DOI: https://doi.org/10.61427/jcpr.v4i2.2024.133.
Lakshmi Himaja Bandaru et al., J.Clin.Pharm.Res., 2024; 4(2): 7-10.

Journal of
Clinical and Pharmaceutical Research

REVIEW OPEN ACCESS

A Brief Review on Korsakoff Syndrome

Lakshmi Himaja Bandaru

Department of Pharmacy Practice, GIET School of Pharmacy, Rajahmundry, Andhra Pradesh, India.

ARTICLE INFO

Article History:
Received: 20.02.2024
Revised: 23.03.2024
Accepted: 21.04.2024

Keywords :
Amnesia
Korsakoff Syndrome
Thiamine

Corresponding Author:
Dr. Lakshmi Himaja Bandaru Pharm.D
Assistant Professor
Department of Pharmacy Practice
GIET School of Pharmacy,
Rajahmundry, Andhra Pradesh, India.
Email: himaja.bandaru@gmail.com

ABSTRACT

Korsakoff Syndrome (KS) is a residual syndrome which is characterized with neuropsychological conditions affecting the daily life of chronic drinkers of alcohol. Sergei Korsakoff is a Russian neuropsychiatrist, in the year 1887 given a note on the Korsakoff syndrome which is characterized by an extraordinary peculiar amnesia which has been associated with peripheral inflammation of the nerves. This syndrome can be chronic in onset and remains permanent. The person suffering with KS can be observed with cognitive and behavioral dysfunction. The symptoms of amnesia, executive dysfunction, confabulation, apathy and social-cognitive impairments can be observed in these affected patients. In the aspect of the pharmacological treatment of KS sufficient concentration of thiamine should be administered parenterally. In alcoholic patients, the doses of thiamine can be administered approximately 500mg or above but the evidence in this aspect is less available. Compared to the pharmacological therapy, the rehabilitation programme can be more helpful to the patients with KS. Among six studies, evidence was produced that some of the techniques which can be helpful for the compensation of memory can include use of agendas, memory cards, gadgets like mobiles and smart watches can be helpful in the patients with KS. For the better improvement of the cognition, interventions associated with errorless learning can be possible theoretically. In this learning process the patients are not permitted to make any errors. This may also support the semantic learning process.

Introduction

Korsakoff Syndrome (KS) is a residual syndrome which is characterized with neuropsychological conditions affecting the daily life of chronic drinkers of alcohol. **S**ergei Korsakoff is a Russian neuropsychiatrist, in the year 1887 given a note on the Korsakoff syndrome which is characterized by an extraordinary peculiar amnesia which has been associated with peripheral inflammation of the nerves. This syndrome can be chronic in onset and remains permanent. The person suffering with KS can be observed with cognitive and behavioral dysfunction. The symptoms of amnesia, executive dysfunction, confabulation, apathy and social-cognitive impairments can be observed in these affected patients. Episodes of Wernicke encephalopathy which is characterized by global amnesia can lead to Korsakoff syndrome [1-4].

Wernicke encephalopathy is a medical emergency condition with an acute onset of neuropsychiatric disorders which might be reversible if treated early. In refeeding syndrome, the patients with thiamine deficiency can be observed with decreased calories due to lack of food intake for few days or weeks or months which can be associated with Wernicke encephalopathy. So, with the help of dietician the calorie intake is reintroduced with the proper diet regimen.

Combination of Wernicke encephalopathy and Korsakoff Syndrome is a rare disease which can be called as the Wernicke-Korsakoff Syndrome (WKS) or Korsakoff symptom complex or the disease of the alcoholics. The thiamine deficiency plays a pivotal role in alcoholics with Wernicke encephalopathy. Alcohol intake causes direct neurological toxicity by decreasing the levels of thiamine which results in intoxication, withdrawal symptoms, cerebrovascular disease, liver impairment, head injury complications and abnormal psychological functioning. In Wernicke encephalopathy, concomitant infections may lead to sepsis where the exact cause and mechanism is not known [5-7].

Prevalence

Certain factors like socioeconomic status and age between 50-60 years can increase the prevalence rate of Korsakoff syndrome. According to some studies, the prevalence of WKS can be higher than 12.5% especially among the alcoholics whereas, in the general population it can be approximately 2%.

