Alcohol withdrawal Syndrome

Withdrawal syndrome primarily affects persons who are habituated (tolerant) to chronic ethanol ingestion who either cease their drinking or markedly reduce their consumption

Symptoms of alcohol withdrawal occur because alcohol is a central nervous system depressant; abrupt withdrawal unmasks compensatory overactivity of certain parts of the nervous system, including sympathetic autonomic outflow.

Altered levels of several neurotransmitters have been noted, and may be important in the pathophysiology of alcohol withdrawal:

Gamma-aminobutyric acid: Gamma-aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the brain.

Its receptor is downregulated and its neuronal activity decreased in alcohol withdrawal, resulting in hyperarousal

Norepinephrine: Elevated levels of norepinephrine are found in the cerebrospinal fluid of patients withdrawing from alcohol and are believed due to a decrease in the alpha-2 receptor-mediated inhibition of presynaptic norepinephrine release

Serotonin: Serotonin and its degradation products have been implicated in both tolerance and craving for alcohol

Characterized by a hyperadrenergic state that develops 6-8 hours after the cessation of drinking and may last up to 5 days

Enhanced excitatory neurotransmission

Increased levels of plasma and urine catecholamines

Decreased inhibitory activity of presynaptic ?2 receptors

Symptom severity determined by the amount of endogenous norepinephrine released during withdrawal

Diagnosis

DSM-IV Diagnosis

The essential feature of Alcohol Withdrawal is the presence of a characteristic withdrawal syndrome that develops after the cessation of (or reduction in) heavy and prolonged alcohol use

The withdrawal syndrome includes two or more of the following symptoms:

Autonomic hyperactivity (e.g. sweating or pulse rate greater than 100)

Increased hand tremor

Insomnia

Psychomotor agitation

Anxiety

Nausea or vomiting

Grand mal seizures

Transient visual, tactile, or auditory hallucinations or illusions

Withdrawal symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning (Criterion C)

The symptoms must not be due to a general medical condition and are not better accounted for by another mental disorder (e.g., Sedative, Hypnotic, or Anxiolytic Withdrawal or Generalized Anxiety Disorder) (Criterion D).

Treatment

Basic principles

The major objective of drug therapy in the alcohol withdrawal period is prevention of seizures, delirium, and arrhythmias

Specific drug treatment for detoxification in severe cases involves two basic principles: substituting a long-acting sedative-hypnotic drug for alcohol and then gradually reducing ("tapering") the dose of the long-acting drug.

Because of their wide margin of safety, benzodiazepines are preferred for treatment of alcohol withdrawal syndrome

After the alcohol withdrawal syndrome has been treated acutely, sedative-hypnotic medications must be tapered slowly over several weeks.

Initial stabilization

ABCs

Correct hypoglycemia

IV fluids

Initiate tranquilization to prevent the progression of the syndrome to more severe levels and to

relieve the symptoms

Administer thiamine

Restore Inhibitory Tone to the CNS

Benzodiazepines:

Examples: diazepam, lorazepam, chlordiazepoxide

Uses: Standard therapy, high doses required owing to cross-tolerance with chronic ethanol ingestion, anticonvulsant effect and may halt progression to DTs

Dosage: Diazepam: 5-20 mg PO for mild reactions; 5-10 mg i.v.

Diazepam is administered 10 to 20 mg po every hour until the patient's symptoms are relieved and the patient is sedated.

Chlordiazepoxide (Librium): 25-100 mg, PO or i.v. q6h

Barbiturates (phenobarbital)

Uses: Cross-tolerant with alcohol, anticonvulsant effect, and useful if severe withdrawal or DTs refractory to large doses of benzodiazepines

Butyrophenone antipsychotics

Examples: Haloperidol (low doses)

Uses: Indicated as adjuncts in the hallucinating patient

Dosage: Haloperidol: 2-10 mg PO, i.v., or i.m.

Thiamine: 100 mg i.v.

Folate: 1 mg i.v. or PO

Major tranquilizer: SYN: antipsychotic *agent*.

Disulfiram

Disulfiram (tetraethylthiuram), a widely used antioxidant in the rubber industry, causes extreme discomfort to patients who drink alcoholic beverages.

Disulfiram causes: flushing, throbbing headache, nausea, vomiting, sweating, hypotension, and confusion occur within a few minutes after drinking alcohol

The effect may last 30 minutes in mild cases or several hours in severe ones

After the symptoms wear off, the patient is usually exhausted and may sleep for several hours.

Disulfiram acts by inhibiting aldehyde dehydrogenase.

Thus, alcohol is metabolized as usual, but acetaldehyde accumulates.

The symptoms resulting from disulfiram plus alcohol are typical of acetaldehyde toxicity: the reaction is reproduced by acetaldehyde infusion in humans.

The usual oral dose is 250 mg daily taken at bedtime.

Naltrexone

Naltrexone is an orally available opioid receptor antagonist that blocks the effects of exogenous and, presumably, endogenous opioids.

Naltrexone is taken once a day in a dose of 50 mg for treatment of alcoholism.