Wernicke-Korsakoff Syndrome Related to Alcohol Abuse: A Literature Review

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Abstract. Alcohol abuse has become more prevalent in recent years and it's a causal factor for numerous diseases. Among the consequences of alcohol, thiamine deficiency, also known as vitamin B1, can be highlighted. Amid the diseases caused by thiamine deficiency, we can draw attention to Wernicke's encephalopathy and Korsakoff's psychosis, which are generally referred together as Wernicke-Korsakoff syndrome. Wernicke-Korsakoff Syndrome is a neurological syndrome that can have irreversible consequences for the patient's life, including amnesia. In this context, it is important for clinicians to know about the syndrome and how to prevent possible complications. The goal of the present study is to analyse the articles published in the last 10 years in PUBMED, covering the themes: clinical presentation, diagnosis and treatment of Wernicke-Korsakoff syndrome.

Keywords. Alcoholism; Wernicke Encephalopathy; Korsakoff Syndrome; Thiamine Deficiency; Clinical significance;

1. Introduction

Alcohol abuse is something quite common today, which generates numerous consequences to the health of the population. Among them we highlight the deficiency of Thiamine. The lack of this vitamin can progress to a neurological syndrome called Wernicke-Korsakoff (WKS) if left untreated.

According to the World Health Organization (WHO), worldwide, 3 million deaths per year result from the harmful use of alcohol, computing 5.3% of all deaths (1). Given the above, we see how serous alcohol abuse is.

Alcohol as an intoxicant affects a wide range of structures and processes in the central nervous system and increases the risk for intentional and unintentional injuries and adverse social consequences (1). It has considerable toxic effects on the digestive and cardiovascular systems. Alcoholic beverages are classified as carcinogenic by the International Agency for Research on Cancer and increase the risk of several cancer types (1). Alcohol as an immunosuppressant increases the risk of communicable diseases, including tuberculosis and HIV (1). Chronic alcohol consumption is believed to contribute directly to neurotoxicity via thiamine deficiency, metabolite toxicity and neuroinflammation, leading to the development of serious conditions, such as Wernicke's encephalopathy (WE) and Korsakoff's Psychosis (KP), and to the acceleration of neurodegeneration more generally (2).

As already mentioned, alcohol abuse can cause thiamine deficiency, also called vitamin B1. Thiamine plays a role in several biological processes and is therefore an important vitamin for the body (3). The deficiency of this vitamin is a critical issue because it is still underdiagnosed and is associated with high morbidity and mortality (3). Mortality rates close to 20% have been seen in untreated or inadequately treated patients, and up to 85% of survivors can develop an irreversible neurological condition (3). One of the conditions that thiamine deficiency can lead to is Wernicke-Korsakoff syndrome.

Wernicke-Korsakoff syndrome is the junction of WE and KP, and is often referred to as WKS. The WE occur when the patient is with thiamine deficit, and if left untreated, can evolve to KP, often bringing irreversible neurological changes.

Although this syndrome is a very serious health problem, it's not well understood among the clinicians. The importance of the knowledge about WKS it's related to the consequences, possibly irreversible, if not treated prematurely. It's important to cite the high percents of Korsakoff amnesia for the rest of the living (80%) (4), if not treated the WE.

In this context, this review proposes to make an analysis of the literature available in PUBMED, on the clinical presentation, diagnosis and treatment of WKS. In order to synthetize and make available the knowledge about the main aspects for longer survival of patients with WKS.

2. Methodology

A search was performed in the PUBMED database on 17 September 2023, filtering the results to the last 10 years, written in English, which covered the topics: clinical aspects, diagnoses and treatment of Wernicke-Korsakoff syndrome. For the research, the following keywords were used: "Wernicke-Korsakoff syndrome" AND "alcohol abuse". 50 results were found, then excluded those that were not related to the theme, duplicate articles and unavailable articles. Based on the following criteria, 8 articles were selected. Furthermore, the book "Merritt's Neurology", 12th edition, and the guideline of The European Federation of Neurological Societies (EFNS) were used to embassy the review, besides the articles selected on the PUBMED database.

