

Alcohol Content in Pediatric Liquid Formulations

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Purpose

- Ethanol is a solvent and preservative in liquid formulations of drugs.
- The American Academy of Pediatrics (AAP) suggests blood ethanol concentration (BEC) \leq 25 mg/100 mL (0.025%) following a single dose of an alcohol containing medication.
- The amount of alcohol containing medication that is considered toxic to a pediatric patient is still unclear.
- Toxic effects reported with acute ingestion of alcohol include hypoglycemia and CNS effects.

Objectives

- To examine alcohol content of medications commonly used in hospitalized pediatric patients
- To analyze current practices that institutions have implemented to minimize administration of alcohol containing medications to pediatric patients

Methods

- A list of formulary oral liquid medications at the University of Maryland Medical Center (UMMC) was obtained.
- Alcohol content was determined with the medication package inserts.
- The ten most commonly used medications in the neonatal population were identified based on clinical judgment.
- 3.5 kg was used for weight-based dosing calculations.
- “Ethanol per dose” was calculated from the dose of medication (mL) multiplied by alcohol concentration (% v/v).
- Calculation for the volume of each drug to produce a BEC of 25 mg/100 mL was adapted from the literature (Pruitt et al., 1984).
- An eight question prospective survey of convenience was sent via email to a pediatric listserv to identify institutional practices in place to minimize alcohol content in oral liquid medications.

Table 1. 31 Alcohol Containing Medications

Drug	mg/mL	Alcohol (v/v)
APAP-codeine soln	120-12 mg/5mL	7%
Chlorothiazide susp	250 mg/5mL	0.50%
Cyclosporine soln	100 mg/mL	12.5%
Cyproheptadine soln	1mg/mL	5%
Diazoxide susp	50 mg/mL	7.25%
Digoxin soln	50 mcg/mL	10%
Diphenhydramine elixir	12.5 mg/5mL	14%
Ferrous sulfate syrup	300 mg/5mL	0.20%
Fluoxetine soln	20 mg/5mL	0.23%
Fluphenazine elixir	2.5 mg/5mL	14%
Griseofulvin susp	125 mg/5mL	0.20%
Indomethacin susp	25 mg/5mL	1%
Lamivudine soln	10 mg/mL	5%
Lithium citrate soln	300 mg/5mL	0.30%
Loperamide soln	1 mg/5mL	0.50%
Megestrol susp	40 mg/mL	0.34%
Methadone soln	5 mg/5mL	8%
Nystatin susp	100,000 U/mL	<1%
Phenobarbital soln	20 mg/5mL	13.5%
Phenytoin susp	125 mg/5mL	0.35%
Prednisolone soln	15 mg/5mL	1.80%
Prednisone soln	5 mg/5mL	5%
Propranolol soln	20 mg/5mL	0.60%
Pyridostigmine soln	60 mg/5mL	5%
Ritonavir soln	80 mg/mL	43%
Sertraline conc. soln	20 mg/5mL	12%
Sirolimus soln	1 mg/mL	1.5-2.5%
Sodium polystyrene susp	15 mg/60mL	0.20%
SMZ-TMP susp	200-40 mg/5mL	0.04%
Theophylline anhydrous elixir	80 mg/15mL	20%
Valproate sodium soln	250 mg/5mL	<0.05%

Top ten medications are bolded
 Abbreviations: APAP, acetaminophen. SMZ-TMP, sulfamethoxazole-trimethoprim.

Table 2. Volume of alcohol per dose and volume of drug to produce BEC=25mg/100 mL for the top 10 medications

