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# Differences Between Alcoholic and Nonalcoholic Patients With Wernicke Encephalopathy: A Multicenter Observational Study

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## Abstract

**Objective:** To analyze the differences in characteristics and prognosis between alcoholic and nonalcoholic patients with Wernicke encephalopathy (WE).

**Patients and Methods:** A retrospective observational cohort of 468 patients diagnosed with WE with at least 2 Caine criteria was selected from all patients discharged with a diagnosis of WE from 21 medical centers in Spain from January 1, 2000, through December 31, 2012. Demographic, clinical, and outcome variables were described.

**Results:** Among the 468 patients, the most common risk factor was alcoholism (n=434 [92.7%]). More than one-third of patients (n=181 [38.7%]) had the classic WE triad of symptoms (ocular signs, cerebellar dysfunction, and confusion). Among 252 patients for whom magnetic resonance imaging data were available, 135 (53.6%) had WE-related lesions and 42 (16.7%) had cerebellar lesions. Of the 468 patients, 25 (5.3%) died during hospitalization. Alcoholic patients presented more frequently than nonalcoholic patients with cerebellar signs ($P$=.01) but less frequently with ocular signs ($P$=.02). Alcoholic patients had a significantly higher frequency of hyponatremia ($P$=.04) and decreased platelet count ($P$=.005) compared with nonalcoholics. Alcoholic patients were diagnosed earlier than nonalcoholics (median time to diagnosis, 1 vs 4 days; $P$=.001) and had shorter hospitalizations (13 vs 23 days; $P$=.002).

**Conclusion:** Compared with nonalcoholic patients, alcoholic patients with WE are more likely to present with cerebellar signs and less likely to have ocular signs. Diagnosis may be delayed in nonalcoholic patients. Mortality in the present series was lower than described previously.

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Wernicke encephalopathy (WE) is a neurologic disorder caused by thiamine deficiency and characterized by ocular abnormalities (nystagmus and/or ophthalmoplegia), mental status changes, and gait disturbances.[1] Carl Wernicke[2] first described this disease in 1881, coining the term *polioencephalitis hemorrhagica* to describe the autopsy findings from 3 patients with this clinical picture.

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However, the classic triad of ocular signs, cerebellar dysfunction, and confusion is found in less than half of patients with WE,[1,3] which prompted Caine et al[4] to develop and validate a set of 4 criteria for the clinical diagnosis of WE (dietary deficiencies, oculomotor abnormalities, cerebellar dysfunction, and altered mental state or mild memory impairment). In patients with chronic alcoholism who do not have hepatic encephalopathy, the presence of 2 of these criteria had a sensitivity of 100% for the clinical diagnosis of WE.[4]

Despite the establishment of these criteria, one of the main clinical problems associated with WE is the high rate of underdiagnosis, which can be due to the lack of suspicion in certain clinical settings (eg, cases not associated with alcoholism) or to atypical presentation.[1,5] Several authors have suggested that clinical features differ between alcoholic and nonalcoholic patients with WE. In a review of published data, Galvin et al[1] reported that the occurrence of the classic triad or the presence of specific signs, such as ocular or cerebellar alterations, was significantly more frequent in alcoholics. A recent systematic review, however, did not replicate these findings.[6] Apart from the application of clinical criteria, magnetic resonance imaging (MRI) is the most useful test to support the diagnosis of WE, with a sensitivity and specificity of 53% and 93%, respectively.[7] Some authors have found differences in MRI findings between alcoholic and nonalcoholic patients,[8] although other authors have not confirmed these findings.[9]

Evidence for many aspects of this disease is lacking, and most data come from autopsy series[10,11] or single-center retrospective studies.[3,12-14] Because of the lack of large recent studies of patients with WE and the absence of studies allowing direct comparison between alcoholic and nonalcoholic patients with WE, we performed the present study of a large multicenter sample to analyze the characteristics and prognosis of patients with clinically diagnosed WE and to examine differences between alcoholic and nonalcoholic patients with this disease.

## PATIENTS AND METHODS

### Patient Selection and Data Collection

The Wernicke Spanish Society of Internal Medicine (SEMI) study group was created by SEMI in 2011 with the aim of analyzing a large cohort of patients from Spain who had been admitted to hospitals with WE. Cases were first identified by searching all hospital discharge diagnoses in each participating center recorded from January 1, 2000, through December 31, 2012, using codes from the *International Classification of Diseases, Ninth Revision* (291.1, 294.0, 265.1) and *Tenth Revision* (E51.2, F04). Medical records were reviewed retrospectively according to a specific protocol, and epidemiological, clinical, laboratory, and radiologic data (including age, sex, comorbidities, risk factors for WE, signs and symptoms of WE, imaging and laboratory findings, treatment, duration of hospital stay, and hospital outcome) were recorded. To avoid the inclusion of patients with an unlikely diagnosis of WE, only patients with a clinical diagnosis of WE and at least 2 Caine criteria[4] were included in our study. Data from individuals with alcoholism were compared with those from nonalcoholic individuals.

A single-center pilot study was first performed to test the feasibility of the study and to design the final version of the database. Data were collected in a standardized database by investigators from each hospital and checked for consistency before they were merged into a single data set. The study was performed in accordance with the ethical standards of the Helsinki Declaration, and the ethics committees of all participating hospitals approved the study protocol.

### Definition of Terms

Criteria for the diagnosis of WE were recorded according to Caine criteria[4]: oculomotor abnormalities (ophthalmoplegia, nystagmus, or gaze palsy), cerebellar signs (ataxia, gait disturbances, or other signs of cerebellar dysfunction), dietary deficiencies (body mass index [calculated as weight in kilograms divided by height in meters squared] $<18.5$ kg/m$^2$, clinical data such as hypoalbuminemia and/or a record


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