Wernicke encephalopathy can also be associated with other diseases like Crohn's disease, hyperthyroidism, acute pancreatitis and others [8-10].

Genetics and neurochemistry

In WKS, three genetic variants have been identified based on the direct genomic sequences of SLC19A2 which is a high affinity transporter gene. In thiamine deficiency, the transketolase enzyme can alter the six types of neurotransmitter system which includes acetylcholine and GABA. The involvement of the genetic predisposition in the aspect of developing this syndrome remained unclear.

Etiopathogenesis

In thiamine deficiency and Wernicke encephalopathy, changes in the microglia and the astrocytes can be observed. These changes in astrocyte can cause decrease in the ketoglutarate-dehydrogenase activity. The thiamine deficiency includes the loss of the functioning of glutamate transporters and specific proteins of the astrocytes. Both of them causes the accumulation of the glutamate extracellularly resulting in the excitotoxicity of the neural cell damage involving in the focal neuronal damage. Reduction in the usage of the glucose and oxidative stress can be observed secondary to the endothelial cell abnormality due to decreased levels of transketolase which is dependent on the activity of the thiamine. This results in cytotoxic effect and vasogenic edema within the astrocytes initially and then in the neurons. In these neurons, the blood brain barrier is altered and local petechiae of the brain regions can be observed among the thiamine deficient patients. Thereafter, the fragmentation of the DNA in neurons and lactic acidosis can take place within the astrocytes & neurons as well, which can be associated with the irreversible structural damage of the brain.

In some studies, it is explained that in thiamine deficiency there is a loss of functioning of neurons locally where inflammation along with hyperactive microglia and pro-inflammatory cytokines are involved in the cellular response. The actual function of the microglia is defensive, but due to over stimulation and hyperactivity of microglia it can further trigger the neuronal toxicity and can lead to damage of the neurons until unless the cholinergic neurons are no longer showing their inhibitory action. In thiamine deficiency, there can be decreased bioavailability of acetylcholine due to the involvement of acetyl-cholinergic synaptic transmission. In this transmission, the acetylation rate might be low which can be related to acetylcholine production but the exact mechanism is unknown [11-13].

Clinical characteristics

Chronic amnesia is the major issue of concern in WE, observed among the chronic alcohol abusers and non-alcoholics also. It can be characterized by asking the same questions repeatedly, reading the same pages for longer period of time, failure to recognize the people at the onset of illness. Generally, the patients of Wernicke encephalopathy were observed with the triad of the symptoms that include mental confusion, ophthalmoplegia and ataxia.

Confabulation is a neuropsychological disorder which can be associated with false recollections or shuffled memories. The cognitive or behavior symptoms can also affect the emotional perception and also the social cognition. In case of thiamine deficiency, the patient can be observed with anorexia, dizziness, elevated heart rate, retention of the urinary bladder where all these symptoms can be a triad of anticholinergic autonomic dysfunction. Alcoholics and non-alcoholics have the symptoms of vomiting, weight loss and vision impairment due to thiamine deficiency [14,15].

Neuroimaging

Based on the MRI, many of the alcoholic KS patients can be observed with the volume deficits of gray and white matter where as in non-alcoholic KS patients, no volume reductions can be observed. Atrophy of the mammillary bodies or the thalamus or cerebellar vermis can be observed in the non-alcoholic KS patients where as in the alcoholics severe damage of the structures can be identified, but we can't completely rely on MRI because the diagnostic aspects varies among the different individuals where the nutritional deficits can also be associated [16-19].

Prognosis

Based on the study by Palm et al which was conducted in 2022, the median survival of patients with WKS was found to be 10.7 years and dementia caused due to alcohol intake was found to be 5.9 years. Other disease complications like cardiovascular

diseases, cancers, gastrointestinal disorders, psychiatric & behavioral disorders and others external etiological factors can be the reasons for the mortality of the patients diagnosed with WKS [20].