Drug	mg/mL	Alcohol (% v/v)	Usual Dose	Usual dose ^a in mL for 3.5 kg neonates	Ethanol per dose (mL)	Volume of drug to produce BEC=25mg/100mL ^b (mL)
Chlorothiazide susp	250 mg/5mL	0.50%	10 - 20 mg/kg/dose q12h	0.7-1.4	0.0035 - 0.007	222.25
Digoxin soln	50 mcg/mL	10%	5 mcg/kg/dose q12h	0.35	0.035	1667.75 - 22225
Ferrous sulfate syrup	75 mg/mL	0.20%	3 mg/kg/day in 1 to 2 divided doses	0.07 - 0.14	0.00014 - 0.00028	22.23
Methadone soln	5 mg/5mL	8%	0.01 - 0.1 mg/kg	0.035 - 0.35	0.0028 - 0.028	98.62
Nystatin susp	100,000 U/mL	<1%	1 - 2 mL q6h	1 - 2	<0.01 - 0.02	22.23
Phenobarbital soln	20 mg/5mL	13.50%	1 - 4 mg/kg/dose q12h	0.88 - 3.5	0.12 - 0.47	5.83 - 14.04
Phenytoin susp	125 mg/5mL	0.35%	4 - 8 mg/kg/day in 2 divided doses	0.28-0.56	0.00098 - 0.00196	254 - 285.75
Prednisolone soln	15 mg/5mL	1.80%	2 mg/kg/day in 1 to 2 divided doses	1.17	0.021	13.58-43.22
Propranolol soln	20 mg/5mL	0.60%	0.25 - 1 mg/kg/dose q6h	0.22 - 3.06	0.0013 - 0.018	740.83
SMZ-TMP susp	200-40 mg/5mL	0.04%	TMP: 6 -12 mg/kg/day divided q12h	1.31 - 2.63	0.00052- 0.0011	4167.19

^aDose of each medication is based on Neofax® or Neonatal Lexi-Drugs

^bCp (BEC, 25 mg/100 mL) x Vd (L/kg) = Dose of alcohol

For example, Vd of phenobarbital is 0.71 L/kg. For 3.5 kg infant, Dose of ethanol = 621.25 mg. Using specific gravity=0.789, 621.25 mg = 0.787 mL; 0.787 mL x 13.5% of alcohol =5.83 mL.

Figure 1. Alcohol content in the 31 liquid medications

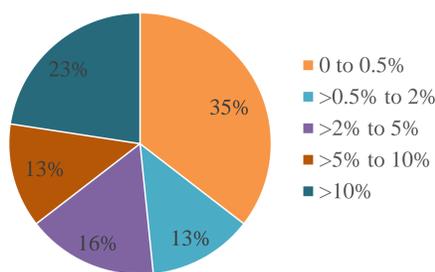
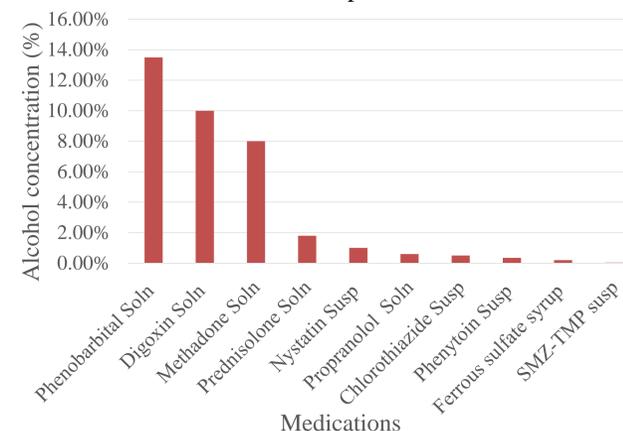


Figure 2. Top 10 commonly used medications in neonatal patients



Results

- The alcohol content of 31 oral liquid medications ranged from <0.05% to 43%.
- About 1/3 (n=11) of medications contained \leq 0.5% of alcohol.
- About 1/4 (n =7) of medications contained >10% of alcohol.
- Among the ten most commonly used medications, the median alcohol concentration was 1.2% (range 0.04% to 13.5%).
- Survey results included nine respondents.
- Five institutions (56%) have converted some of their alcohol containing medications (i.e. phenobarbital, dexamethasone) to non-alcohol containing medications.
- If specified, the acceptable alcohol content cut-off for neonates varied by respondent and ranged from 0% to 10%.

Conclusions

- The volume of drug that would need to be consumed to produce a BEC of 25 mg/100 mL was found to be higher than the usual dose given to full-term neonates weighing 3.5 kg.
- Alcohol containing medication should be administered cautiously to neonates and children due to lack of data regarding effects of short- and long-term exposure to alcohol.
- More information is needed to determine practice standards for alcohol containing medications used in pediatric patients.

Disclosures

- None