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Selected Topics: Toxicology

PERSISTENT EFFECTS AFTER CAMPHOR INGESTION: A CASE REPORT AND LITERATURE REVIEW

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☐ **Abstract—Background: Camphor is a well-known toxin responsible for thousands of poisonings per year. It can be found in many over-the-counter remedies and illegally imported substances. The toxidrome manifests within minutes and includes gastrointestinal, neurologic, pulmonary, and cardiac effects. Severe ingestions may progress to seizures, apnea, and coma. Most individuals are no longer symptomatic outside the 24–48 h window, but physiologic derangement may persist for far longer in some instances. Case Report: This is a case report of a 25-year-old Guatemalan woman with no past medical history who ingested a cube of camphor for a facial rash. She presented to the Emergency Department with persistent delirium and headache 6 days after ingestion. She had a protracted recovery but returned to her baseline state of health 19 days after ingestion. Why Should An Emergency Physician Be Aware Of This?: Persistent toxic effects of camphor are not well described, and most sources state that the toxidrome resolves in 24–48 h. Given the frequency of camphor poisoning, it is crucial to increase public awareness of camphor toxicity, to understand the biological mechanism of the effects, and to develop more targeted treatments. From the emergency physician's perspective, it is important to realize that toxic effects of camphor poisoning may persist far beyond the 24–48 h window and require attention.** © 2015 Elsevier Inc.

☐ **Keywords—camphor; poisoning; toxicity; neurotoxic; seizure; ingestion; poison; toxin; altered mental status**

INTRODUCTION

Camphor (2-bormanone, 2-camphonone) is a well-known toxin responsible for thousands of poisonings per year. Camphor derives naturally from the bark of the *Cinnammomum camphora* tree, and it is a major essential oil in many aromatic plants, such as Greek sage (*Salvia fruticosa*), Spanish sage *(Salvia lavandulifolia)*, Lavender cotton (*Santolina insularis*), and sweet wormwood (*Artemisia annua*). In addition, camphor may be biosynthetically synthesized, using turpentine as a starting material (1).

Camphor has been used medicinally since ancient times in China and since the Middle Ages in Europe (1). Currently, camphor is used as an antitussive, antimicrobial, antiviral, and analgesic agent, as well as an insecticide and a skin penetration enhancer. Camphor is also found in many cosmetics, air fresheners, and food products (2).

Camphor's toxic properties have been recognized since at least the 19th century (1). In 1983, the U.S. Food and Drug Administration (FDA) placed an 11% limit on the amount of camphor allowed in medical products due to a number of poisoning cases in children (3). Despite the dangers of camphor, substances containing <11% camphor remain available in any retail drug store. These products include Vicks VapoRub (Proctor & Gamble, Cincinnati OH), Tiger Balm (Prince of Peace

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Enterprises Inc., Hayward, CA), Chapstick (Pfizer, New York, NY), and Campho-Phenique (Bayer Healthcare LLC, Pittsburgh, PA), among others.

Despite these regulations, pure camphor cubes and products containing up to 20% camphor are heavily imported into the United States from countries such as India and China. They are illegally marketed in the United States to combat colds, skin conditions, headaches, abdominal pain, and pregnancy, as well as for use in spiritual rituals (4). These products may be purchased in many ethnic grocery stores and bodegas, and they often fail to indicate the percentage of camphor they contain.

The availability of camphor-containing substances leads to common poisonings in the United States and across the world. In fact, the American Association of Poison Control Centers Toxic Exposures Surveillance System reported more than 10,000 cases of single-drug camphor exposure through topical agents in the United States in 2011 alone (5).

The mechanism of camphor toxicity is not well understood. Camphor is a highly lipophilic cyclic terpene, which allows it to diffuse rapidly across membranes and to fill a volume of distribution ranging from 2–4 L/kg (2). Absorption occurs via the gastrointestinal tract, transdermally, by inhalation, and across mucous membranes. Once absorbed, camphor is oxidized and conjugated by the liver, then excreted by the kidneys. Active metabolites are stored in fat and eventually released through the urine (2).

Toxic effects usually occur within 5–90 min of ingestion (3). The first effect is often a burning oral and abdominal sensation, followed by nausea and vomiting. Aspiration of camphor-containing emesis or fumes may cause pulmonary irritation. Severe poisonings may also result in postictal respiratory depression and apnea. Fatty infiltration of the liver, hepatic enzyme elevation, encephalopathy, and renal toxicity may occur, and can resemble Reye syndrome. Neurologic manifestations begin rapidly after ingestion and include headache, irritability, hyper-reflexia, confusion, tremors, and myoclonus. Severe ingestions may progress to seizures, apnea, and coma (5–16).

The lethal dose of camphor in adults ranges from 50 to 500 mg/kg (2). Death is usually due to respiratory failure or complications of status epilepticus. In adults, a dose of 2 grams or more usually causes toxic effects, and 4 grams is potentially lethal. In contrast, the lethal oral dose is estimated to be 0.5–1 g in children and 70 mg/kg in infants. Neurologic effects are common above 50 mg/kg, whereas toxicity has not been reported below 30 mg/kg (2). The threshold limit value-time-weighted average for camphor, as set by the Occupational Safety and Health Administration, is 2 mg/m^3 (0.3 ppm) (17).

Camphor metabolism seems to follow first-order kinetics. It has a half-life of approximately 15 h and is initially metabolized via cytochrome P450-mediated reactions (18). Camphor is then oxidized by alcohol dehydrogenase and aldehyde dehydrogenase in the liver and conjugated with glucuronic acid to become water-soluble for urinary excretion (18,19). Oral ingestion of camphor can lead to high concentrations of camphor in the fetal brain, liver, kidney, and blood, as well as in amniotic fluid (18,19). Fetuses lack the enzymes to hydroxylate and conjugate camphor with glucuronic acid, which can lead to spontaneous abortion in pregnant women (20). In those cases that do not result in abortion, camphor has not been found to produce teratogenic effects in animal models after oral ingestion or in humans after topical exposure (2,21). Based on such information, topical camphor exposure is categorized as FDA Pregnancy Category C (2).

The mechanism of camphor's toxic effects remains unknown, and few studies have examined this question. A study published by Park et al. in 2001 indicates that camphor noncompetitively inhibits nicotinic acetylcholine receptors and therefore decreases catecholamine secretion (22). However, in vitro studies conducted by Perry et al. in 2000 involving human erythrocyte acetylcholinesterase exposed to camphor from the salvia plant showed that camphor also noncompetitively inhibits acetylcholinesterase (23). These actions seem to counteract each other, and their clinical significance is unclear.

Toxic effects of camphor are widely thought to resolve by 24–48 h after ingestion, and the majority of case reports support this conclusion (6–13,15,16). However, the following case report demonstrates persistent neurologic effects weeks after ingestion. This case suggests that although most individuals are no longer symptomatic outside the 24–48 h window, physiologic derangement may persist for far longer in certain instances.

CASE REPORT

A 25-year-old Guatemalan woman with no past medical history presented ambulatory to the Emergency Department (ED) from work for altered mental status. According to her husband, she had seemed very confused at her job in a restaurant that day, and her employer advised her to seek medical treatment. Upon arrival at the ED, the patient was continuously singing and holding her head and abdomen. With redirection, she reported that she had purchased "medicine from a man on the street" 1 week prior to presentation to treat a facial rash. The medicine consisted of 0.25-ounce camphor resin tablets imported from China, advertised to contain 99% pure camphor (Figure 1). The product was packaged as a