Fatal ethylene glycol intoxication[1]

Report of a case and review of the literature

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The authors describe a 27-year-old man with signs of acute ethylene glycol intoxication, including coma, absent pupillary reflexes, hypotonia, and hyporeflexia, plus laboratory evidence of a high-anion-gap metabolic acidosis, an osmolal gap, calcium oxalate monohydrate crystalluria, and elevated serum ethylene glycol levels. He failed to respond to sodium bicarbonate and ethanol therapy and died immediately before hemodialysis. The diagnosis, clinical presentation, pathophysiology, and treatment of acute ethylene glycol intoxication are reviewed.

Index terms: Ethylene glycol • Poisoning

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Originally prepared during a glycerine shortage in World War I,[1,2] ethylene glycol (EG) is a colorless, odorless, water-soluble saturated polyalcohol with a variety of commerical uses.[3–5] It is used as a freezing-point depressant in antifreezes, de-icers, and coolants; as a solvent for detergents, paints, lacquers, polishes, cosmetics, and pharmaceuticals; and has been improperly used as a preservative in juices and some Austrian wines.

See also the editorial by Freed (pp 255–257).

Nicknamed the "sweet killer,"[7] EG's warm, sweet taste and ready availability have made it a popular ethanol substitute, a suicide agent, and an accidental intoxicant.[1–7] It was initially promoted as a benign medicinal solvent, but EG's toxicity began to be recognized after the first cases of fatal EG intoxication were described in 1930.[8] Since then, many additional cases have been reported. Forty to 60 fatalities annually have been thought to occur in the United States,[2,3] but Field[9] has suggested recently that this estimate may be high because of earlier diagnosis and aggressive treatment.

We saw a patient who was fatally intoxicated with EG during an attempted suicide. To increase the awareness of physicians at this and other institutions we describe the clinical syndrome of EG intoxication, its pathophysiology, diagnosis, and current treatment.

Case report

An otherwise healthy 27-year-old man with a history of chronic relapsing paranoid schizophrenia was admitted to the psychiatric unit after he had talked of suicide to his family by telephone. He was confused and combative, but

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there were no significant physical findings. Four hours after admission, he became unresponsive. At that time, he was pale, with a blood pressure of 120/70 mm Hg; apical rate, 100 beats per minute; respirations, 32 per minute of Kussmaul quality; and oral temperature, 36.5°C. There were no signs of trauma, and there was no odor of ethanol on his breath. He was comatose and completely unresponsive to stimuli and had small (2 mm), equal, unreactive pupils; normal retinas, optic discs, and venous pulsations; diminished corneal reflexes; absent doll's eyes reflex; generalized muscular hypotonia and hyporeflexia; and flexor plantar responses.

He was immediately given one ampule of $D_{50}W$, two ampules of naloxone, and 100 mg of thiamine hydrochloride intravenously, without effect. An arterial blood gas with the patient breathing room air showed a pH, 6.96; arterial oxygen partial pressure, 98 mm Hg; arterial carbon dioxide partial pressure, 14 mm Hg; bicarbonate, 4.5 mEq/L; and arterial oxygen saturation, 99%. Three ampules of sodium bicarbonate were given intravenously. An endotracheal tube was placed, he was transferred to the intensive care unit, and mechanical ventilation was begun.

Laboratory investigation revealed the following: a white blood cell count (WBC), 21,000 cells/mm^3, with a normal differential; hematocrit, 44.5%; sodium, 135 mEq/L; potassium, 8.4 mEq/L; chloride, 100 mEq/L; bicarbonate, 4.0 mEq/L; anion gap, 31 mEq/L; blood urea nitrogen (BUN), 21 mg/dL; creatinine, 2.0 mg/dL; albumin, 4.6 g/dL; calcium, 7.2 mg/dL; glucose, 158 mg/dL; creatine phosphokinase (CPK), 270 U/L, with a skeletal muscle (MM) fraction of 99% and a myocardial (MB) fraction of 1%; venous lactate, 2.2 mEq/L; serum ketones, absent; measured serum osmolality, 378 mOsm/kg; and osmolal gap, 70 mOsm/kg. A urinalysis showed a specific gravity, 1.010; trace protein; 1+ hemoglobin; and numerous needle-shaped calcium oxalate monohydrate crystals. An electrocardiogram showed sinus tachycardia and hyperacute T waves. A chest radiograph was normal. Blood and urine cultures had no growth. Qualitative serum and urine toxicology screens showed the presence of ethylene glycol, with ethanol, methanol, salicylates, paraldehyde, and other drugs absent. The serum EG level was 14 mg/dL six hours after admission.

