Rev Bras Psiquiatr 2004;26(Supl I):47-50

Psychiatric complications of alcoholism: alcohol withdrawal syndrome and other psychiatric disorders

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Abstract

Alcohol withdrawal syndrome is an acute condition secondary to total or partial reduction of alcohol consumption, characterized by self limited signs and symptoms and different degrees of severity. It can be complicated by several clinical and/or other psychiatric related problems. The objective of this article is to review the most important psychiatric complications to alcohol withdrawal syndrome as well as other psychiatric disorders associated with alcohol dependence as Wernicke Korsakoff and Marchiava Bignami syndromes. We aim to promote early diagnosis and treatment of these conditions, minimizing morbidity and mortality associated with them.

Keywords: *Substancial withdrawal syndrome. Korsakoff syndrome. Convulsion. Delirium tremens.*

Introduction

Alcohol withdrawal syndrome (AWS) is responsible for a significant increase in the mortality and morbidity associated with alcohol consumption and is one of the diagnostic criteria of alcohol dependence syndrome. It is characterized by signs and symptoms stemming from total or partial interruption of intake of alcoholic beverages on dependent subjects who show a significant previous consumption. These signs and symptoms are not specific only to alcohol withdrawal syndrome and may be present on other withdrawal syndromes (e.g., benzodiazepines). They are, also, insidious and hardly specific, what makes their recognition and assessment complex processes; they vary in their intensity and severity, and may appear, as already said, after a partial or total decrease in the dose usually ingested. The most common signs and symptoms of AWS are, among others, restlessness, anxiety, mood alterations (dysphoria), trembling, nausea, vomiting, tachycardia and arterial hypertension.

This article aims to describe the main complications secondary to AWS, as well as their treatment. Some of them are very common (seizures and hallucinations), and others are more severe and less common (delirium tremens). Besides, it describes and proposes the treatment of other complications associated with alcohol dependence such as Wernicke Korsakoff and Marchiava Bignami syndromes.[12]

Seizures

Convulsive pictures secondary to alcohol abuse/dependence are not rare, as well as it is not uncommon the worsening of the control of seizures on patients with previous history of convulsions (idiopathic or not).[10] Seizures secondary to alcohol withdrawal pictures are often

tonic-clonic (or grand mal), isolated and occur in the first 48 hours (with a peak between 13 and 24 hours) after the suspension or reduction of alcohol consumption. However, focal symptoms may appear in nearly 5% of convulsive pictures secondary to alcohol withdrawal. The appearance of convulsions is almost always associated with the severest pictures of alcohol withdrawal and most patients who are not adequately treated evolve to delirium tremens.[7 18]

There is indication for imaging assessment in case of convulsions secondary to alcohol withdrawal (e.g., computerized tomography), in order to detect comorbid diseases (e.g., chronic subdural hemorrhage and brain trauma). Nearly 4% of tomographies of patients with convulsive conditions secondary to alcohol withdrawal show structural lesions. Computerized tomography is also indicated in cases of seizures other than grand mal, in abstinent patients, due to the higher prevalence of co-occurrence of lesions in this group.[16]

The chance of recurrence of convulsive crisis, in a six-month period, is 41%, and this prevalence increases with time, reaching 55%, within three years.[11 16] New episodes of convulsive crises could trigger secondary alterations in the brain excitability (kindling) which seem to be additive, i.e., at each new convulsive crisis, the condition worsens. Kindling is defined as a phenomenon in which a weak electrical or chemical stimulus, which normally would not cause an important behavioral response, when administered for several times, triggers the process. Kindling may result from alterations on brain neurotransmitters (mainly GABA and NMDA) which, consequently, increase brain excitability, predisposing to the risk of new convulsive crises, anxiety pictures and increase of neurotoxicity.[1] If structural alterations are not identified in patients with seizures secondary to alcohol withdra- wal, not having previous history of convulsive crises and not having previously used anticonvulsants, they do not seem indicated, and may in some cases trigger the occurrence of seizures due to withdrawal (including of anticonvulsants).

