THE GUIDELINES FOR MANAGEMENT OF ETHANOL, METHANOL AND ETHYLENE GLYCOL POISONING AT THE EMERGENCY ROOM

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Ethanol Overdose  Introduction  Pharmacokinetics  Absorption and Metabolism
Clinical Symptoms Produced by Ethanol Overdose  Diagnosis, Laboratory Analysis and Treatment

Ethanol is the most commonly abused drug in the United States, with approximately 10 percent of the adult population qualifying as alcoholics. Approximately 40 percent of the medical hospital admissions are related to ethanol abuse and multisystem organ dysfunctions secondary to chronic alcohol intake. The chronic alcohol intake can lead to numerous metabolic complications such as hypoglycemia, ketoacidosis, electrolyte disorders, neurologic disorders, withdrawal seizures, delirium tremens, gastritis, hepatitis, pancreatitis, as well as hematologic disorders. It is very important for the emergency physicians to recognize these patients. The adolescents and young adult suicide rates are frequently associated with ethanol abuse and overdose. It is also important to remember that the depressed level of consciousness in alcoholics could also be due to subdural hematoma, meningitis, and other central nervous systems lesions. Alcohol abuse is often associated with suicide, homicide, drowning, physical abuse, and motor vehicle accidents. The forms of alcohols are: Ethyl alcohol (ethanol) Ethylene glycol Isopropyl alcohol (isopropanol) Methyl alcohol Propylene glycol Diethylene glycol All of these forms of alcohol are low molecular weight, water soluble substances with prominent multiorgan toxicity.

Pharmacokinetics of Ethanol
Ethanol is absorbed in an unaltered state from the stomach and small intestine, metabolized by the liver and excreted through the kidneys. It has been recently postulated that the presence of alcoholic dehydrogenase in gastric mucosa degrades some of the absorbed ethanol, and histamine H-2 antagonist inhibits alcohol dehydrogenase hence patients taking acid suppressing drugs are more prone to alcohol toxicity with ethanol intake. Several hepatic enzymes convert ethanol to acetaldehyde. These enzymes are cytoplasmic alcohol dehydrogenase, catalase, and a microsomal ethanol oxidizing system.

Metabolism of Ethanol

\[
\text{Ethanol} \rightarrow \text{Acetaldehyde} \rightarrow \text{Acetic acid} \rightarrow \text{Carbon dioxide and water}
\]

The alcohol dehydrogenase pathway is the predominant system for alcohol metabolism. The second pathway is the microsomal ethanol oxidizing system located in the endoplasmic reticulum. This system may be associated with cytochrome P-450 mixed function oxidase system in the liver. The third system involves the catalase located in the peroxisomes. The rate of metabolism of ethanol is in the range of 15 to 25 milligrams per deciliter per hour. 12 mg/dl/hour in nondrinkers 15 mg/dl/hour in social drinkers 30 mg/dl/hour in alcoholics A 150 pound person metabolizes 10 ounces of beer in one hour. Effects Produced by Ethanol Metabolism

1. Drug Interactions
2. Carbohydrate Metabolism

A. Hypoglycemia in the presence of inadequate food intake. B.
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Inhibition of galactose metabolism  C. Hyperglycemia  D. Hypomagnesemia.  3. Protein Metabolism A. Increased synthesis of lipoproteins  B. Decreased synthesis of albumin and other proteins.  4. Lipid Metabolism A. Increase in liver lipids (fatty liver)  B. Increase in serum triglycerides  5. Increase in Lactate Production A. Lactic acidosis  B. Decrease in uric acid secretion and resultant Hyperuricemia.  6. Other Effects A. Ketoacidosis  B. Increased catecholamine release  C. Interference with citric acid cycle  D. Decreased serum level of phosphate

The acute organ toxicity directly related to ethanol:  A. Central nervous system  Acute intoxication syndromes  Withdrawal syndromes.  B. Gastrointestinal system  Acute gastritis  Acute pancreatitis  Acute fatty liver of alcoholism  Alcoholic hepatitis  C. The other common manifestations  Alcoholic cardiomyopathy  Alcoholic skeletal myopathy  Hematologic abnormalities  Endocrine disorders

The early manifestation of intoxication such as altered mood and impaired cognition are seen at an alcohol blood level of 25 to 50 mg/dl. Impaired performance and judgement are seen in individuals with alcohol levels of 40 to 60 mg/dl. The legal intoxicated blood level of alcohol is 100 mg/dl. When ethanol concentration exceeds 250 mg/dl patient is at High risk of coma. A level about 450 to 500 mg/ml may be fatal. The symptoms of acute ethanol ingestion are further complicated by the use of other drugs, sedatives, or other toxic alcohols such as isopropyl alcohol.  The Acute Symptoms Related to Ethanol Blood Level