Gastric lavage was performed, and 50 grams of an activated charcoal-sorbitol mixture was instilled. Two ampules of calcium chloride were given intravenously. A loading dose of 0.6 g/kg of 50% ethanol was given by nasogastric tube, and a maintenance dose of 110 mg/kg/h of 20% ethanol was begun by the same route. After a total of 11 ampules of sodium bicarbonate were given intravenously, a repeat arterial blood gas with the patient breathing room air showed a pH, 7.21; arterial oxygen partial pressure, 100 mm Hg; arterial carbon dioxide partial pressure, 14 mm Hg; bicarbonate, 5.0 mEq/L; and arterial oxygen saturation, 99%. A repeat serum potassium was 4.3 mEq/L. Femoral vein cannulation was performed for emergency hemodialysis, but before dialysis could be started, sustained ventricular tachycardia and ventricular fibrillation developed that did not respond to resuscitation.

The postmortem examination revealed abnormalities mainly in the liver, lungs, and kidneys with no pathological findings in the spleen, pancreas, heart, large intestine, or brain. The liver weighed 2,275 g. The external and the cut surfaces were reddish brown. Microscopically, severe fatty metamorphosis was seen. The right and left lungs (925 g and 875 g, respectively) had a moderate decrease in crepitus and increase in consistency in all lobes. The cut surfaces were reddish pink, moist, and covered with abundant, frothy pink fluid. Microscopically, acute passive congestion was seen. The kidneys (right, 190 g; left, 195 g) had a smooth, reddish brown surface. The cut surface disclosed normal corticomedullary demarcation. Microscopically, numerous birefringent sheaf-shaped crystals in the lumen of tubules were seen. Incidentally, black foreign material consistent with charcoal was seen on the microscopic examination of the mucosal surfaces of the stomach, small intestine, and esophagus.

Comment

As in this case, EG intoxication should strongly be suspected in a patient who appears to be inebriated without the presence of ethanol on his breath or in his blood, or who has confusion or coma plus laboratory evidence of a high-anion-gap metabolic acidosis and an osmolal gap, with or without calcium oxalate crystalluria.[3,5,9–15]

Diagnosis

The diagnosis of EG intoxication can be made from a history of ingestion; the patient's clinical presentation; the identification of the compound in a container,[2,12] body fluids (serum, urine, gastric contents),[2,3,5,10] or postmortem tissues[1–3,7]; or from elevated serum oxalate levels.[2,3,5,10] EG may be identified by boiling point determination, ultra-red spectroscopy, and paper chromatography.[2] Both EG and a major metabolite, glycolate, may be detected by colorimetric or gas chromatography or by mass spectroscopy, the preferred methods.[16–18] Recently, a rapid enzymic spectrophotometric assay using yeast alcohol dehydrogenase has been developed for detecting EG in body fluids.[16,17] Regardless of the method of detection, specimens should be evaluated immediately because prolonged refrigeration may decrease EG levels.[19]

