Progressive Toxemia with Acetaldehyde in a Reactive Form of Alcohol Withdrawal Syndrome

A. G. Remennik, L. M. Nepomnyashchikh, and V. I. Remennik

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 139, No. 6, pp. 704-706, June, 2005
Original article submitted December 8, 2004

We carried out a complex clinical and laboratory examination of 169 patients with reactive form of alcohol withdrawal syndrome. Progressive toxemia with acetaldehyde (key pathogenetic stage) and volemic changes were followed by homeostasis disorders and gradual decompensation of the natural detoxification system. The patients with this form of alcohol withdrawal syndrome did not exhibit physical and psychic dependence on alcohol. The proposed therapeutic algorithm for the treatment of various pathogenetic stages rapidly and efficiently restored homeostasis parameters and prevented the development of serious and life-threating complications.

Key Words: *alcohol withdrawal syndrome; progressive toxemia; acetaldehyde*

Consumption of alcoholic beverages increases constantly throughout the world. It is accompanied by an increase in the number of patients with alcoholism, which becomes a social disease. In the present time alcoholism runs a progredient course and has a variety of life-threating complications that require intensive clinical care [1,2].

Alcohol withdrawal syndrome (AWS) is one the most serious complications of alcoholism. AWS is associated with massive alcohol consumption and pronounced changes in homeostasis. The dependence on alcohol concentration in the organism causes dipsomania. This critical state is the most severe and life-threating manifestation of AWS associated with progressive polyorgan insufficiency due to alcohol intoxication and release of aggressive mediators formed during alcohol metabolism [3,5].

Intensive care usually starts from correction of alcohol intoxication, AWS, and associated psychosomatic disturbances. A variety of abnormalities observed in this period are related to systemic metabolic changes leading to brain dysfunction. Structural and metabolic changes in the heart contribute to progressive hypoxia of the brain and liver. Liver dysfunction is accompanied by accumulation of secondary endogenous toxins, which aggravates systemic disturbances [3].

Intensive care is aimed at correction of homeostasis parameters and recovery of functions or systems. The methods of sorption detoxification (*e.g.*, enterosorption and hemosorption) are widely used in narcology. The mechanisms underlying the positive therapeutic effect of these methods remain unclear.

This work was designed to develop a pathogenetically substantiated therapeutic method suitable for rapid and effective correction of AWS and based on principles of intensive care.

MATERIALS AND METHODS

We performed complex clinical and laboratory examination of 169 patients with a reactive form of AWS (127 men and 42 women).

Anamnesis of patients was thoroughly evaluated. A special inquiry system allowed us to estimate objectively the mental state and stage of alcoholism in patients. Laboratory and instrumental studies involved standard clinical, biochemical, and functional tests (evaluation of hemodynamics, electrocardiogram, acid-base metabolism, and oxygen saturation). The patients

Institute of Regional Pathology and Pathomorphology, Siberian Division of the Russian Academy of Medical Sciences, Novosibirsk

0007-4888/05/1396-0732

were examined before therapy and 4-6 h (completion of the main stage of correction of homeostasis) or 1 day after the start of treatment.

The therapeutic treatment of AWS includes four major components of intensive care: correction of volemic changes and restoration of diuresis; cellular and metabolic therapy for the correction of metabolic disorders and detoxification; correction and stabilization of major mental processes in the central nervous system (excitation and inhibition, therapeutic narcosis); and nonspecific (situational) therapy for the correction of iatrogenic disorders.

Intravenous multicomponent infusion therapy was performed to normalize blood volume (correction of deficits) with regard to the degree of hypovolemia (50 ml/kg) [4]. The treatment included 300-500 ml 5% mannitol or 200-400 ml 5.8% NaCl, 150-300 ml 3-5% sodium hydrocarbonate, 1000-2000 ml Hartman's solution, 1000 ml 5% glucose and KCl (1 mmol/kg), and 200-400 ml Gemodez.

Cellular and metabolic therapy is required to normalize acid-base metabolism, inhibit peroxisomal and microsomal oxidation, and correct activity of adrenoreactive structures in the organism. It is based on combined use of various medicinal preparations with regard to their action on the major pathogenetic stages. We used corticosteroids (1 mg/kg prednisolone), neuroleptics (0.05-0.15 mg/kg droperidol, bolus dose), β-adrenoceptor antagonists (obsidan and propranolol, 5-7 mg), magnesium sulfate (2.5-5.0 g), unithiol (250-500 mg), vicasol (50-100 mg), ascorbic acid (500-1000 mg), pyridoxine phosphate (500-1000 mg), thiamine chloride (500 mg), furosemide (above 5 mg), and Euphyllin.

Infusion detoxification therapy (method of forced diuresis) and standard extracorporeal sorption procedures were used for the correction of toxemia.

Mental disorders were corrected and stabilized using multicomponent balanced controlled intravenous therapeutic narcosis with spontaneous breathing (0.1-0.2 mg diazepam, 20-30 mg/kg sodium hydroxybutyrate, and sodium thiopental or hexenal or diprivan, *quantum satis*).