3. Results and discussions

3.1 Clinical Presentation

The classic clinical triad of the Wernicke syndrome consists of mental status changes, ophthalmoplegia, and gait ataxia (5). However, the incidence of all three symptoms in patients is rare (≈17%) and most patients present with delirium alone (6). The cognitive changes range from apathy and mild neurocognitive symptoms to severe symptoms including, in rare situations, coma (5).

Abnormal eye movements include nystagmus, paralysis of the lateral rectus, paralysis of the conjugated gaze, progressing to complete ophthalmoplegia (4). Although the slowness of the pupillary reaction is common, total loss of reactivity to light and ptosis are rare (4).

Ataxic gait is not just a manifestation of cerebellar pathology; it is the combination of vestibular paralysis and polyneuropathy. The stance of the patients changes from normal to wide with bradykinesia, and patients in the acute stage of the disease have vestibular dysfunction (which mostly does not result in auditory impairment) (6).

Patients with WE commonly present signs of nutritional deficiency or liver involvement, as well as autonomous signs (4). Acute tachycardia, exertional dyspnoea, and postural hypotension not explained by hypovolemia are common, usually signs and symptoms explained by thiamine deficiency (4).

Due to nonspecific clinical manifestations, often the diagnosis is made after death, by autopsy. When not diagnosed the WE after alcohol abuse, it's quite probably the evolution to KP.

The Korsakoff syndrome is generally known as a disorder of memory, but it has many others cognitive and behavioural symptoms. The symptom of memory disorder is primarily related to declarative memory, which affects both episodic memory and semantic memory, being the anterograde memory processes typically more severely affected than retrograde memory processes (7).

There are other symptoms besides the memory disorder, like executive disfunction, apathy, disorders of affect, emotion perception, and social cognition (7).

3.2 Diagnosis

In addition to the clinical presentations mentioned, we can make use of laboratory and imaging tests to help diagnose the syndrome.

In line with the clinical suspicion, The European Federation of Neurological Societies (EFNS) guideline recommends a blood sample for measurement of total thiamine drawn immediately before administration of thiamine and sent for HPLC analysis (GPP) (8). The sample should be taken before administration of thiamine and should be protected from light (8). However, the diagnosis cannot be based only on blood levels of thiamine (6).

Regarding imaging, computed tomography is typically non-contributory in the diagnosis of either condition(9). Magnetic Resonance should be used to support the diagnosis of acute WE in patients both with and without alcoholism (9). MRI findings in acute Wernicke's relate to oedema of the affected tissue and include T2-weighted and FLAIR signal hyperintensity in the grey matter of the periventricular region, mammillary bodies, thalamus and the superior and inferior colliculi (9). Contrast enhancement of the mammillary bodies and colliculi is highly specific for WE (9).

MR findings in KS include T2-weighted and FLAIR hyperintensities within the periventricular areas, the anterior nucleus of the thalamus, the mammillary bodies and posterior midbrain and the peri-aqueduct grey matter (9). Imaging features of both WE and KS are similar, except that damage to the anterior nucleus of the thalamus appears more severe in KS (9).

3.3 Treatment

The basis of treatment is the administration of thiamine. In view of the difficulty and delay of diagnostic confirmation, a high clinical suspicion should prompt the clinician to start treatment as soon as possible (5). This practice is adopted because thiamine is safe and not expensive (5).

When a suspected case of WE, glucose must be administered, especially alcoholics presenting with hypoglycaemia, it is recommended that thiamine infusion is given before or along with the glucose load to prevent the exacerbation of symptoms (6).

Evidences from randomized controlled clinical trials are insufficient to guide clinicians in determining the

dose, frequency, route, or duration of thiamine treatment for prophylaxis against or treatment of WKS due to alcohol abuse(10,11).

EFNS's guideline recommends that thiamine should be given 200 mg three times daily and preferably via intravenous instead of intramuscular route (8). Thiamine should be given before any carbohydrate, and a normal diet should be instituted immediately after thiamine (8). Treatment should be continued until there is no further improvement in signs and symptoms (8)

As a residual syndrome after WE, KS can be seen as a form of acquired brain damage. After treating WE with thiamine replacement and after a convalescence phase, the effect of pharmacological interventions is necessarily confined to enhancing the skills that remain, or to suppress symptoms that interfere with normal functioning (7). In KS, however, there is no evidence of any beneficial effect of pharmacological therapy, the perspectives for rehabilitation programs are more promising than those of pharmacological interventions (7).

