



International Journal of Pharmacognosy and Chemistry

Short Communication

WERNICKES KORSAKOFF SYNDROME

Syam Prashanth Pedada*, Jyotsna Allamsetty, Ujwala Mukthipudi.

Department of Pharmacy Practice, Avanthi Institute of Pharmaceutical Sciences, Cherukupally (Vil), Bhogapuram (M), Vizianagaram (Dist), A.P-531162.

Abstract

Wernickes korsakoff syndrome (WKS) is a combined disorder of Wernicke's encephalopathy and korsakoff psychosis which is a neurological disorder. Wernicke enchplaophaty and korsakoff psychosis are the acute and the chronic phase respectively, wernickes korsakoff syndrome is mostly observed in chronic alcoholism and rarely with non-alcoholics. It includes symptoms of diplopia, ophthalmoplegia, ataxia, retrograde and anterograde amnesia. It is easily diagnosed by a dietary deficiency, ocular abnormalities, cerebellar dysfunction, memory impairment. WKS also include gliosis and microhemorrhages in periaqueductal and paraventricular grey matter, atrophy in the mamillary bodies and thalamus, volume deficits in the hippocampus, cerebellar hemispheres, pons, and anterior superior vermis. In the early stages of the Wernicke's korsakoff can be preventable to the chronic stage irreversible stage of korsakoff psychosis by treating it with thiamine for few days and the improvement of the symptoms is observed after few weeks.

Keywords: Wernickes korsakoff syndrome, encephalopathy, cerebellar dysfunction, korsakoff psychosis.



Article Info

Received: 15-07-2020

Revised: 25-08-2020

Accepted: 18-09-2020

*Corresponding Author

Syam Prashanth Pedada

Email: shyamprashanth1995@gmail.com



INTRODUCTION

Wernicke's Korsakoff syndrome is the type of spectrum of the neurological disorder. It is commonly seen in the patient with chronic alcoholism. The main complication of this syndrome is the deficiency of thiamine (vitamin-B). It is also seen in nonalcoholics (rarely). Wernicke's Korsakoff syndrome is a combined neurological disorder, which is preventable and also a life-threatening neuropsychiatric syndrome. Wernicke's encephalopathy is an acute reversible stage because it can be treated by the vitamin -B and if it is left untreated then it may lead to Korsakoff syndrome which is chronic and irreversible [1,2,3,4]. Prevalence rate is high in older individuals living alone or with psychiatric inpatients. Sometimes prevalence is not associated with alcohol consumption per capita. Korsakoff syndrome damages nerve cells and supporting cells in the body and spinal cord as well and also the part of the brain which is involved in the memory.

HISTORY

Wernicke's Korsakoff syndrome was discovered by Carl Wernicke and Sereji Korsakoff in the 18th century.

Carl Wernicke:1881

- Onset of paralysis of eye disorder
- Ataxia of gait
- Mental confusion

Sereji Korsakoff :1887 and 1897

- Amnesic syndrome
- Polyneuropathy
- Psychosis polyneuritica
- Two facets of the same disease.
- He observed these symptoms in three patients, two alcoholics and a patient with persistent vomiting after ingestion of the sulphuric acid, who presented with progressive stupor and coma, progressing to death.
- Wernicke described punctate hemorrhages affecting grey matter around the third and fourth ventricles and aqueduct of Sylvius and designated the pathology "polioencephalitis hemorrhagica superioris".
- In 1852, Magnus Huss mentioned a disturbance of memory in alcoholics, elucidated between 1887 and 1891 by the Russian psychiatrist Sereji Korsakoff, who considered that the polyneuropathy and the memory of

disorder represented 'two facets of the same disease', which was designated psychosis polyneuritica.

- The postulation that a single cause was responsible for both Wernicke's disease and Korsakoff psychosis was first made by Murawieff in 1897 [5].
- "polioencephalitis superior hemorrhagica" was published by Wernicke in the second volume of *Lehrbuch der Gehirnkrankheiten* [6].
- Karl Bonhoeffer was the first German neuropsychiatrist who said that Wernicke's encephalopathy and Korsakoff syndrome are the combined disorder. He also often saw that the Wernicke's encephalopathy phase if untreated it later goes to Korsakoff syndrome and sometimes Wernicke's encephalopathy can be misdiagnosed due to the mental condition [7,8].
- Korsakoff, Wernicke, and Bonhoeffer knew nothing about the real cause of WE and KS. Only after the concept of "vital amines" or "vitamins" had evolved (in 1912), and thiamine was isolated (in 1926) and synthesized (in 1936), the etiology of WE and KS could be fully clarified (in 1952) [9,10].