Nonspecific (situational) therapy was applied in patients with AWS-nonspecific symptoms resulting from therapeutic treatment. The goal of this therapy was to stimulate the impaired or temporarily lost of vital functions. The most common symptom was arterial hypotension associated with administration of neuroleptics and β-adrenoceptor antagonists to patients with inadequately corrected hypovolemia. Controlled hypotonia in the pulmonary circulation was rarely required (only upon sharp increase in preload). Artificial ventilation was applied in patients with abnormal external respiration function associated with administration of medicinal preparations in high doses during therapeutic narcosis.

RESULTS

The clinical picture was characterized by serious polyorgan dysfunction (toxemia with acetaldehyde) and decompensation of the natural detoxification system. The symptoms of reactive AWS are similar but more pronounced compared to those observed during therapeutic treatment with disulfiram and its analogues. These preparations inhibit acetaldehyde dehydrogenase, which contributes to accumulation of acetaldehyde in the organism.

This state developed after excessive and long-term alcohol consumption. The mean duration of alcohol excess in this group was 3-4 days. In most patients the last alcohol excess occurred several hours or several days before examination. The patients with reactive AWS had a negative attitude toward alcohol because of severe nausea, vomiting, and headache. However, the state of patients slightly improved, when they take alcohol again.

The somatic state was characterized by pronounced autonomic dysfunction manifesting in hyperdynamic blood flow, arrhythmia, and tremor. Mean blood pressure was 110-160 mm Hg. The decrease in central venous pressure and other symptoms (mucosa and skin dryness, low turgor pressure, and oligo- or anuria) reflected the development of serious hypovolemia.

Hypovolemia and metabolic disorders contributed to the development of renal failure. The degree of renal failure differed in AWS patients. Most patients with reactive AWS did not have severe mental illness. However, manifestations of encephalopathy (psycho-

TABLE 1. Clinical and Laboratory Parameters in Patients with Reactive AWS

Parameter	Before therapy	Immediately after therapy	One day after therapy
Hematocrit, %	48-54	42-44	44-45
Osmolarity, mmol/liter	320-340	284-286	280-286
Urea, mmol/liter	14.5-19.0	8.5-12.0	7.8-9.6
Venous blood pH	7.28-7.35	7.35-7.48	7.40-7.50

motor agitation, sleep disorders and sometimes insomnia) were observed in all patients.

Laboratory tests revealed increased blood viscosity, neutrophilic leukocytosis, increase in erythrocyte sedimentation rate, moderate anemia, increase in urea concentration, decrease in fibrinogen content and prothrombin index, and moderate glycemia (Table 1). Transaminase activity exceeded the normal by 1.5-2 times. Compensated (pH 7.45-7.35) or decompensated metabolic acidosis (pH value ≤7.28) was revealed in all patients.

Homeostasis parameters returned to normal 4-6 h after major procedures of intensive care (correction of hypovolemia, stabilization of hemodynamics, and restoration of diuresis). A positive change was revealed in the results of laboratory tests (normalization of hematocrit, acid-base metabolism, and blood glucose level). Other laboratory parameters remained practically unchanged.

Homeostasis parameters can be corrected much more easily and rapidly compared to functional indexes. The period necessary to achieve complete correction and stabilization of functional indexes directly depended on the degree and duration dipsomania, premorbid state of the organism, and hystory of alcoholism.

Previous complaints of patients disappeared after therapy. Alcohol aversion was seen in all patients. Twenty-two patients (13%) complained weakness and dizziness. Eighteen patients (10.6%) noted the feel of inner tension, restlessness, and slight tremor. Microcirculatory disturbances were absent. Hemodynamic parameters were stabilized and corresponded to a satisfactory state in most patients. Arterial hypertension and tachycardia were found in only 27 patients (15.9%). Complete stabilization occurred in a later period. Despite voleme compensation (normal values of central venous pressure, hematocrit, and diuresis), 81 patients (47.9%) suffered from thirst. The volume of consumed fluid reached 1.5-2.0 liters per day. Diuresis returned to normal in all patients (without stimulation).

The proposed therapeutic algorithm to treat various pathogenetic stages of reactive AWS rapidly and efficiently restores homeostasis parameters and prevents the development of life-threating complications.

REFERENCES

1. V. B. Al'tshuller, *Pathological Alcohol Attraction. Clinical and Therapeutic Problems* [in Russian], Moscow (1994).
2. D. P. Bilibin and V. E. Dvornikov, *Pathophysiology of Alcoholism and Drug Addiction* [in Russian], Moscow (1991).
3. E. A. Luzhnikov, *Anesteziol. Reanimatol*., No. 3, 4-10 (1995).
4. A. G. Remennik and L. M. Nepomnyashchikh, *Sibirsk. Nauch. Vestnik*, No. 7, 53-56 (2004).
5. V. V. Tyutikov, V. V. Tkachev, I. A. Ognev, and G. G. Efremushkin, *Clinical Morphology in Nephrology* [in Russian], St. Petersburg (1994), pp. 128-129.