The treatment of choice is the control of the convulsive crisis by means of an infusion of benzodiazepines and a specific treatment to control alcohol dependence.[11] The maximum dose of not diluted diazepam should be 10 mg in 4 minutes, and the intravenous administration of benzodiazepines requires a specific technique and medical support to manage occasional respiratory failure.[12] The chronic use of anticonvulsants (phenytoine and phenobarbital, among others) has a limited action in the prevention of convulsions secondary to alcohol withdrawal, as the central problem of these patients is alcohol use and, in the great majority of cases in which there is maintenance of alcohol consumption (therefore, risk for new convulsive crises), non-compliance with pharmacological treatment is almost a rule, and this action may, by itself, trigger a new seizure. However, in patients with previous use of anticonvulsants, the medication should be maintained.

The most effective prevention in this group of patients is undoubtedly the treatment to stop the consumption of alcohol and, whenever necessary, it is indicated the use of long-term action benzodiazepines 10 to 20mg (e.g., diazepam) or the use of lorazepam, in an equivalent dose, in hepatopathic or senile patients.[1 12] The introduction of anticonvulsants in this population is not justified neither for the treatment nor the prevention of convulsive crises.

Status epylpeticus is a severe condition, with high mortality (nearly 10%) and it is not rare among patients with alcohol withdrawal syndrome. One study performed in 1980 demonstrated that 21% of patients with tonic-clonic status were alcohol-abstinent. The treatment of this condition should be started the earliest possible, in emergency care units.[7 12]

Delirium tremens (DT)

Delirium is a common cause of altered behavior among subjects with any physical disease which was not adequately diagnosed or treated. Several terms have been used to describe this syndrome, including acute confusional states, acute brain syndrome, acute brain psychosyndrome and acute organic reaction.

DT is a specific picture of delirium, related to alcohol withdrawal. Delirium conditions usually have floating symptoms, with significant worsening in the evening. Cognitive, memory and attention alterations and temporo-spacial disorientation are common. Decreased attention and thought disturbances result in incoherent speech. Relatives and other informants may report a rapid and drastic decline in the premorbid functioning of patients, what makes them different from those with demential conditions. Sensoperceptive alterations (hallucinations and illusions) are common, being visual hallucinations very common. Delusions are also frequent, often persecutory and related to temporospacial disorientation. Mood alterations are usual and vary from intense apathy up to intense anxiety conditions; the presence of alterations in the sleep-vigil cycle is constant. Unfortunately, as it has been said, many cases are not adequately detected and, therefore, are not treated.[3]

Not all abstinence is DT. In fact, DT is a condition hardly frequent among alcohol-dependent subjects, occurring in less than 5% of the abstinent population. Nevertheless, it is responsible for the high morbidity and mortality associated with AWS, as DT pictures are not, as has been already said, adequately diagnosed. DT as a rule starts up to 72 hours (although it may start after up to seven days) after withdrawal and comprises varied signs and symptoms, such as mental confusion, hallucinations, trembling, fever (with or without signs of infection) and autonomic hyperresponsiveness, with hypertension, tachycardia and diaphoresis. DT may be suspected in all cases of agitation in a patient with AWS whose arterial pressure is above 140/90mm Hg, heart frequency higher than 100 bpm, and temperature, above 37C. Mortality rates are high, varying from 5% to 15% of patients with this condition. Few studies, however, define adequately DT conditions taking into account clinical/psychiatric comorbidities, traumas, etc. The most frequent cause of death is cardio-respiratory failure. The patophysiology of DT pictures is still hardly understood. The physiological alterations resulting from DT would stem from interactions of neuro-receptors (mainly the gabaergic and catecolaminergic systems), as well as ionic alterations (especially potassium and magnesium).[5 8]