CLINICAL MANIFESTATIONS

WERNICKE'S ENCEPHALOPATHY

- Ophthalmoplegia- Weakness or Paralysis of Eye Muscle.
- Nystagmus
- Peripheral Neuropathy
- Ataxia and unsteady gait
- Changes in mental state - confusion, apathy, difficulty in concentrating.
- If untreated leads to coma and death

KORASOKOFF SYNDROME

Targets limbic system.

- Severe memory impairment
- Anterograde amnesia : inability to create new memories.
- Retrograde amnesia: inability to recall previous memories.
- Confabulation which creates stories to fill the gaps in their memory

ETHIOLOGY

MAIN CAUSES

- Alcohol misuse of malnutrition
- Recurrent vomiting and chronic diarrhoea
- Unbalanced nutrition
- Magnesium depletion
- Chemical compounds and drugs (tolazamide, high dose of nitroglycerine)

OTHER CAUSES

- Terminal cancer
- Starvation
- Inflammatory bowel disease
- Aids
- Breast feeding without supplements
- Systemic disorders like TB, uremia.

SYMPTOMS OF VITAMIN –B DEFICIENCY

- Loss of appetite
- Nausea and vomiting
- Fatigue, weakness, apathy
- Giddiness, diplopia
- Insomnia, anxiety
- Difficulty in concentration.
- Loss of memory
- Decompensation: confusion, disorientation, confabulation, hallucination.

PATHOPHYSIOLOGY

- Thiamine is stored in liver and it is absorbed to duodenum and then it moves throughout the body. It also involves in numerous cellular processes that require thiamine. Thiamine is converted to thiamine pyrophosphate. It is metabolically active form of thiamine. It consists of enzymes such as
 - Pyruvate dehydrogenase
 - Transketolase
 - Alpha keto glutarate dehydrogenase
- Thiamine pyrophosphate is useful for glucose metabolism and also helps in the metabolism of lipids and carbohydrates and maintains normal amino acids and neurotransmitter levels. Thiamine deficiency leads to impaired glucose metabolism and decreased cellular energy.
- Thiamine pyrophosphate also helps for propagation of neural impulse of axon.

- Alcohol interferes with the conversion of thiamine to thiamine pyrophosphate by blocking thiamine pyrophosphate synthetase. Chronic alcohol leads to cirrhosis which also interferes with storage of thiamine.
- Brain atrophy and chronic alcoholism leads to dysfunction or damage of mammillary bodies, cerebellum, thalamus, frontal lobe, periaqueductal grey matter, walls of fourth ventricle, cortex.
- Ocular lesions occur by the damage of abducens nuclei, midbrain and damage of superior vermis leads to ataxia.

DIAGNOSIS

- BLOOD BY MEASURING B1 LEVEL
- LIVER FUNCTION TEST
- MRI-DEGENERATION OF MAMMILARY BODIES

DIFFERENTIAL DIAGNOSIS

- Anoxic encephalopathy
- Alzheimer's disease
- Temporal lobe epilepsy
- Concussive head injury
- Temporal lobe infarction
- Third ventricular tumor

PROGNOSIS

- Mental state complication
- Ataxic complications
- Ocular complications.

TREATMENT

Identifying this diagnosis is relatively simple but the management is unsatisfactory because this disorder has high mortality and morbidity rate. Most of the patients need long term care for the Wernicke-Korsakoff syndrome because of the long term hospitalization. Infusion of thiamine for few days (500mg-1500 mg for thrice daily) will improve the symptoms of Wernicke-Korsakoff syndrome then after have to give glucose to normalize the levels of the B1 level [11,12,13,14]. Korsakoff syndrome can be prevented due to earlier administration of the thiamine for few days when the patient is suffering from the Wernicke-Korsakoff encephalopathy. Due to the thiamine administration we can see the improvement in the patients within few weeks (2-6 weeks). Proper nutrition combined

with the thiamine supplement leads to prevention of the risk of this syndrome.

