Scientific Article

Acute ethanol toxicity from ingesting mouthwash in children younger than 6 years of age

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Abstract

The purpose of our study was to analyze reports of the American Association of Poison Control Centers (AAPCC) of suspected overingestion of ethanol from mouthrinses by children younger than 6 years of age between 1989 and 1994. Annual incidence rates of reported ethanol exposures attributed to mouthrinses were calculated. Lethal and toxic amounts of several mouthrinses were calculated using peak blood ethanol concentrations of 500 and 50 mg per 100 mL, respectively. In 1994, there were 2937 calls reported by poison control centers related to ethanol-containing mouthrinses, an estimated incidence of 168 reported exposures per 100 000 children younger than 6 years of age. A 15-kg child who ingests 212 mL (7.2 oz.) of Listerine® (26.9% ethanol) ingests 57 mL (1.9 oz.) of ethanol, which is potentially lethal. Approximately one-tenth that amount of ethanol can produce a toxic reaction. Physicians, dentists, and other health care providers should inform parents of the dangers associated with accidental ingestion of mouthrinse and encourage them to keep mouthrinse out of the reach of children. The Food and Drug Administration (FDA) should require readily visible warning labels and child-resistant caps for containers with potentially toxic volumes of ethanol. The American Dental Association (ADA) should re-evaluate its acceptance criteria for advertising cosmetic mouthrinses in its publications and consider including child-resistant caps and warning labeling. (Pediatr Dent 19:405–408, 1997)

Mouthrinse is generally considered a safe product. However, mouthrinse that contains ethanol can be fatal if ingested by a small child. In a case reported in *Clinical Pediatrics*, a 4-year-old boy died after drinking approximately 585 mL (20 oz.) of a mouthwash containing 10% ethanol.[1] While fatalities or life-threatening toxicity from ingestion of ethanol-containing products by children is rare, mouthrinse ingestion does occur frequently, sometimes with nonlethal, toxic reactions.[2] Hornfeldt reported that 75 mL (2.6 oz.) of mouthwash containing 12.35% ethanol "caused hypoglycemia, coma, and manifestations of tonic seizure activity" in a 23-month-old child.[2]

Mouthrinse has great potential to cause ethanol toxicity in children because of its prevalence, appeal, and ease of use. It is ubiquitous, used by an estimated 63% of the US adult population.[3] Unlike other ethanol-containing products such as perfumes, colognes, and aftershave lotions, it is formulated to taste good. In addition, it is colorful and available in large containers that generally do not have child-resistant caps. Children see their parents placing it in the mouth and may mimic their actions. Last, children are capable of drinking large amounts in relation to their body weight and achieve high blood-alcohol levels rapidly.[4]

Background

Mouthrinses are classified as cosmetics under the Food, Drug and Cosmetics Act.[5] They are composed of flavoring agents, coloring agents, surface-active ingredients, water, and generally, denatured ethanol. Denaturing agents are added to ethanol to discourage people from ingesting ethanol-containing products.[6] However, the denaturing agents used in mouthrinse are only minimally toxic as mouthrinses may be inadvertently swallowed in normal use.[7]

Ethanol-containing mouthrinses comprise most of the mouthrinses currently on the market. The product with the highest ethanol concentration, Listerine® (Warner–Lambert), contains 26.9% ethanol by volume (53.8 proof), more than five times the ethanol concentration of beer and more than twice that of table wines. Table 1 shows the ethanol concentration, volume, and largest container size available to the public of over-the-counter mouthrinses. Because of the toxicity concerns associated with accidental ingestion of ethanol from mouthrinses, the American Dental Association Council on Dental Therapeutics now requires child-resistant packaging on ..."all [containers of] Council-Accepted mouthrinses containing three or more grams of alcohol"[8] (one-tenth the lethal dose for a 10-kg child). Further, mouthrinses containing more than three grams of ethanol must have the following warning: "WARNING: KEEP OUT OF REACH OF CHILDREN. This product contains alcohol. Do not swallow. Use only as directed."[8] However, this applies only to therapeutic