Metabolism

EG is a nontoxic compound, but its metabolites are highly toxic.[3,10,13,14,20] Once ingested, EG is rapidly absorbed from the gastrointestinal tract and distributed throughout the body fluids and tissues.[11] The metabolism of EG follows saturation kinetics; therefore, the half-life is highly variable after ingestion.[3,5,10,11,13,21] Twenty-four hours after ingestion, no EG is usually detectable in body fluids.[11] Its volume of distribution is 0.83 L/kg,[21] and the volume of distribution of a major metabolite, glycolate, is 0.55 L/kg.[22] Approximately 10 g of EG is metabolized by the liver per hour, and the production of acid metab-

olites can be as high as 150 mEq per hour.[23] The lethal dose of EG is thought to be 100 mL (1.4 to 1.6 mL/kg),[1,3–6,12–14,17] but as little as 30 mL has proven fatal,[9] and recovery has occurred after the ingestion of as much as 2 L.[11,20]

In the liver, EG is first oxidized to glycoaldehyde by nicotinamide adenine dinucleotide (NAD)–dependent alcohol dehydrogenase. Glycoaldehyde is rapidly oxidized to glycolate, which in turn is oxidized to glyoxylic acid in a rate-limiting step.[22] Glyoxylic acid may be converted to either formic acid and carbon dioxide; to glycine; to oxalomalate, alpha-hydroxy-beta-ketoadipate, and gamma-hydroxy-alpha-ketoglutarate; or to oxalate. EG and its metabolites are excreted by the kidney.[3,11,13,18]

The aldehyde metabolites (glycoaldehyde, glycolate, glyoxylic acid) inhibit protein synthesis, DNA replication, ribosomal RNA synthesis, oxidative phosphorylation, respiration, and glucose metabolism.[3,10,14] Oxalate may produce renal damage and acidosis and may cause hypocalcemia by chelating the calcium ion.[3,10,13,14] Lactic acid is formed during the breakdown of EG because of nicotinamide adenine dinucleotide (NADH) production and through inhibition of the citric acid cycle by the products of glyoxylic acid oxidation.[5,10,11,13,14] Oxalate, glycolate, and glycine contribute to the acidosis.[2,3,11,18,19] Pyridoxal phosphate is consumed during the transamination of glyoxylic acid to glycine, and thiamine pyrophosphate is used during the formation of alpha-hydroxy-beta-ketoadipate.[3]

Differential diagnosis

Sodium and potassium account for 95% of extracellular cations, while chloride and bicarbonate account for 85% of extracellular anions, so the sum of the measured cations exceeds the sum of the measured anions. This difference is known as the anion gap, and it is normally 10 to 14 mEq/L. The anion gap consists of unmeasured anions, including albumin, sulfate, phosphate, negatively charged proteins, and organic acids. The addition of an organic acid with a nonchloride anionic moiety to the extracellular fluid causes the loss of bicarbonate and results in a high-anion-gap metabolic acidosis. A high-anion-gap metabolic acidosis occurs with established renal failure, ketoacidosis (starvation, alcoholic, diabetic), lactic acidosis, and ingestion of certain toxic substances.[11,14,15,24,25] These substances include salicylates, methanol, paraldehyde, phenformin, iron, isoniazid, and EG.[11,24] Salicylate intoxication causes a pure respiratory alkalosis or a combined respiratory alkalosis and metabolic acidosis, plus elevated serum salicylate levels.[11,12,14,24] Three drops of 10% ferric chloride added to 1 mL of boiled urine result in a positive test (purple color) in the presence of salicylates, and an Ames Phenistix® dipstick turns brown in the presence of either salicylates or phenothiazines; addition of one drop of 20 N sulfuric acid bleaches the dipstick if phenothiazines are present.[11] Methanol intoxication causes inebriation, visual blurring, abdominal pain, and neurological signs (e.g., seizures, coma)[5,14,24]; physical examination shows retinal edema, optic disc hyperemia, and papillitis[5,11,12,14,24]; laboratory evaluation shows leukocytosis, an elevated mean corpuscular volume, and both a high-anion-gap metabolic acidosis and an osmolal gap.[5,14] Paraldehyde ingestion is seen in ethanol and/or drug abusers, and it can be diagnosed at bedside by its characteristic odor.[11,12,14,24] Phenformin ingestion causes prolonged hypoglycemia. Iron intoxication causes severe emesis and diarrhea, whereas isoniazid causes seizures.[11]

