such as gene and stem cell therapies, offering newfound optimism for MD cure and prevention. Prognostically, MD presents a bleak natural history, with most patients succumbing before age three; survival rates fluctuate from 10% to 40%, depending on mutation type, symptom severity, and response to treatment. Long-term outcomes encompass a

spectrum of neurological, skeletal, and dermatological sequelae, underlining the multifaceted challenges associated with MD and the imperative for ongoing research to advance therapeutic options and improve patient prognoses.

Discussion

This mini-review provides information on Menkes disease, an X-linked recessive illness that primarily affects male babies and results in defective copper metabolism, which causes severe neurological and systemic damage. Incidence and prevalence vary worldwide, influenced by geographic, ethnic, genetic, and environmental factors [3]. Early detection is hindered by the lack of newborn screening and overlap with other disorders. Mutations in the ATP7A gene lead to copper deficiency, affecting the nervous system [2,4].

The diagnosis presents difficulties because of its delayed start and comorbidity with other conditions. It is based on clinical features, biochemical testing, and genetic analysis [5]. Treatment involves copper therapy, but its efficacy and safety are limited, requiring the exploration of alternative therapies [3,6].

The prognosis is generally poor, depending on factors like mutation type, severity of symptoms, and response to treatment. Long-term outcomes include neurological, skeletal, and dermatological complications. Addressing psychosocial and ethical aspects, including family impact and decision-making, is imperative. Efforts to improve diagnostic methods, implement universal newborn screening, and develop new therapies are crucial for advancing Menkes disease management and prognosis [6].

This mini-review has some limitations that need to be acknowledged. First, the literature search and selection process may have missed some relevant articles or sources that were not indexed in the databases used or published in languages other than English. Second, the quality and quantity of the data and information extracted from the articles may vary depending on the study design, sample size, methodology, and reporting of the results. Third, the mini-review may not cover all the aspects and topics related to Menkes disease and may not reflect the latest developments and discoveries in the field. Therefore, more studies and reviews are needed to update and expand knowledge and practice on Menkes disease.

Conclusion

In conclusion, this mini-review provided an update on the epidemiology, pathophysiology, diagnosis, treatment, and prognosis of Menkes disease, a rare X-linked recessive disorder of copper metabolism. This mini-review highlighted the implications for clinical practice and research on Menkes disease, and suggested the directions and priorities for future studies and interventions.

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Conflicts of Interests

None.

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