CONCLUSION

WKS is a neuropsychiatric disorders associated with thiamine deficiency. The absence of the thiamine in alcoholic patients leads to chronic cognitive impairment and Korsakoff syndrome. The contribution of the alcohol abuse lead to the development of the wernicke encephalopathy (WE) and korsakoff syndrome (KS). Alcohol abuse play an important cause for the WKS which leads to the extension of wernickes encephalopathy to korsakoff syndrome. Thiamine deficiency is seen in both alcohol and non-alcoholic due to genetic susceptibilities and acquired deficiency. Long term care is needed for the WKS patients by guiding them with the memory rehabilitation and also require more attention from neuropsychiatrists, neurologists, psychiatrists, dieticians. To get the good outcome for the WE is to treat the patient with the thiamine in the early WE.

REFERENCES

- Gerridzen IJ, Joling KJ, Depla MF, Veenhuizen RB, Verschuur EML, Twisk JWR, Hertogh CPM. Awareness and its relationships with neuropsychiatric symptoms in people with Korsakoff syndrome or other alcohol-related cognitive disorders living in specialized nursing homes. *Int J Geriatr Psychiatry*. 2019 Jun;34(6):836-845. [PMC free article] [PubMed]
- Yoon C, Gedzior J, DePry D. Wernicke-Korsakoff syndrome: Focus on low-threshold diagnosis and prompt treatment in the primary care setting. *Int J Psychiatry Med*. 2019 May;54(3):172-180. [PubMed]
- van Dongen LCM, Wingbermühle E, van der Veld WM, Vermeulen K, Bos-Roubos AG, Ockeloen CW, Kleefstra T, Egger JIM. Exploring the behavioral and cognitive phenotype of KBG syndrome. *Genes Brain Behav*. 2019 Apr;18(4):e12553. [PMC free article] [PubMed]
- Polegato BF, Pereira AG, Azevedo PS, Costa NA, Zornoff LAM, Paiva SAR, Minicucci MF. Role of Thiamin in Health and Disease. *Nutr Clin Pract*. 2019 Aug;34(4):558-564. [PubMed]
- Harper C, Gold J, Rodriguez M, Perdices M. The prevalence of the Wernicke-Korsakoff syndrome in Sydney, Australia: a prospective necropsy study. *J Neurol Neurosurg Psychiatry*. 1989 Feb;52(2):282-285. [Europe PMC free article] [Abstract] [Google Scholar]
- w ernicke C. *Lehrbuch Der Gehirnkrankheiten Für Aerzte Und Studirende, Band II*. Kassel: Fischer; 1881. [Google Scholar]
- Bonhoeffer K. *Die Akuten Geisteskrankheiten Der Gewohnheitstrinker*. Jena: Fischer; 1901. [Google Scholar]
- Bonhoeffer K. *Der Korsakowsche Symptomenkomplex in seinen Beziehungen zu den verschiedenen Krankheitsformen*. *Allg Z Psychiat*. 1904;61:744-752. [Google Scholar]
- Wuest H. The history of thiamine. *Ann N Y Acad Sci*. 1962;98:385-400. [PubMed] [Google Scholar]
- Phillips BGB, Victor M, Adams RD, Davidson CS. A study of the nutritional defect in Wernicke's syndrome; the effect of a purified diet, thiamine, and other vitamins on the clinical manifestations. *J Clin Invest*. 1952;31(10):859-871. [PMC free article] [PubMed] [Google Scholar]
- Isenberg-Grzeda E, Chabon B, Nicolson SE. Prescribing thiamine to inpatients with alcohol use disorders: how well are we doing? *J Addict Med*. 2014 Jan-Feb;8(1):1-5. [PubMed].
- Feeney GF, Connor JP. Wernicke-Korsakoff syndrome (WKS) in Australia: no room for complacency. *Drug Alcohol Rev*. 2008 Jul;27(4):388-92. [PubMed]
- Harper C. The neurotoxicity of alcohol. *Hum Exp Toxicol*. 2007 Mar;26(3):251-7. [PubMed].
- Day E, Bentham P, Callaghan R, Kuruvilla T, George S. Thiamine for Wernicke-Korsakoff Syndrome in people at risk from alcohol abuse. *Cochrane Database Syst Rev*. 2004;(1):CD004033. [PubMed]