The treatment of this condition is usually performed with benzodiazepines, aiming to decrease the autonomic hyperactivity and the risk of psychomotor restlessness. There is preference for diazepam, in higher doses than usual (60 mg/day) or lorazepam (12 mg), being the patient hepatopathic or senile. Occasionally the association with neuroleptics, in low doses, may be indicated (haloperidol 5 mg/day). In case of neuroleptic-induced dystonia (particularly when parenterally administered), it may be controlled with anticholinergics (biperidene 2mg).[5 12]

Wernicke Korsakoff Syndrome(WKS)

WKS is a potentially fatal complication associated with deficiency of B1 or thiamine. It was described as two distinct entities Wernicke's encephalopaty and Korsakoff's psychosis.

A triad of clinical abnormalities described by Wernicke oftalmoplegy, ataxia and mental confusion, composes the syndrome. They would be the cornerstones of the syndrome's diagnosis; however, the presence of all these symptoms is not necessary for the diagnosis of WKS, being more frequent the presence of isolated signs (oftalmoplegy and/or mental disorientation and/or stupor and/or coma). Eye movements may consist of horizontal and vertical nystagmus, weakness or paralysis of the lateral rectus eye muscle and of conjugated eye movement. In advanced cases, complete oftalmoplegy may be found. Mental confusion is characterized by a decrease in the consciousness and attention state and senso-perceptual and memory alteration. Confabulation is

common among this group of patients. Sometimes there is progression to coma.[14]

The daily needs of thiamine are estimated at 1.0 1.5 mg/day for normal patients. Thiamine is an important co-factor of the piruvate dehydrogenase enzyme and dehydrogenase alpha-cetoglutarate, involved in the metabolism of carbohydrates and transcetolase, an important enzyme of pentose cycle. Thiamine is naturally present in cereals and many flours. However, the processing of these grains results in the loss of most part of this vitamin. Several countries (US, England, Canada and Denmark) enrich their flours with thiamine; with this measure, the deficiency of thiamine became restricted to some groups of patients. WKS is a syndrome commonly associated with alcohol dependence and, in some cases, with some types of cancer, pregnancy hyperemesis, obstruction of the small intestine, anorexia nervosa and gastroplasty. The chronic consumption of alcohol is related to the low absorption of thiamine by intestinal cells, as well as to its lower phosphorilation, in its active form, and decrease in the hepatic store of thiamine. These factors, associated with the lower intake of food with thiamine, may be one of the causes of low concentration of thiamine on alcohol-dependent subjects.[9]

Several mechanisms have been implied in the pathogenesis of this syndrome, but they are not yet fully understood. One of the explanations are the neuronal losses, and the mechanisms for this cerebral death include brain energetic deficiency, excitoxicity mediated by glutamate, focal lactic acidosis and alteration of the blood brain barrier. Focal lactic acidosis may be one of the mechanisms which lead to cerebral thiamine deficiency (reducing the brain permeability to thiamine). The most plausible explanation for this phenomenon seems to be a decrease in the oxidation of piruvate, resulting from a decrease in the activity of the thiamine-dependent deshydrogenases. With the accumulation of lactate in neurons, there is a pH alteration (acidosis), generating cell death. The intensive formation of free radicals is also associated with WKS. The chronic administration of alcohol in rats, with subsequent AWS, causes an increase in the formation of free radicals in several brain regions, as well as an increase in the nitric oxide molecule through the metabolization of ethanol.[6]

In animals in which the deficiency of thiamine was experimentally induced, microdialysis showed a significant increase of extracell glutamate, selective for the ventral posterior thalamus. These changes are reversible with the administration of thiamine in the brain cortex and pons, but not in the thalamus. In the regions in which there is excess of glutamatergic activity, there may occur excitotoxic neurodegeneration. However, direct evidence is needed to support a relationship between deficiency of thiamine and alteration in the NMDA receptor.[6 19]

