EXPERIENCE WITH HIGH-DOSE THIAMINE (VITAMIN B1) THERAPY IN THE MANAGEMENT OF KORSAKOV-TYPE ALCOHOLIC ENCEPHALOPATHY: CLINICAL EFFICACY AND NEUROPSYCHOLOGICAL OUTCOMES

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Annotation: *Alcoholic encephalopathies remain a serious complication of chronic alcohol dependence and are associated with high levels of disability and poor prognosis. Therapeutic outcomes largely depend on the timeliness and adequacy of pathogenetic treatment. Korsakov-type alcoholic encephalopathy most commonly develops during the resolution of severe alcohol withdrawal delirium and is closely linked to thiamine deficiency. This study evaluates the clinical effectiveness of thiamine megadoses compared to standard complex therapy in patients with Korsakov syndrome following prolonged alcoholic delirium. The findings demonstrate that high-dose thiamine therapy contributes to faster regression of psychopathological symptoms, shorter duration of consciousness disorders, and more pronounced recovery of neurological functions.*

Keywords: *alcoholic encephalopathy, Korsakov syndrome, thiamine megadoses, alcohol withdrawal delirium, vitamin B1 therapy.*

Introduction

Alcohol-related brain damage represents one of the most severe and disabling consequences of chronic alcohol dependence, leading to persistent neurocognitive, emotional, and behavioral disturbances [1-3]. In cases where alcohol withdrawal

delirium persists for more than 7-10 days, the clinical picture frequently evolves into alcoholic encephalopathy, reflecting profound metabolic and structural damage to the central nervous system [4-6]. The outcomes of such conditions may range from transient cognitive impairment and Korsakov syndrome to persistent amnestic psychosis with varying degrees of cognitive recovery or long-term disability [7–9]. In the majority of patients, cognitive dysfunction is accompanied by peripheral polyneuropathy, autonomic disturbances, and gait abnormalities, underscoring the systemic nature of alcohol-induced neurotoxicity [10-12].

The pathogenesis of alcoholic encephalopathies is multifactorial and involves a complex interaction of direct neurotoxic effects of ethanol and its metabolites, chronic metabolic disturbances, oxidative stress, nutritional deficiencies, neuroinflammation, and impaired neurotransmitter balance [13-16]. Among these pathogenetic mechanisms, thiamine deficiency occupies a central and well-documented role [17-19]. Chronic alcohol consumption leads to insufficient dietary intake of thiamine, reduced intestinal absorption, impaired hepatic storage, and inhibition of its phosphorylation into biologically active forms, particularly thiamine pyrophosphate [20-22]. As a result, neuronal energy metabolism is disrupted, mitochondrial dysfunction develops, axonal transport is impaired, and selective vulnerability of diencephalic and limbic brain structures emerges, often leading to irreversible structural damage [23-26].

Alcohol abuse remains a major global medical and social problem with profound health, economic, and demographic consequences [27-29]. According to international health statistics, excessive alcohol consumption is among the leading contributors to preventable mortality and morbidity worldwide, accounting for a significant proportion of deaths from liver disease, cardiovascular pathology, trauma, and neuropsychiatric disorders [30-32]. Chronic alcohol intoxication affects nearly all organ systems, with particularly detrimental effects on the central and peripheral nervous systems [33-35]. Both acute and long-term exposure to ethanol is associated with neurodegenerative changes, progressive cognitive decline, affective instability, impaired executive functions, and behavioral disturbances, which significantly reduce social adaptation and quality of life [36-38].

Thiamine (vitamin B1) is a key coenzyme involved in carbohydrate metabolism, oxidative phosphorylation, neurotransmitter synthesis, and maintenance of neuronal membrane integrity [39]. Its deficiency results in lactate accumulation, intracellular calcium overload, oxidative stress, excitotoxic neuronal injury, and myelin damage, all of which substantially enhance alcohol-related neurotoxicity [40]. These pathogenetic

mechanisms provide a strong scientific rationale for the use of parenteral high-dose thiamine as a cornerstone of pathogenetic therapy in alcoholic encephalopathies, particularly in the acute and subacute stages, aimed at preventing irreversible brain damage and improving neurological and cognitive outcomes.