Pharmacological treatment

In the aspect of the pharmacological treatment of KS sufficient concentration of thiamine should be administered parenterally. In alcoholic patients, the doses of thiamine can be administered approximately 500mg or above but the evidence in this aspect is less available. According to the Cochrane review of 2008, limited information was available in the aspect of dose, frequency, route of administration and duration of the thiamine therapy. According to the European Federation of Neurological Societies (EFNS) patients suffering with any two of the following such as dietary deficits, dysfunction of the cerebellum, memory impairment or the altered mental state and abnormal oculomotor malfunctioning can be preferred with 200mg of IV parenteral therapy thrice daily until the symptoms are resolved [21-24].

In some studies, parenteral therapy of thiamine can result in pruritis which is observed to be the major reaction. Anaphylactic reactions can also be reported. Especially in alcoholics, hypo-magnesia levels can be observed which can result in the alteration of therapeutic response of the thiamine. Patients with decreased hypomagnesia, alcohol withdrawal, untoward reactions of PPI's and diuretics do not respond to the thiamine [25,26]. Starvation, malnutrition, malabsorption and vomiting can lead to decreased availability of the thiamine. Improper utilization of thiamine can be caused due to the decreased enzyme activity and accelerated usage can be observed due to excessive or hypermetabolism [7].

Course of illness

In patients with WKS, delirium can lead to cognitive reductions. Ataxia can be observed before reaching the plateau phase within few months which can also be associated with the chronic Korsakoff stage. Alcohol abstinence is required for at least 6 weeks for the neuropsychological evaluation of the KS. Patients can be observed with the agnosia and memory gaps. At the initial phases itself efficient treatment is required within the limited duration [27].

Cognitive rehabilitation

Compared to the pharmacological therapy the rehabilitation programme can be more helpful to the patients with KS. Among six studies, evidence was produced that some of the techniques which can be helpful for the compensation of memory can include use of agendas, memory cards, gadgets like mobiles and smart watches can be helpful in the patients with KS. For the better improvement of the cognition, interventions associated with errorless learning can be possible theoretically. In this learning process the patients are not permitted to make any errors. This may also support the semantic learning process [28].

References

1. Nicolaas JM Arts, Serge JW Walvoort et al. Korsakoff's syndrome: A critical review. Neuropsychiatr Dis Treat. 2017; 13: 2875–90.

2. Victor M, Adams R, Collins G, Eds: The Wernicke-Korsakoff syndrome and related neurologic disorders due to alcoholism and malnutrition. Philadelphia: FA Davis. 1989; 3:142–5.

3. Delay J, Brion S. Le Syndrome de Korsakoff. Paris: Masson; 1969.

4. Fama R, Pitel AL, Sullivan EV. Anterograde episodic memory in Korsakoff syndrome. Neuropsychol Rev. 2012; 22(2): 93–104.

5. Wijnia JW, van de Wetering BJ, Zwart E, Nieuwenhuis KG, Goossensen MA. Evolution of Wernicke-Korsakoff syndrome in self-neglecting alcoholics: Preliminary results of relation with Wernicke-delirium and diabetes mellitus. Am J. Addict. 2012; 21:104–10.

6. Hershkowitz E, Reshef A, Munich O, Yosefi B, Markel A. Thiamine deficiency in self-induced refeeding syndrome, an undetected and potentially lethal condition. Case Rep Med. 2014; 605707.

7. Elie Isenberg-Grzeda MD, Haley E, Kutner MA, Stephen E, Nicolson MD. Wernicke-Korsakoff-Syndrome: Under-Recognized and Under-Treated. Psychosomatics. 2012; 53: 507–16.

8. Torvik A: Wernicke's encephalopathy—prevalence and clinical spectrum. Alcohol Alcohol (Suppl) 1991; 1:381–4.

9. Torvik A, Lindboe CF, Rogde S: Brain lesions in alcoholics. A neuropathological study with clinical correlations. J Neurol Sci. 1982; 56(2–3):233–48.

10. Lishman WA: Cerebral disorder in alcoholism: syndromes of impairment. Brain. 1981; 104(Pt 1):1–20.

11. Michael D, Kopelman, Allan D, Thomson, et al. The Korsakoff Syndrome: Clinical Aspects, Psychology and Treatment. Alcohol & Alcoholism. 2009; 44(2): 148–54.