The serum osmolality is a reflection of the number of particles per given weight of solvent and can be almost entirely accounted for by sodium, urea, and glucose.[11,12,14,24,26,27] The serum osmolality can be calculated[14] by doubling the serum sodium concentration and adding approximately 10, or by using the following formula[11,12,24,27]: 2(Na) + BUN/2.8 + glucose/18. The normal serum osmolality is 285–295 mOsm/kg. The difference between the measured serum osmolality and the calculated serum osmolality is known as the osmolal gap. Normally, the osmolal gap is less than or equal to 10 mOsm/kg and may be accounted for by proteins, lipids, and calcium.[12,24,25] An osmolal gap greater than 10 mOsm/kg suggests the serum presence of high levels of low-molecular-weight, osmotically active compounds.[11,12,14,15,24,26,27] An osmolal gap can occur with hyperglycemia, hyperlipidemia, hyperproteinemia, parenteral hyperosmolar solutions, and ingestion of certain toxic substances.[14,25,27] The latter includes ethanol, isopropanol, methanol, EG, mannitol, glycerol, acetone, ethyl ether, and trichloroethane. Of these, only methanol and EG cause both a high-anion-gap metabolic acidosis and osmolal gap.[11–15,25,26] An EG level of 21 mg/dL increases the serum osmolality by 4.0 mOsm/kg.[26] We emphasize that a measured osmolal gap may be significantly higher than the osmolal gap calculated based on

the molecular weight of EG. The other metabolites of EG (glyoxylic acid, formic acid, etc.) also contribute to the clinically observed osmolal gap.

Clinical presentation

As described by Berman et al,[1] the syndrome of EG intoxication can be divided into three successive stages. The severity of each stage and the progression from one stage to the next depend upon the amount of EG ingested and the timing of medical intervention.[3,10,11,20] Death may occur at any stage, but early mortality is due to shock, central nervous system (CNS) depression, or cardiopulmonary failure,[3–5,19] and late mortality is due to renal failure.[2,5]

The first stage of EG intoxication occurs 30 minutes to 12 hours after ingestion, resembles ethanol intoxication, and is dominated by depressive CNS signs and symptoms, accompanied by a profound high-anion-gap metabolic acidosis.[1,3,4,11,19,24,28] The CNS signs and symptoms correlate with maximal production of aldehyde metabolites from EG and probably with the development of cerebral edema and calcium oxalate deposition.[3,5,10,11,13] Nonspecific nausea, emesis, pyrosis, abdominal cramps, and hematemesis are seen early after ingestion, reflecting gastric irritation.[1–6,10,12] With small amounts of EG, the patient appears intoxicated, despite the absence of ethanol odor on the breath.[1–6,10,13,14]

With larger amounts, common neurological findings include depression, hallucinations, confusion, coma, meningismus, focal or generalized seizures, hypotonia, hyporeflexia or hyperreflexia, ataxia, tremors, myoclonic jerks, and tetany.[1–6,10,13,14,18,28] Coma may last a week or more.[3,29] Common ocular findings include decreased or absent pupillary reflexes, nystagmus, decreased visual acuity, optic disc blurring and pallor, internuclear ophthalmoplegia, strabismus, blue/red/green color blindness, papilledema, and optic atrophy.[2–5,10,13,14,19,29,30] Additional cranial nerve palsies may present as bilateral facial paralysis, dysarthria, dysphagia, and absent gag reflexes.[18] Other early physical findings include tachycardia, mild hypertension, low-grade fever, Kussmaul respirations, and abdominal tenderness.[2,3,5,14]

