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Barbiturate Overdosage

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Barbiturates are physically addicting sedative-hypnotic agents that can cause severe withdrawal symptoms. Their original role was to treat anxiety and insomnia, but they became popular drugs of abuse in the 1960s and 1970s and the most commonly used drugs in suicide attempts. Use of barbiturates has decreased significantly with stricter governmental regulations and with the advent of the much safer benzodiazepines. Current therapeutic uses of barbiturates are to treat seizure disorders, headaches, gastrointestinal disorders, and increased intracranial pressure and for anesthesia induction, but they have no analgesic properties. Adolescents abuse barbiturates to achieve a euphoric “high,” to offset the undesirable anxiety caused by stimulant drugs, and to attempt suicide.

Monitoring the Future is a national survey of high school students that investigates their use of different substances as well as their beliefs about substance use. This survey showed that barbiturate use among 12th grade students peaked in the mid-1970s, reached an all-time low in the early 1990s, and since then has risen slowly. This rise may be due to an increase in “social approval of use” as well as to a lack of recognition of “perceived risk” that was found in the survey. Overall, 6% of students reported use in the last 12 months, which has been fairly consistent over the past 6 years.

Barbiturates inhibit synaptic transmission in all areas of the central nervous system (CNS) by binding to sites for gamma-aminobutyric acid (GABA), a major inhibitory neurotransmitter. Excitatory neurotransmitters are also blocked, adding to the CNS depressive effects. Barbiturates are metabolized in the liver, and the inactive metabolite is excreted in the urine. These drugs are classified by duration of action. Ultra short-acting types, such as thiopental, act within 30 minutes and are used for anesthesia induction. Short-acting agents, such as pentobarbital and secobarbital, take 3 to 8 hours to demonstrate their effects, which are sedative and hypnotic. Long-acting phenobarbital takes 1 to 2 days and is used as an anticonvulsant. The shorter-acting agents that are more lipid-soluble and protein-bound are metabolized almost entirely in the liver to inactive products via P450 microsomal enzyme induction.

Barbiturates may diminish the action of other drugs that are taken concomitantly and are dependent on the P450 enzyme system, such as oral contraceptives, corticosteroids, and anticoagulants. Short-acting agents are used more commonly as drugs of abuse because of their rapid onset of action and prompt crossing of the blood-brain barrier. Longer-acting agents are less lipid-soluble, accumulate more slowly in the body, and are excreted in the urine mostly as active drug.

Symptoms of barbiturate overdose include CNS, cardiovascular, and respiratory depression. CNS manifestations range from confusion, vertigo, ataxia, and slurred speech to lethargy and coma. Miosis and nystagmus are common, as are hypothermia and diminished deep tendon and brainstem reflexes. Patients may appear delirious, irritable, combative, or paranoid. Respiratory suppression may occur at toxic doses with resultant hypoxia and acidosis. In severe overdoses, barbiturates exert direct depressive effects on the myocardium and vascular tone, leading to hypotension, poor perfusion, and eventually, cardiac arrest. Hypothermia between 30°C and 36°C is common and contributes to cardiac depression and rhythm disturbances. Physical dependence can occur, and overdose may be unintentional given the narrow therapeutic range of these agents. Withdrawal can be severe and can manifest as tremors, weakness, seizures, and cardiac arrest.

Mortality is related primarily to hypoxia and hypotension. Thus, the first priority in evaluating a patient suspected of having a barbiturate overdose...
is assessing the airway, breathing, and circulation. Endotracheal intubation may be necessary to secure the airway and maintain adequate ventilation. Administration of intravenous (IV) fluids, vasopressor agents, and IV dextrose should be considered, as should administration of naloxone because polysubstance abuse is common, especially with opiates. Although not effective in reversing barbiturate ingestion, naloxone can be used both as a diagnostic and therapeutic tool to distinguish if opiates were taken and to treat a concomitant ingestion of opiates.

Rectal temperatures need to be monitored for hypothermia, and an electrocardiogram should be obtained. Urine and serum toxicology screens (including acetaminophen, salicylate, and alcohol concentrations) should be undertaken, and electrolytes, anion gap, blood gases, blood urea nitrogen, and creatinine should be measured. Barbiturate concentrations aid in the diagnosis, with toxic signs occurring when values exceed 10 to 30 mcg/mL for short-acting and 50 to 80 mcg/mL for long-acting agents.

Barbiturates may be taken as drugs of abuse, and intervention is tailored to the degree of toxicity. Because most are taken orally and toxic doses decrease gastrointestinal motility, gastrointestinal decontamination is an effective intervention and should be started for those who have a secure airway by administering 1 g/kg of activated charcoal, which binds barbiturates and most other ingested drugs. Doses of 0.25 g/kg every 4 to 6 hours can be given for severe ingestions. Induction of emesis is not recommended unless the patient presents within 1 hour of ingestion and aspiration risks are minimized by the patient having either a secure airway or an alert mental status. Cathartics are not effective, may cause large fluid shifts in children, and should be avoided.

Alkalization of the urine to a pH of more than 7.5 with sodium bicarbonate promotes renal elimination of the metabolites of long-acting agents, which are physiologically active. The effects of short-acting barbiturates do not respond as well because those agents produce inactive urinary products. Although both urine alkalinization and gastrointestinal decontamination are effective, a comparative study found that decontamination led to more rapid elimination. Hemodialysis and charcoal hemoperfusion are last resorts for patients who have ingested long-acting barbiturates, are clinically unstable despite aggressive intervention, or have rising barbiturate levels despite appropriate gastrointestinal decontamination. Short-acting barbiturates are poorly eliminated by this method because they are highly protein-bound and have a large volume of distribution.

Barbiturates may lead to addiction. Sudden discontinuation of use may lead to withdrawal symptoms similar to those of alcohol withdrawal. When no longer indicated, these drugs must be weaned slowly.
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