12. Cullen KM, Halliday GM, Caine D, Kril JJ. The nucleus basalis (Ch4) in the alcoholic Wernicke-Korsakoff syndrome: reduced cell number in both amnesic and non-amnesic patients. J Neurol Neurosurg Psychiatry. 1997; 63(3):315–20.

13. Baker KG, Halliday GM, Harper CG. Effect of chronic alcohol consumption on the human locus coeruleus. Alcohol Clin Exp Res. 1994; 18(6):1491–6.

14. Sharp CS, Wilson MP, Nordstrom K. Psychiatric emergencies for clinicians: Emergency department management of wernicke-korsakoff syndrome. J Emerg Med. 2016; 51:401–4.

15. Arts NJ, Walvoort SJ, Kessels RP. Korsakoff's syndrome: A critical review. Neuropsychiatr Dis Treat. 2017; 13:2875–90.

16. Pitel AL, Chételat G, Le Berre AP, Desgranges B, Eustache F, Beaunieux H. Macrostructural abnormalities in Korsakoff syndrome compared with uncomplicated alcoholism. Neurology. 2012; 78(17): 1330–3.

17. Le Berre AP, Pitel AL, Chanraud S, et al. Chronic alcohol consumption and its effect on nodes of frontocerebellar and limbic circuitry: comparison of effects in France and the United States. Hum Brain Mapp. 2014; 35(9):4635–53.

18. Nikolakaros G, Ilonen T, Kurki T, Paju J, Papageorgiou SG, Vataja R. Non-alcoholic Korsakoff syndrome in psychiatric patients with a history of undiagnosed Wernicke's encephalopathy. J Neurol Sci. 2016; 370:296–302.

19. Gasquoine PG. A case of bariatric surgery-related Wernicke–Korsakoff syndrome with persisting anterograde amnesia. Arch Clin Neuropsychol. 2017; 32(5):610–7.

20. Palm A, Vataja R, Talaslahti T, Ginters M, Kautiainen H, Elonheimo H, Suvisaari J, Lindberg N, Koponen H. Incidence and mortality of alcohol-related dementia and Wernicke-Korsakoff syndrome: A nationwide register study. Int. J. Geriatr. Psychiatry 2022; 37: e5775.

21. Pruckner N, Baumgartner J, Hinterbuchinger B, Glahn A, Vyssoki S, Vyssoki B. Thiamine substitution in alcohol use disorder: A narrative review of medical guidelines. Eur Addict Res. 2019; 25, 103–10.

22. Praharaj SK, Munoli RN, Shenoy S, Udupa ST, Thomas LS. High-dose thiamine strategy in Wernicke-Korsakoff syndrome and related thiamine deficiency conditions associated with alcohol use disorder. Indian J Psychiatry. 2021; 63: 121–6.

23. Thomson AD, Guerrini I, Marshall EJ. The evolution and treatment of Korsakoff's syndrome: Out of sight, out of mind? Neuropsychol Rev. 2012; 22:81–92.

24. Galvin R, Brathen G, Ivashynka A, Hillbom M, Tanasescu R, Leone MA, EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy. Eur J Neurol. 2010; 17:1408–18.

25. Dingwall KM, Delima JF, Gent D, Batey RG, Hypomagnesaemia and its potential impact on thiamine utilisation in patients with alcohol misuse at the Alice Springs Hospital. Drug Alcohol Rev. 2015; 34: 323–8.

26. Parrish CR, Thomson AD, Guerrini I, Marshall EJ. Nutrition Issues in Gastroenterology: Series #75. Wernicke's Encephalopathy: Role of Thiamine. Practical Gastroenterology. 2009.

27. Schrader M, Bamborschke S, Lenk U, Sterr A. Case report: Intensive inpatient neurorehabilitation achieves sustained real-world benefits in severe alcohol-related Wernicke-Korsakoff syndrome: A case study with 7-years follow-up. Front. Psychol. 2021; 12: 693920.

28. Oudman E, Nijboer TCW, Postma A, Wijnia JW, Van der Stigchel S. Procedural learning and memory rehabilitation in Korsakoff's syndrome – a review of the Literature. Neuropsychol Rev. 2015; 25(2):134–48.