Laboratory evaluation may show a moderate leukocytosis (10,000–40,000 cells/mm^3), with a neutrophil predominance, a high-anion-gap metabolic acidosis with hypobicarbonatemia (less than 10 mEq/L), an osmolal gap (greater than 10 mOsm/kg), and hyperkalemia concomitant with the acidosis. Hypocalcemia may also be present.[2–6,10,13,14] A typical urinalysis shows low specific gravity, proteinuria, microhematuria, pyuria, cylinduria, renal tubular epithelial cells, and profuse crystalluria,[1–6,10,13,14] with either spindle-shaped calcium oxalate monohydrate crystals, or octahedral or dumbbell-shaped calcium oxalate dihydrate crystals.[9,31–33] Crystalluria may be absent, depending on the time elapsed since ingestion.[1,9,14,29] Hippurate crystals are not present, as formerly thought.[5,9,32] An electrocardiogram may be normal or may show hyperacute T waves consistent with hyperkalemia.[2] An electroencephalogram may show mild, diffuse, slow wave activity seen with a metabolic encephalopathy.[2,3] A cerebrospinal fluid examination can be compatible with a chemical meningoencephalitis, with a cloudy or bloody appearance, increased pressure, increased protein, xanthochromia, a neutrophilic or monocytic pleocytosis, and sterile cultures.[3–5,10,13,14,28,29] A cerebral computed tomogram (CT) may be normal or show central edema, with sparing of the corona radiata and the cortical gray matter but with compression of the lateral and third ventricles and the sulci.[29,34]

The second stage of EG intoxication occurs 12–48 hours after ingestion, and is marked by cardiopulmonary failure caused by the toxicity of the acid metabolites of EG.[1,4,15,19,24,28] Neurogenic influences,[1,4] hypocalcemia,[3,11,13] and calcium oxalate deposition in the myocardium, pulmonary parenchyma, and the vasculature[5] have also been suggested as causes. Physical findings may include tachypnea, tachycardia, cyanosis, ventricular gallop, inspiratory rales, and mild hypertension. Pulmonary edema, bronchopneumonia, cardiac dilatation, and cardiac arrhythmias have been described.[1–6,10,13,14,18] Recently, noncardiogenic pulmonary edema (adult respiratory distress syndrome, ARDS) from EG intoxication has been reported.[15] Cardiopulmonary arrest is less common now because of more aggressive correction of acidosis and hypocalcemia,[3,11] plus earlier use of ethanol therapy and hemodialysis.[18]

The third stage of EG intoxication occurs 48 hours or more after ingestion and is characterized by acute renal failure caused by the toxicity of the acid metabolites of EG.[1–4,10,11,13,14,18,28] Acute tubular necrosis occurs and is predominantly proximal, but can also be distal.[5,18]

Renal edema and renal deposition of calcium oxalate crystals contribute to the renal failure.[1,3,10,11] In severe cases, renal cortical necrosis has been found.[2,5] Costovertebral angle tenderness is the most common physical finding,[1–6,10,13] but oliguria or anuria may also be seen.[2–6,13,14] Laboratory evidence of renal impairment may range from mild proteinuria and azotemia to frank renal failure.[1–4,10,11,13] Plain abdominal radiographs may show indistinct renal margins, suggesting perirenal edema.[2] Renal ultrasound has been reported to show renal enlargement, with increased echogenicity and partial obstruction of the corticomedullary junction, as seen with primary hyperoxaluria. Abdominal CT has shown enlarged, low-attenuation kidneys.[35] Recovery of renal function may require more than 50 days to occur.[3,36] Serial renal biopsies may be useful in predicting the reversibility of renal failure if the latter is prolonged more than 30 days[36]; permanent renal insufficiency from interstitial fibrosis and tubular atrophy is rarely seen.[3,13,36]

Additional aspects of EG intoxication include a myopathy suggested by myalgias, muscle tenderness, and elevated serum creatine phosphokinase levels[2,3,14] and possible toxic bone marrow suppression, with peripheral pancytopenia and bone marrow maturation arrest seen in bone marrow biopsies.[29]