Aim of the Study

The aim of this study was to evaluate the clinical efficacy of thiamine megadoses in the treatment of Korsakov-type alcoholic encephalopathy that developed during the resolution phase of severe alcoholic delirium.

Materials and Methods

The study included 47 male patients aged 44,3 ± 4,5 years with a confirmed diagnosis of stage II alcohol dependence. The duration of alcohol use disorder ranged from 9 to 18 years. All patients were admitted to the emergency department and subsequently hospitalized. According to ICD-10 criteria, all participants were diagnosed with F10.4 – Alcohol withdrawal delirium.

In all cases, the delirium followed a severe course and evolved into Korsakov-type alcoholic encephalopathy within 8–10 days. Patients were divided into two therapeutic groups.

All patients received standard detoxification therapy. Glucose-containing solutions were excluded, and carbohydrate intake was restricted due to increased thiamine demand during glucose metabolism. Sedative therapy included parenteral diazepam (up to 30 mg/day for 7–10 days), followed by oral phenazepam (up to 2 mg/day).

Group 1 (n = 23): Patients received high-dose thiamine therapy. Thiamine was administered intravenously at a dose of 1500 mg/day for 7 days, followed by oral administration (400 mg three times daily for 2 weeks, then 200 mg three times daily for 1 month).

Group 2 (n = 24): Patients received complex therapy with standard doses of thiamine (200 mg/day), pyridoxine (200 mg/day), piracetam, mexidol, ademetionine, and neuromidine, administered sequentially intravenously, intramuscularly, and orally.

The average duration of inpatient treatment ranged from 4 to 6 weeks.

Assessment Methods

Treatment efficacy was evaluated using:

- the Brief Psychiatric Rating Scale (BPRS-17) at baseline and on days 7, 14, 21, 28, 35, and 42;
- the Clinical Global Impression (CGI) scale before and after therapy.

The primary endpoint was regression of Korsakov syndrome to an asthenic variant of psycho-organic syndrome.

Results

In Group 1, clinical improvement became evident between days 14 and 16 of therapy. Episodes of confusion gradually decreased, and memory impairment became the dominant symptom, characterized by confabulations and pseudoreminiscences. Emotional elevation with elements of euphoria was observed. Neurological examination revealed residual coordination disturbances and dizziness during ambulation.

By days 21-28, memory impairment persisted mainly for recent events, emotional lability was noted, and neurological symptoms showed marked improvement. By days 35-42, patients demonstrated stable orientation, improved memory for current events, partial insight into their condition, and significant regression of polyneuropathy. Asthenic symptoms predominated.

A significant or very significant therapeutic effect was observed in 20,8%, while a moderate effect was noted in 23,1% of patients. In nearly half of the patients, Korsakov syndrome was transient and resolved within 10 days.

In Group 2, clinical improvement began later, between days 18 and 21. Confusion, amnestic disorientation, confabulations, and psychomotor inhibition persisted longer. Neurological symptoms, including polyneuropathy, were more resistant to therapy.

By day 42, gradual improvement was observed; however, Korsakov syndrome persisted in 62,5% of patients. Significant improvement was recorded only in 12,5%, with a moderate effect in 21,7%.

The results demonstrate that thiamine megadoses lead to faster regression of cognitive and neurological symptoms compared to standard complex therapy. Accelerated recovery of consciousness and memory functions supports the central role of thiamine deficiency in the pathogenesis of Korsakov-type alcoholic encephalopathy. Improved outcomes in polyneuropathy further confirm the neurotrophic and metabolic importance of vitamin B1.

Conclusion

High-dose thiamine therapy significantly shortens the duration of Korsakov syndrome and promotes more complete neurological recovery in patients with alcoholic encephalopathy. The use of thiamine megadoses should be considered a key pathogenetic strategy in the treatment of severe alcohol-related brain damage, particularly during the resolution phase of prolonged alcoholic delirium.

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