The traditional view that KS is a static condition that does not permit further recovery is obsolete and therefore gradually abandoned, thanks to accumulating evidence that memory rehabilitation is possible in KS (7). Memory compensation techniques such as using agendas, memory cards, smartphones, and smartwatches are promising (7).

With thiamine replacement, eye abnormalities (especially abducens and gaze paralysis) improve within a few hours and usually regress completely within 1 week; In about 35% of cases, horizontal nystagmus persists indefinitely (4). The overall confusion may improve in a few hours or days and usually regresses within 1 month, although more than 80% of patients continue with Korsakoff's amnesia (4). In less than 25% of these patients, the memory deficit eventually disappears (4). Ataxia may improve in a few days, but less than 50% of patients recover completely and about 35% show no improvement (4).

4. Conclusion

It is concluded that WKS is a syndrome that can generate irreversible consequences for the patient's life, so it is of paramount importance the diagnosis and early treatment of the disease, in order to prevent more serious complications. In addition to early diagnosis and treatment, it is important to raise awareness of the population about the abuse of alcohol use and its consequences for the human body, especially thiamine deficiency.

There is also a need for studies involving the treatment of KP, both pharmacological therapy and behavioural therapy. Finally, it's concluded by reaffirming, once again, the importance of the clinician to know the clinical manifestations of WKS, to be made the diagnosis and treatment as soon as possible, avoiding the possible complications to the life of the individual.

5. References

1. World Health Organization (WHO). https://www.who.int/health-topics/alcohol#tab=tab_1. 23AD. Alcohol.
2. Nutt D, Hayes A, Fonville L, Zafar R, Palmer EOC, Paterson L, et al. Alcohol and the brain. Nutrients. 2021 Nov 1;13(11).
3. Polegato BF, Pereira AG, Azevedo PS, Costa NA, Zornoff LAM, Paiva SAR, et al. Role of Thiamin in Health and Disease. Vol. 34, Nutrition in Clinical Practice. John Wiley and Sons Inc.; 2019. p. 558–64.
4. Rowland LP, Pedley TA, editors. Merritt's Neurology. 12th ed. Lippincott Williams & Wilkins; 2010.
5. Sinha S, Kataria A, Kolla BP, Thusius N, Loukianova LL. Wernicke Encephalopathy—Clinical Pearls. Vol. 94, Mayo Clinic Proceedings. Elsevier Ltd; 2019. p. 1065–72.
6. Chandrakumar A, Bhardwaj A, T'Jong GW. Review of thiamine deficiency disorders: Wernicke encephalopathy and Korsakoff psychosis. Vol. 30, Journal of Basic and Clinical Physiology and Pharmacology. De Gruyter; 2019. p. 153–62.
7. Arts NJM, Walvoort SJW, Kessels RPC. Korsakoff's syndrome: A critical review. Vol. 13, Neuropsychiatric Disease and Treatment. Dove Medical Press Ltd; 2017. p. 2875–90.
8. Galvin R, Bråthen G, Ivashynka A, Hillbom M, Tanasescu R, Leone MA. EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy. Eur J Neurol. 2010 Dec;17(12):1408–18.
9. Logan C, Asadi H, Kok HK, Looby ST, Brennan P, O'Hare A, et al. Neuroimaging of chronic alcohol misuse. J Med Imaging Radiat Oncol. 2017 Aug 1;61(4):435–40.
10. Dingwall KM, Delima JF, Binks P, Batey R, Bowden SC. What is the optimum thiamine dose to treat or prevent Wernicke's encephalopathy or Wernicke–Korsakoff syndrome? Results of a randomized controlled trial. Alcohol Clin Exp Res. 2022 Jun 1;46(6):1133–47.

11. Day E, Bentham PW, Callaghan R, Kuruvilla T, George S. Thiamine for prevention and treatment of Wernicke-Korsakoff Syndrome in people who abuse alcohol. Vol. 2013, Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd; 2013.