Pathology

Generalized edema and hyperemia involving the brain, lungs, heart, kidneys, and liver have been described in the majority of cases.[1–4,10,13,14,28,37–39] Widespread petechiae in the brain, lungs, heart, pleura, pericardium, and great vessels are common.[1,3–5,13,15,28,29,39] Focal mucosal hemorrhages in the esophagus and stomach and intraparenchymal hemorrhages in the brain, lungs, and heart have been observed.[15,39] Diffuse calcium oxalate crystal deposition occurs in the brain parenchyma, leptomeninges, choroid plexuses, vessel walls, and perivascular spaces[1–5,10,13,14,19,28,37,38]; in the pulmonary parenchyma and vessels[1,10,19,37,38]; the renal collecting system[1–3,10,13,14,37–39]; and less often in the myocardium,[14,19] pericardium,[5] liver, and spleen.[2,5,19,37] Deposition probably also occurs in the lymph nodes, adrenals, pancreas, and prostate.[37]

The brain may show evidence of a sterile meningoencephalitis.[2–4,10,13,14,28,38] Perivascular infiltration with neutrophils, lymphocytes, and red blood cells; diffuse neuronal satellitosis; focal Betz and Purkinje cell chromatolysis; and astrocytosis in the cerebrum, brainstem, and cerebellum have been seen microscopically.[1,2,10,13,14,28,37–39]

Diffuse pulmonary edema and focal hemorrhagic bronchopneumonia are found.[1,4,10] Cardiac enlargement is usually present.[1–3,10] There may be microscopic interstitial pneumonitis and myocarditis.[2,37,39]

Bilateral focal hemorrhagic renal cortical necrosis has been seen.[2,5] Microscopically, dilated proximal tubules with hydropic degeneration of the tubular epithelium are present.[2,3,10,13,37] Large numbers of light yellow, brilliantly birefringent calcium oxalate crystals are found, primarily within the lumens and also within the epithelial cells of the proximal tubules.[1–3,10,13,14,37–39] To a lesser extent, these crystals may occur in the distal tubules and collecting ducts.[2,3,10,14,37] Renal calcium oxalate crystal deposition has been found in all stages of EG intoxication and may also occur during intoxication with EG monoacetate, ethanol amine, glyoxal, and glycolate, as well as with primary hyperoxaluria and chronic renal failure.[14,19] Eosinophilic casts may be present, and interstitial edema and nephritis have been found.[2,3,5,13,37] The renal glomeruli are generally spared, except for increased cellularity, focal thickening of the basement membrane, and deposition of protein in Bowman's space.[2,3,10]

Other pathological findings include central hydropic or fatty degeneration and parenchymal necrosis in the liver[2,3,37,39]; parenchymal and interstitial inflammation in the muscles[2,3]; focal hyperplasia and pseudoacinar transformation in the adrenals; and interstitial inflammation in the pancreas and the diaphragm.[2,37]

Treatment

EG intoxication should be treated rapidly and aggressively.[3,20] The objectives of therapy are to reduce the load of ingested EG, to inhibit the metabolism of EG to its toxic metabolites, and to prevent calcium oxalate formation and deposition, particularly in the kidney.[20]

If the patient is alert and cooperative, emesis should be induced[4]; if the patient is confused or comatose, intubation should be performed before gastric lavage.[4,6,11,19,20] Activated charcoal should be administered to remove any residual EG from the gastrointestinal tract.[18] A cathartic such as sorbitol should also be given to decrease the intestinal transit time of EG. Fluid resuscitation and intravenous pressor support are appropriate for

dehydration and shock.[5,10] Although not clearly proven, forced diuresis with intravenous fluids, mannitol, and loop diuretics may increase renal clearance of EG during the early stages of intoxication and, if effective, should be continued until the crystalluria is gone.[3,11,13,18,20] Meticulous fluid and electrolyte balance should be maintained to avoid causing acute pulmonary edema or electrolyte abnormalities.[4,5] Intubation and mechanical ventilation should be instituted for cardiopulmonary failure.[4,10] Hypocalcemia should be corrected with intravenous calcium salts in order to prevent seizures, tetany, and cardiac failure.[5,6,10,11,13,19] Thiamine and pyridoxal phosphate cofactors should be given parenterally to help decrease calcium oxalate deposition because they function as cofactors in the metabolism of glyoxylate to alpha-hydroxy-beta-ketoadipate and glycine instead of oxalate.[11,18] Intravenous sodium bicarbonate should be used to treat acute metabolic acidosis[3–6,10,11,13,19]; massive doses up to 1,000–2,000 mEq may be required.[5]