<table>
<thead>
<tr>
<th>Concentration (mg per 100 ml)</th>
<th>Symptoms</th>
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<tbody>
<tr>
<td>Mild muscle incoordination 50 -100 mg/ml</td>
<td>Decreased motor skill</td>
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<tr>
<td>Slow reaction time</td>
<td>Stupor</td>
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<tr>
<td>Blurred vision</td>
<td>Hypoglycemia</td>
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<tr>
<td>Incoordination</td>
<td>Hypothermia</td>
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<tr>
<td>Decreased inhibition 50 mg/100 ml</td>
<td>Coma</td>
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<tr>
<td>100 - 300 mg/ml</td>
<td>Death</td>
</tr>
<tr>
<td>Stupor</td>
<td>Respiratory failure</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>&gt;400 mg/ml</td>
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</table>
| Hypothermia | The initial management of the over-dosed patient is control of airways, intravenous fluids, drawing blood for electrolytes and alcohol level and drug screening, gastric lavage, activated charcoal, and close monitoring of vital signs. If patient presents with altered mental status, 2 mg of Naloxone, 25 gm of glucose and 50 to 100 mg of thiamine should be given. A continuous infusion of glucose saline should be administered with multivitamins.

Treatment of Ethyl Alcohol Overdose

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Altered mental status</td>
<td>Naloxone</td>
</tr>
<tr>
<td>Glucose</td>
<td>Thiamine</td>
</tr>
<tr>
<td>Hypoventilation</td>
<td>Mechanical ventilation</td>
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<tr>
<td>Ketoacidosis</td>
<td>Normal saline</td>
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<tr>
<td>Vasopressor</td>
<td>Normal saline</td>
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<tr>
<td>Alcohol Withdrawal Seizures</td>
<td>Trendelenburg’s position;</td>
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<tr>
<td>Mechanical ventilation</td>
<td>Normal saline</td>
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<tr>
<td>Valium</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Ativan</td>
<td>Normal saline</td>
</tr>
</tbody>
</table>
| Dilantin | Intravenous Valium, Ativan and Dilantin. A recommended regimen consists of intravenous Valium 2 mg every two minutes, or 1 mg of Ativan I.V., followed by Dilantin I.V. 40 mg per minute for a total dose of 15 mg/kg. Delirium tremens is the most serious and delayed manifestation of ethanol withdrawal that usually occurs two to four days after cessation of drinking, and is characterized by severe confusion state with delirium, visual and sensory Hallucinations and sign of increased autonomic activities like tachycardia, Hyperpyrexia, and diaphoresis. The symptoms usually subside in two to three days and may be fatal in 5 to 15 percent of patients. 1. I.V. Fluids  2. Valium 5 to 10 mg or Ativan 2 mg frequent I.V. injections until symptoms subside.  3. Haldol 5 mg I.V. every six hours as needed  4. Propranolol 0.5 to 1 mg I.V., or 40 to 80 mg po to control tremors.  5. Atenolol up to 100 mg po per day with Valium shorten the duration of withdrawal syndrome. Dehydration is due to profound agitation, decreased oral intake, and diaphoresis, and is
corrected by I.V. fluid therapy. Wernicke's encephalopathy is another fatal complication of alcoholism and is characterized by cerebellar ataxia, mental confusion, and oculomotor disturbance. The patient should receive 100 mg I.V. thiamine. However, severely malnourished alcoholics might need up to 1000 mg of thiamine I.V. to reverse the ophthalmoplegia. Since thiamine is a co-factor in glucose metabolism, the administration of glucose to a thiamine deficient patient may exacerbate this deficiency; hence, patient should receive thiamine before glucose. Since Hypomagnesemia may cause thiamine resistance, intramuscular magnesium 1 to 2 cc of 50 percent solution should be given with thiamine. Drug Interaction Ethanol is synergistic with narcotics and sedative-hypnotics. Abuse of combinations of drug with alcohol may lead to respiratory arrest and coma. Disuifiram, a drug used for detoxification, blocks the activity of the enzyme aldehyde dehydrogenase, leading to accumulation of acetaldehyde in the blood. Within five to ten minutes of ethanol ingestion, the patients on Antabuse develop headache, nausea, flushing, tachycardia, and hypotension secondary to vomiting and dehydration. Treatment is supportive with intravenous fluids and norepinephrine for severe hypotension. Isopropyl Alcohol This is the second most commonly ingested alcohol and is present in rubbing alcohol, skin and hair products and antifreeze. Children might suffer toxicity from inhalation, and from transdermal absorption during sponging. Pharmacology and Metabolism The absorption of isopropyl alcohol is rapid, and within 30 minutes of ingestion, 80 percent of the alcohol circulates in the blood, leading to CNS depression. The potential lethal dose of isopropyl alcohol is 2 to 4 cc/kg. Isopropyl Alcohol