The anatomical-pathological characteristics vary according to the stage and severity of the pathology. Patients in the acute phase may have alterations in mamillary bodies, hypothalamus, thalamic periventral region (above the aqueduct). The mamillary bodies, especially medial nuclei, are the most often affected structures and they are affected in almost all the cases. Hystopathological exams, in acute cases, show edema, necrosis, desmielinization, mild neuronal loss, spongiform degeneration and increase of blood vessels as a result of hyperplasia; when there is petequial hemorrhage, erythrocytes and hemossiderine are present, as well as macrophages. In chronic cases, there is more remarkable neuronal loss and gliosis. The diagnosis is clinical, being magnetic nuclear ressonance a useful complementary exam to detect these brain lesions, while cerebral tomography is, in many cases, inefficient. WKS is one more of the complications of alcohol dependence which is frequently subdiagnosed.[3 8]

The treatment of this condition is not still adequately established regarding the route and the dose of thiamine needed both for the prevention and the treatment, not being known to the authors of this article any well-conducted study; most of the recommendations of vitamin supplementation is empirically based.[8] Consensual thiamine dose for alcohol withdrawal syndrome was intramuscular doses above 300 mg/day, for a period between 7 and 15 days. Oral use is not indica- ted for the prevention of Wernicke Korsakoff syndrome as the absorption of thiamine may be impaired due to alcohol consumption and, therefore, a decrease in its efficacy may occur. In England, after the suspension of high-potency complex B vitamins (250 mg of thiamine at each flask) there was an increase in the cases of "alcoholic psychosis" and the authors suggest that this may be secondary to low doses of vitamin suplementation.[17]

Marchiava Bignami syndrome

Also called "corpus callosum body primary degeneration", it is a disease most commonly defined by its pathological than its clinical aspects. The main alteration is found in the medial portion of the corpus callosum, in which, at naked eye, a decrease in the tissue density is seen, with a mild reddish or yellowish depression, depending on the time of lesion. Microscopically, clearly demielinizating zones with abundant macrophages may be seen, although without inflammatory alterations. Less consistent lesions of similar nature are found in the central portion of the anterior, posterior commissures and pons.

It is a rare disease which affects elderly people and, with few exceptions, all ill patients are alcohol-dependent. Some of them show, in terminal stages, stupor and coma, and others, symptoms compatible with chronic intoxication and withdrawal syndrome. In some cases, progressive dementia has been described, with symptoms such as dysarthria, slow and unstable movements, transient sphincter incontinence, hemiparesis and aphasia. The diagnosis is rarely performed in life, but as a rule, in autopsy, by means of an anatomical-pathological exam. The occurrence among alcohol-dependent patients of symptoms similar to frontal lobe syndrome, Alzheimer disease or symptoms found in frontal tumors, which remit spontaneously, suggests the occurrence of Marchiava Bignami syndrome, and imaging exams will help in the diagnosis. The etiology and pathology of this condition are not well known up to the moment.[20]

Conclusion

Despite having dealt above with severe complications of alcohol dependence which arise independently from the level of alcohol consumption, all dependent subjects need and should have access to treatment at any phase of their disease as well as their relatives. This article exposes the basis for the recognition of these complications and proposes some interventions for their treatment, which would minimize the morbidity and mortality.

There are efficient interventions and some of them, such as the use of thiamine in the prevention of Wernicke Korsakoff syndrome, still lack further research to establish the dose, way of administration and time of use. Other ones, however, are well established, such as the use of benzodiazepines, aiming to prevent the progression of AWS towards the severest conditions such as DT. This use should be instituted the earliest possible in patients with history of severe AWS, for whom it is proposed abstinence or when they are abstinent for less than three days and have an important symptomatology justifying the use of this medication.

The involvement of the family in the treatment of the patient is fundamental, as it enables higher compliance as well as a higher quality of life for the members of the familial nucleus. Hospitalization may be needed to assure abstinence when an outpatient treatment is not possible or the severity of the condition demands. All these measures can and should be implemented in the public and private health systems and, for its appropriate functioning, more professionals should be adequately trained to perform them.

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