Ethanol has a hundred-fold greater affinity for hepatic alcohol dehydrogenase, and it should be given as soon as possible after EG ingestion to act as a competitive inhibitor of EG so that the latter cannot be metabolized to its toxic intermediates.[3,5,6,10,11,13,14,20,29] A loading dose of 0.6 g/kg of 50% ethanol is given orally or by nasogastric tube and should be followed by a maintenance dose of 109 mg/kg/h of 20% ethanol by the same route.[5,13,21] The oral dose of ethanol should not exceed a concentration of 20% in order to avoid gastritis. CNS depression and hypoglycemia are also possible consequences of ethanol administration.[11] A continuous intravenous infusion of 5–10% ethanol may be given instead if the patient is comatose,[23] if prolonged emesis[40] or adynamic ileus[29] are present, or if the gastric contents (e.g., lipids, charcoal)[21,23,29] may interfere with oral ethanol absorption.

Simultaneously, or as rapidly as possible, hemodialysis should be initiated to correct metabolic acidosis,[3,14] treat crystalluria and renal failure,[3,4,11,40] prevent or treat fluid overload,[14] and remove both EG and its toxic metabolites, particularly glycolate and oxalate.[3,11,14,29,41] The half-life of EG during hemodialysis and oral ethanol therapy is 2.5 hours. The mean clearance of EG is 210 ± 3.0 mL/min when the dialysis blood flow rate is 227 mL/min, similar to the clearance of urea.[5,21] During hemodialysis, 237 mg/kg/h of 20% ethanol should be given.[5,13,21] Alternatively, 95% ethanol can be added to the dialysate bath to achieve a dialysate level of 100 mg/dL and, thus, more stable blood ethanol levels.[5,18,29,40] Regardless of the route of administration, serum ethanol levels should be checked hourly to maintain a level between 100 mg/dL and 200 mg/dL to assure saturation of hepatic alcohol dehydrogenase.[10,11,13,18,20,21,29,35] Chronic ethanol abuse, hemodialysis, and activated charcoal may decrease ethanol levels after oral or intravenous administration and increase the required loading and maintenance doses of ethanol by as much as 50%.[11,21,29] Bicarbonate dialysis is most appropriate for long-term control of metabolic acidosis.[5,13,18] Dialysis should be continued until serum EG levels are undetectable, the metabolic acidosis is resolved, and the urine output is adequate.[5,18] Ethanol therapy should be instituted promptly and continued to maintain ethanol concentrations within the range of 100–200 mg/dL until EG levels are undetectable. EG levels may transiently increase after hemodialysis as a result of fatty tissue release or from continued intestinal absorption.[16,18,20,21] Peritoneal dialysis is also effective,[6,10,13,42] but it is less efficient than hemodialysis in removing EG and its metabolites,[13,18] so it should be used only if hemodialysis is not available. Activated charcoal hemoperfusion is effective but least desirable because acid-base imbalances cannot be corrected and the charcoal columns must be changed regularly at 1.5–2.0 hour intervals because they easily become saturated with EG.[5,43]

Experimental therapy for the treatment of EG intoxication includes 4-methyl pyrazole, a potent and specific inhibitor of alcohol dehydrogenase used successfully to treat methanol intoxication in monkeys[44] and EG intoxication in rats and monkeys.[5,44,45] Four-methyl pyrazole is not currently available for treating EG intoxication in humans, and it has been used in humans only for experimental studies of ethanol metabolism.[44]

As a means of prevention, prominent labeling of all commercial glycol-containing solutions has been recommended.[2] Public and professional education regarding the hazards of EG is important. Old antifreeze and other glycol preparations should be discarded and not saved. An unpalatable but benign taste deterrent might be incoporated into glycol-containing products.[7,46]

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