TABLE 1. ETHANOL CONCENTRATION AND LARGEST WIDELY AVAILABLE MOUTHRINSE CONTAINER

Product	*Manufacturer*	*Percent Ethanol*	*Largest Container (Oz.)*	*Ethanol Content (Oz.)*
Listerine®	Warner-Lambert		58	
Original Formula		26.9		15.6
Cool Mint		21.6		12.5
Fresh Burst		21.6		12.5
Cepacol®	J.B. Williams Co.	14.0	40	4.8
Scope®	Procter and Gamble	18.9	72	24.5
Plax®	Pfizer		58	
SoftMint®		8.5		4.9
Original Flavor		7.5		4.4
Viadent®	Colgate	10.0	30	3.0
Mentadent®	Cheeseboro Ponds	12.0	30	3.6
Lavoris®	Dep Corporation		32	
Peppermint		7.0		2.2
Spearmint		7.0		2.2
Crystal Fresh		6.0		1.9
Cinnamon		5.0		1.6

mouthrinses. Because the majority of mouthrinses are cosmetic, few must comply with this ADA requirement, although many do include a warning of some type.

The American Academy of Pediatrics Committee on Drugs took similar measures. The committee reviewed the literature on ethanol-related central nervous system effects in children and recommended to the FDA that the blood ethanol level after a single dose of any medication should not exceed 25 mg/100 mL.[9]

Ethanol is highly lipid-soluble and is rapidly absorbed from the gastrointestinal tract. Under ideal conditions, approximately 80–90% of ingested ethanol is absorbed within 30–60 min.[10] However, because ethanol is primarily absorbed in the small intestine, anything that delays gastric emptying will also delay absorption. The presence of food, gastrointestinal motility, ingestion of drugs, rates of ingestion, and individual variables all influence the rate of absorption and may delay absorption 2–6 hr. In the liver, ethanol is eliminated primarily by enzymatic oxygenation. A byproduct of this process, reduced nicotinamide adenine dinucleotide, impairs glucogenesis leading to hypoglycemia.[10]

Symptoms of ethanol intoxication in adults vary according to the concentration of alcohol in the blood. Blood-alcohol concentrations are expressed in terms of weight/volume (w/v) or volume/volume (v/v). For example, 100 mg ethanol per 100 mL blood may be expressed as w/v: 100 mg/100 mL, 100 mg/dL, 0.1g/100 mL, 100 mg %, or 0.1% and a v/v : 21.7 mmol/L, or 0.127%. The blood-ethanol concentration, in turn, depends on the quantity of ethanol ingested, the rate of ingestion, physiologic tolerance to ethanol, body weight, and stomach contents. At lower dosages, intoxication appears as mild euphoria, loquacity, decreased inhibitions, and some muscular uncoordi-nation. In many states, a blood-ethanol level of 100 mg/100mL (0.10% w/v) defines legal intoxication. As the amount of ingested ethanol increases, blood plasma levels also increase and the symptoms become more life-threatening. As the blood-ethanol concentration approaches 300 mg/100 mL, clinical signs of toxicity include the inability to stand or walk, vomiting, and impaired consciousness. Complete unconsciousness, coma, and depressed reflexes result from increasing blood-alcohol levels. At blood-ethanol levels more than 500 mg/100 mL, death from respiratory paralysis usually occurs.[10] While the generally accepted lethal dose of ethanol for adults ranges from 5–8 g/kg,[11] it is influenced by many factors such as age, the presence of other depressants, nutritional status, and physiologic tolerance level.

While children exhibit many of the same symptoms as adults, irritability is often an early symptom of acute ethanol toxicity. Other reported symptoms range from hypotonia, unconsciousness, unresponsiveness, and possibly convulsions. As the blood-ethanol levels increase, symptoms become more severe. Deep coma, hypotension, bradycardia, and death from respiratory arrest may occur.[12]

The generally accepted lethal dose of ethanol for children is 3 g/kg[11,12] but toxic reactions have been reported from doses as small as 0.6 g/kg.[2] Children are more likely than adults to suffer severe hypoglycemia from ethanol ingestion. Such ethanol-induced hypoglycemia is not dose-related and can lead to irreversible brain damage and death if untreated.[13] As in adults, ingestion of certain drugs such as diazepam may increase the absorption of alcohol.[14]

Our study reviews the literature on ethanol toxicity in children, analyzes reports of suspected overingestion of ethanol-containing mouthrinses by children younger than 6 years of age published by the AAPCC, and estimates incidence rates that adjust for the lack of national poison control data.

