



Motherisk Update

Exposure to alcohol-containing medications during pregnancy

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ABSTRACT

QUESTION A pregnant patient consulted her physician after discovering that a diphenhydramine preparation (Benadryl elixir) she used for allergy symptoms during the first trimester of her pregnancy contained 15% alcohol. Should she be concerned about fetal alcohol spectrum disorder in her baby?

ANSWER Most ethanol-containing medical preparations are safe during pregnancy. Adult doses of some elixirs with high ethanol concentrations might produce blood levels similar to those achieved by drinking 1 alcoholic beverage. Caution is advisable when prescribing ethanol-containing elixirs to pregnant women, as is informing them about the alcohol content.

RÉSUMÉ

QUESTION Une patiente enceinte a consulté son médecin après avoir découvert qu'une préparation de diphenhydramine (l'éllixir Bénadryl), qu'elle prenait durant le premier trimestre de sa grossesse pour des symptômes d'allergie, contenait 15% d'alcool. Devrait-elle s'inquiéter de la possibilité du syndrome d'intoxication fœtale à l'alcool chez son bébé?

RÉPONSE La plupart des préparations médicales contenant de l'éthanol sont sécuritaires durant la grossesse. Une dose pour adulte de certains élixirs à forte concentration d'éthanol pourrait produire des taux d'alcool dans le sang semblables à ceux produits après avoir bu 1 consommation d'alcool. Il est conseillé d'être prudents lorsqu'on prescrit des élixirs contenant de l'éthanol aux femmes enceintes et de bien les renseigner sur le contenu en alcool.

Ethanol is used widely in pharmaceutical formulations and cosmetics as an antimicrobial preservative or as a solvent. Some common ethanol-containing medications are listed in **Table 1**. More than 130 preparations containing ethanol are listed in the 2006 *Canadian Compendium of Pharmaceuticals and Specialties*.¹

If the above patient used Benadryl elixir containing 15% alcohol at an adult dose of 50mg 4 times daily (80mL of elixir daily), she would have ingested about 10g of ethanol daily, equivalent to the amount of alcohol in a glass of wine.

Ethanol is a potent animal and human teratogen. A dose-dependent risk of malformation has been demonstrated repeatedly in animal experiments.²⁻⁴ Epidemiologic studies in humans have provided strong evidence for dose-dependent toxicity, with babies of heavy-drinking pregnant women having a higher risk of fetal alcohol spectrum disorder than those of moderate drinkers.⁵⁻⁷

A threshold level of exposure for fetal toxicity (ie, a level below which there is no toxicity) of ethanol has not been identified so far.^{8,9} Some authors have suggested, based on animal studies, that this threshold level could be exceeded with very low levels of exposure.⁹

Data obtained from animal studies suggest that serum ethanol concentrations are the best risk marker for fetal toxicity. On the other hand, the toxicologic definition of a threshold level of exposure in which no adverse effect is observed must be based on studies evaluating exposure of the most sensitive indicator of toxicity, the brain. Direct measurements of alcohol concentrations in the human fetal brain and correlation with neurotoxicity are not feasible, which precludes a precise estimation of dose-related risk.⁹

Most human data come from studies evaluating fetal ethanol exposure among alcohol-drinking pregnant women. Some experts consider the developmental outcomes observed to be irrelevant to the low blood alcohol concentrations resulting from

Table 1. Common ethanol-containing medications

PREPARATION	ACTIVE INGREDIENTS	ALCOHOL CONCENTRATION (%)
Allernix elixir	Diphenhydramine	10-20
Balminil Night-Time	Ammonium chloride, dextromethorphan, diphenhydramine	1-10
Benadryl elixir	Diphenhydramine	10-20
Benylin DM-E syrup	Dextromethorphan, guaifenesin	1-10
Choledyl elixir	Oxtriphylline	20
Fermentol liquid	Pepsin	10-20
Gravol injection	Dimenhydrinate	20
PMS-Phenobarbital elixir	Phenobarbital	20
Robitussin Cough & Cold syrup	Guaifenesin	1-10
Senokot syrup	Senna concentrate	1-10
Septra injection	Trimethoprim, sulfamethoxazole	20
Tylenol with codeine elixir	Codeine, acetaminophen	1-10
Zantac oral solution	Ranitidine	7.5

Data from the 2006 *Compendium of Pharmaceuticals and Specialties*.¹

physicians' recommending use of consumer products containing ethanol.^{10,11} Small quantities of ethanol in the blood are metabolized rapidly, unlike the medium-to-large amounts ingested in beverages, which saturate alcohol-metabolizing enzymes and lead to disproportionately high blood alcohol concentrations.¹²⁻¹⁴

Experiments in primates have established that the threshold level of exposure for ethanol blood concentration is 400 mg/L,¹⁰ a level higher than most ethanol-containing medications would produce. Elixir formulations taken in adult doses would lead to exposures similar to those following 1 average alcoholic drink (9 to 14 g of ethanol), which produces serum levels around 150 mg/L.¹⁰ Most of these medications would be used for only short periods and would be divided into several (eg, 3 or 4) small doses throughout the day, unlike most alcohol exposures among alcoholic beverage drinkers enrolled in epidemiologic studies.

Yet the prospect of pregnant patients' unknowingly consuming alcohol at a dose equivalent to 1 drink a day is troubling.

While most medical, industrial, and domestic uses of ethanol-containing products might be safe during pregnancy, women should still be made aware that they contain alcohol. Adult doses of some elixirs with high ethanol concentrations might produce blood alcohol levels similar to those observed after 1 alcoholic drink.¹⁰ It is important to use caution when prescribing ethanol-containing elixirs to pregnant women.

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MOTHE RISK

Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. **Drs Garcia-Bournissen, Finkelstein, and Rezvani** are members and **Dr Koren** is Director of the Motherisk Program. **Dr Koren** is supported by the Research Leadership for Better Pharmacotherapy during Pregnancy and Lactation and, in part, by a grant from the Canadian Institutes of Health Research. He holds the Ivey Chair in Molecular Toxicology at the University of Western Ontario in London. **Dr Finkelstein** is supported by a research fellowship and **Dr Garcia-Bournissen** is supported by the Clinician Scientist Training Program, both from the Hospital for Sick Children.

Do you have questions about the effects of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the **Motherisk Program** by fax at 416 813-7562; they will be addressed in future **Motherisk Updates**.

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