- alcohol dehydrogenase
- Acetone

- Lungs Kidneys Clinical Symptoms These patients present to the emergency room with headache, dizziness, poor coordination, mental confusion due to alcohol and acetone. The abdominal pain, vomiting, hematemesis, are due to local gastric irritation. These patients do not have the breath odor of ethanol. The obtunded patients might also have hypoglycemia, ketosis, myoglobinuria, and rhabdomyolysis. Laboratory Investigations These include CBC, electrolytes with BUN, creatinine, serum osmolality, ketones, arterial blood gasses, and urinalysis. Treatment and Disposition 1. Gastric lavage and emesis if ingestion is within two hours. 2. Activated charcoal for multi-drug ingestion 3. I.V. Fluids to correct high anion gap acidosis and hypoglycemia 4. Hemodialysis is indicated for serum isopropyl alcohol level greater than 400 mg/cc, refractor Hypotension and deteriorating vital signs. Methanol Ingestion Methanol is a highly toxic alcohol obtained from distillation of wood. Methanol is present in antifreeze and windshield washer fluid, carburetor fluids, glass cleaners, Sterno, paint strippers, and gasoline substitutes. Methanol ingestion can cause serious sequelae due to multiorgan damage, including permanent blindness, and death. Pharmacology and Metabolism Methanol is rapidly absorbed from the gastrointestinal tract and blood levels peak 30 to 90 minutes after absorption. The smallest lethal dose reported is 15 cc of 40 percent methanol. This is metabolized by the liver and excreted through the kidneys.
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- Formaldehyde
- Formic acid
- Folate

C02 and H2O  Clinical Manifestations of Methanol Intoxication  General
Mental Confusion  Metabolic acidosis  Long latent period, often 12 to 24 hours
Gastrointestinal  Nausea  Vomiting  Severe abdominal pain  Neurologic
Headache  Dizziness  Seizures, stupor, coma  Visual  Diminished sensation of light
Photophobia  blurred vision  Retinal edema  Hyperemia of optic disk

Laboratory Investigation
These include: CBC, electrolytes, calcium, amylase, serum osmolality, ethanol and methanol levels, arterial blood gases and urinalysis. A severe anion gap metabolic acidosis is the significant finding of methanol ingestion. Osmolal gap = measured serum osmolality - calculated serum osmolality

Calculated serum osmolality (mosm/kg) = 2 (na+) + glucose + BUN

18 2.8 The normal osmolal gap is less than 10 mosm/1. A High osmolal gap indicates the presence of ethanol, ethylene glycol, methanol, isopropyl alcohol, mannitol, or glycerol in blood. Patients with peak methanol level below 20 mg/di are asymptomatic; a level greater than 25 to 50 mg/di have serious ingestions needing therapy, and those with levels above 150 mg/di often die if not treated early. These same investigations are suggested for patients with ethylene glycol ingestion and the treatment for these two conditions is very similar.

Ethylene Glycol Ingestion
It is a colorless, odorless substance and the ethylene glycol intoxication is usually due to suicide attempt, accidental ingestion, or due to consumption as ethanol substitute. The sources of ethylene glycol are: antifreeze, brake fluid, coolant, windshield fluids, some detergents, lacquers, and polishes.

Pharmacology and Metabolism
Ethylene glycol

Alcohol dehydrogenase  Glycolaidehyde

Alcohol dehydrogenase

Glycolic acid  Lactic dehydrogenase

Glycolic acid oxidase

Pyridoxine  Glyoxylic acid  Thiamine

Glycine
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Oxalic acid
Formic acid
a
Hydroxy-
b
Ketoadipate

Stage I (30 minutes to 12 hours) Intoxicated patient with no alcohol odor
Nausea and vomiting Metabolic acidosis Crystalluria Myoclonus Seizure
and death Stage II (12 to 24 hours) Tachypnea, tachycardia Hypertension
Cyanosis Pulmonary edema Bronchopneumonia Cardiac Enlargement
Stage III (36 to 48 hours) Crystalluria Costovertebral angle tenderness Tubular
necrosis with oliguria Renal failure Treatment of Methanol and Ethylene Glycol
Toxicity 1. Prevent further absorption by Ipecac or lavage, activated charcoal and cathartics. 2) Alkalization by 2 to 3 mg/kg of intravenous sodium bicarbonate. 3. Ethanol therapy 4. Calcium chloride I.V. gm for ethylene glycol ingestion. 5. Thiamine 50 mg to 100 mg for ethylene glycol 6. pyridoxine 2 to 5 gm I.V. for ethylene glycol 7. Folic acid 50 to 100 mg I.V. for methanol 8. Dialysis Ethyl Alcohol Therapy Ethyl alcohol therapy is suggested for management of ethylene glycol and methanol ingestion because it completes with alcohol dehydrogenase--the enzyme responsible for breakdown of methanol and ethylene glycol. Ethyl alcohol saturates this enzyme, increases the half-life of ethylene glycol from 3 to 17 Hours. Therefore, the administration of ethanol leads to increased excretion of unchanged compound through kidneys, hence prevents the body organ damage due to toxic metabolites. Dose 95% Ethanol 40% Ethanol 10% Ethanol Loading 1 cc/kg 2.5 cc/kg 100 cc/kg Maintenance w/o dialysis 0.1 cc/kg/hr 0.3 cc/kg/hr I cc/kg/Hr Maintenance with dialysis 0.3 cc/kg/hr 1 cc/kg/hr 3 cc/kg/hr In summary, the author has discussed the management of ethanol, isopropyl alcohol, methanol, ethylene glycol poisonings with particular emphasis on early diagnosis and proper management of these patients. The Hospitalization, psychiatric, and social service evaluations should be made on these overdosed patients with proper emphasis on long-term management and guidance of the patient.