Methods

Poison Control Center Data

Our data consist of annual summaries of the American Association of Poison Control Centers (AAPCC) Data Collection System published each September in the *American Journal of Emergency Medicine* for 1989–1994.[17,18,19,20,21,22] Our analysis begins with 1989 data, the first year in which AAPCC data distinguished between exposures related to mouthrinses with and without

Table 2. Potentially toxic* and lethal† volumes of ingested ethanol at 5th, 50th and 95th percentiles of body weight (25)

Age (Years)	5th Percentile Weight (kg)	5th Percentile Ethanol (Fluid Oz.) Toxic	5th Percentile Ethanol (Fluid Oz.) Lethal	50th Percentile Weight (kg)	50th Percentile Ethanol (Oz.) Toxic	50th Percentile Ethanol (Oz.) Lethal	95th Percentile Weight (kg)	95th Percentile Ethanol (Oz.) Toxic	95th Percentile Ethanol (Oz.) Lethal
0.5	6.00	0.09	0.77	7.53	0.113	0.97	9.10	0.14	1.17
1.0	8.14	0.12	1.05	9.84	0.120	1.26	11.62	0.17	1.49
1.5	9.26	0.14	1.19	11.15	0.150	1.43	13.10	0.20	1.68
2.0	10.21	0.15	1.31	12.25	0.180	1.57	14.39	0.22	1.85
2.5	11.11	0.17	1.43	13.30	0.210	1.71	15.66	0.23	2.01
3.0	11.94	0.18	1.53	14.31	0.224	1.84	17.25	0.26	2.22
3.5	12.61	0.19	1.62	15.38	0.240	1.98	18.78	0.28	2.41
4.0	13.38	0.20	1.72	16.33	0.256	2.10	20.09	0.30	2.58
4.5	14.14	0.21	1.82	17.25	0.270	2.22	21.44	0.32	2.75
5.0	14.91	0.22	1.92	18.17	0.284	2.33	22.86	0.34	2.94
5.5	15.69	0.24	2.02	19.12	0.298	2.46	24.390	0.37	3.13
6.0	16.49	0.247	2.12	20.11	0.314	2.58	26.050	0.39	3.35

*Toxic dose: blood level of 50 mg/100 mL.

†Lethal dose: 3 g/kg (3.8 mL/kg), or 543 mg/100 mL blood level.

ethanol. The AAPCC consolidates reports from participating local poison control centers that serve approximately 70% of the US population.[22] Each local poison control center records the number of calls by individuals (teachers, parents, caregivers, dentists, physicians) asking for advice about dealing with a suspected overingestion of a potentially toxic substance. Next we adjusted the frequencies of reports for the percent of the population not served by participating poison control centers. For example, in 1993, 70% of the population was served by poison control centers, so the number of reported exposures (2,277) was divided by 0.70. If poison control centers covered 100% of the population, an estimated 3,253 exposures would be reported. We estimated the annual incidence rate by dividing the adjusted number of reports by the proportion of children younger than 6 years of age from the 1991 census (9%).[15] We explicitly assume that the incidence rates of acute toxic reactions to ethanol are the same in the proportion of the population covered by poison control centers and the remaining proportion not covered in any given year.

Estimating ethanol doses

We converted the ethanol concentration from volume percent to grams per ounce for the principal ethanol-containing mouthrinses sold over the counter in the United States. We assumed the threshold lethal level for a bolus dose of ethanol is 3 g/kg[11] and the potentially toxic peak blood ethanol is 50 mg/100 mL. Our toxic threshold of 50 mg/100 mL is twice the blood-ethanol concentration recommended by the American Academy of Pediatrics Committee on Drugs after a single dose of medication[9] and is more appropriate when dealing with accidental ingestion. This is approximately one-tenth the blood level associated with a lethal dose of 3g/kg. To determine the potentially lethal volume (PLV) for each product, we calculated the volume of each product that would have to be ingested to yield a dose of 3g/kg (assuming a bolus dose and rapid absorption) for children age 6 months to 6 years at 6-month intervals at the 5th, 50th, and 95th percentiles of a growth and development table.[16]

The potentially toxic amount of ethanol is the amount that is likely to produce mild symptomatology in a child. To calculate the potentially toxic volume (PTV), we estimated the peak blood ethanol level (C_p) using the formula: C_p=Dose/V_d x body weight. Dose (mg ethanol) is the product of the volume of mouth-rinse ingested, ethanol concentration of the mouthrinse, and the density of ethanol (.789) and, V_d, volume of distribution in plasma, is 0.7 L/kg for adults and 0.6 L/kg for children.[11]

Results

Children younger than 6 years of age comprised 52.5% of the 27 361 reported exposures attributed to mouthrinses with ethanol from 1989 to 1994.[17-22] Outcomes were reported for 1322 of the 2237 children younger than 6 years of age in 1992. Health care facilities treated 272 (12.2% of all children); one died, one had a life-threatening episode (major), 16 (0.7%) had pronounced signs and symptoms with treatment indicated (moderate), 325 (14.5%) had minor signs and symptoms that resolved rapidly, and 979 (74.1%) had no symptoms.[20]

Table 2 shows potentially lethal and toxic amounts of ethanol at the 5th, 50th, and 95th percentiles of a growth and development table. Fig 1 shows the lethal volume of representative over-the-counter ethanol-containing mouthrinses and pure ethanol assuming the lethal amount of ethanol is 3 g/kg. Less than 145 mL (5 oz.) of a high-ethanol product could be fatal to a 10-kg child. Fig 2 shows volumes of mouthrinse that could produce a peak blood-ethanol level of 50 mg/100 mL. Less than 11 mL (0.5 oz.) of a high-ethanol product and less than 66 mL (3 oz.) of the low-ethanol mouthrinse could be toxic to a 10-kg child.

Table 3 shows the total number of reports to the AAPCC related to mouthrinses (column A). The US population for each year is in column B and the proportion of the population covered by the AAPCC each year is in column C. Column D adjusts the number of reports (column A) for the proportion of the population covered by the AAPCC. Column E shows the number of children

TABLE 3. REPORTS TO AMERICAN ASSOCIATION OF POISON CONTROL CENTERS RELATED TO ETHANOL-CONTAINING MOUTHRINSES: CHILDREN, YOUNGER THAN SIX YEARS OF AGE

Year	A Total # of Reports	B U.S. Population (million)	C Population Served by AAPCC (%)	D Adjusted # of Reports (A÷C)	E Population <6 Years (million)	F Adjusted # of Reports: Children <6 Years (C÷ .09)	G Incidence per 100,000 Children <6 ([F/E] x 100,000)
1989	2,494	248.2	73.0	3115	22.3	34,611	155.2
1990	2,317	249.6	76.8	3,017	22.5	33,522	149.0
1991	2,082	250.9	80.4	2,589	22.6	28,767	127.3
1992	2,245	252.2	78.0	2,878	22.7	31,978	140.9
1993	2,277	257.9	70.0	3,253	23.2	36,144	155.8
1994	2,937	260.3	83.0	3,539	23.4	39,322	168.0
Mean				3,115	22.8		149.4

*Approximately 9% of the population is younger than six years of age.

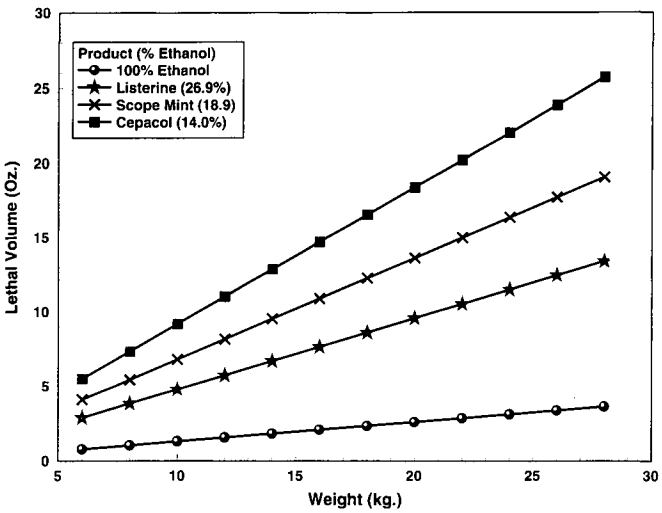

Figure 1. Ingested volume of ethanol and ethanol-containing mouthrinse that will produce a dose of 3 g/kg (potentially lethal dose), by body weight.

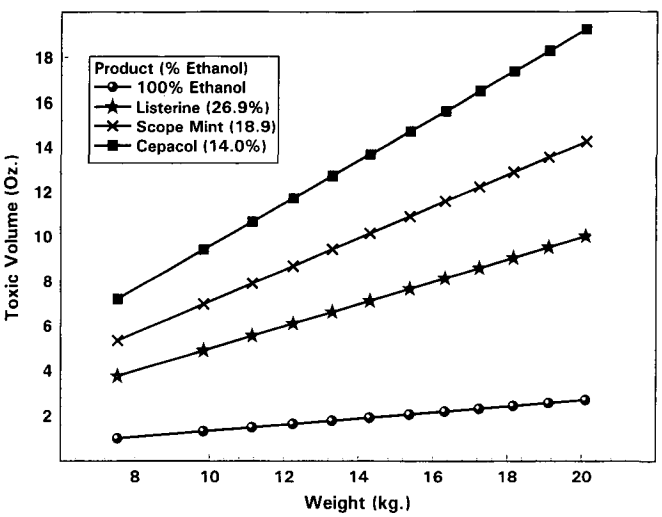

Figure 2. Ingested volume of ethanol and ethanol-containing mouthrinse that will produce a peak blood ethanol level of 50 mg/100 mL (potentially toxic dose), by body weight.

younger than 6 years of age. Column F adjusts the number of reports in the overall U.S. population related to ethanol-containing mouthrinses (column D) for the estimated population of children younger than the age of 6 (Column E). Column G shows the estimated incidence of poison exposures in a population of children younger than 6. In 1994, the estimated incidence of reported exposures was 168 per 100 000 children younger than the age of 6.

Discussion

There are many reports in the literature of children requiring treatment for acute ethanol toxicity following mouthrinse ingestion and several reports of fatalities.[5,7,12-14] However, except for those children requiring emergency treatment, it is difficult to determine the true incidence of mouthrinse-related ethanol toxicity. We believe mild-to-moderate cases of ethanol toxicity are under-reported for several reasons. Early symptoms of ethanol toxicity in children are not necessarily similar to those in adults. Parents and caregivers may not suspect ethanol toxicity if a child is irritable and lethargic. Health care providers, without a reported ingestion of mouthrinse, may not include ethanol toxicity in their differential diagnosis. Parents and caregivers may ignore mild-to-moderate symptoms or be unaware of the potential for toxicity and not seek the advice of the local poison control center or a health care provider. Finally, parents and caregivers might not be aware of the existence of the local poison control center or simply not report a suspected overingestion.

While we used the generally accepted lethal dose of ethanol for children, 3 g/kg, life-threatening reactions can occur at lower dosages. Hypoglycemia, common in children after ingestion of ethanol, is not dose-related and can cause death at levels below 3 g/kg, particularly in children more susceptible to hypoglycemia, or in children who are malnourished or in a fasting state.[13]

For purposes of analysis, we assumed 100% of ingested alcohol was absorbed in a short period of time. Many factors influence absorption and in the presence of food, for example, absorption would be delayed and the potentially toxic dose would be higher.

Besides the risk of acute ethanol toxicity, ethanol-containing mouthrinses have a potential for abuse in older children. A teenager may turn to mouthrinse as a source of alcohol, as it can easily be purchased by the underage drinker. For example, the largest bottle of Listerine,® 58 oz., contains 15.6 oz. of ethanol, four times more than a bottle of wine and 20% more than a quart of hard liquor. Denaturants, added to discourage ingestion of ethanol-containing products, are not likely to deter abuse because they are only mildly toxic and few consumers know that they are present in mouthrinse.

Acute ethanol toxicity is an area of concern for children younger than 6 years of age. While there are many variables which affect the toxic dose, we believe that the ethanol content of ingested mouthrinse can cause mild-to-moderate symptoms of ethanol toxicity in children and has the potential to be life-threatening. We recommend several actions to decrease the likelihood of acute ethanol toxicity in children.

1. Physicians, dentists, and other health care providers should inform parents of the dangers associated with accidental ingestion of mouthrinse and encourage them to keep mouthrinse out of the reach of children.
2. The FDA should require manufacturers to package larger containers of ethanol-containing mouthrinses with child-resistant caps or offer at least one package with a child-resistant cap and warning about the danger of accidental ingestion. The warning should include instructions such as those suggested by the ADA: "WARNING: KEEP OUT OF REACH OF CHILDREN. This product contains alcohol. Do not swallow. Use only as directed."[8]
3. The FDA should mandate readily visible warning labels that include the dangers and symptoms of accidental ingestion, along with emergency instructions.
4. While the ADA requires child-resistant caps and labeling on mouthrinses seeking acceptance as therapeutic agents, it does not have an acceptance program for those considered cosmetic. The ADA should consider requiring cosmetic mouthrinses to use child-resistant packaging as a condition for advertising in its publications and annual meetings.
5. The ADA and AAP should work with the FDA to draft requirements for child-resistant caps and labeling.

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