Osmolality of Medications Administered in the Neonatal Intensive Care Unit

The most recent recommendations regarding enteral feeding solutions for newborns state that they should have a maximum osmolality of 450 mOsm/kg (400 mOsm/L) and that the use of hyperosmolar feeding solutions may be a factor in the development of necrotizing enterocolitis.[1,2] These recommendations are based on historical consensus,[3] and there is little other evidence to guide this practice. For preterm newborns at risk of necrotizing enterocolitis, or infants at risk of osmotic diarrhea because of gastrointestinal abnormalities, enteral medications are often diluted in small amounts of breast milk or formula (usual osmolality about 300 mOsm/kg), both for ease of administration and to reduce the osmolar challenge of the medications. Unfortunately, for many compounded and commercially available oral liquid medications, published osmolality values are not available to clinicians to aid in assessing the osmolar load and the risks associated with enteral administration. The purpose of this study was to measure the osmolality of several proprietary and compounded medications commonly used in the neonatal intensive care unit.

We performed an analytically controlled laboratory study to measure the osmolality of 23 medications, specifically 8 proprietary and 15 compounded medications (Table 1).[4–11] Osmolality was measured with a Micro OSMETTE II model 6002 osmometer (Precision Systems, Natick, Massachusetts), calibrated with aqueous normal sodium chloride in triplicate. The maximum measurable osmolality was 2000 mOsm/kg; medications with higher osmolality were diluted 1:1 or 1:2 with distilled water before measurement, and the resulting osmolality was multiplied by 2 (for 1:1 dilutions) or 3 (for 1:2 dilutions). Osmolality was measured in 2 aliquots of each medication (from the same lot). We planned to measure a third time if 2 osmolality measurements differed by more than 10 mOsm/kg, but this did not occur.

The measured osmolality of the proprietary medications ranged from 624 mOsm/kg to 7480 mOsm/kg, and that of the compounded medications ranged from 25 mOsm/kg to 3385 mOsm/kg (Table 1). Only 3 of the 23 medications had osmolality below the recommended maximum 450 mOsm/kg:

TABLE 1. Osmolality of Commercially Available and Compounded Medications for Neonates

Drug Name and Concentration	Manufacturer	Osmolality (mOsm/kg)
Commercially available		
Digoxin (Toloxin), 0.05 mg/mL	Pendopharm	3670
Fluconazole, 10 mg/mL	Pfizer Canada	2020
Ibuprofen liquid (infant's Motrin, dye-free, berry flavour), 40 mg/mL	McNeil Consumer Healthcare	1775
Pediavit (750 IU vitamin A, 30 mg vitamin C, and 400 units vitamin D per millilitre)	Europharm International Canada	7450
Ranitidine, 15 mg/mL	Apotex Inc	624
Sodium phosphate (4.8 mmol sodium and 4.2 mmol phosphate per millilitre)	Odan Laboratories	7480
Vitamin E (Aquasol E), 50 units/mL	Columbia Laboratories Canada	3563
Zidovudine, 10 mg/mL	ViiV Healthcare	3455
Compounded		
Atenolol, 2 mg/mL	Nahata et al.[4]	3385
Caffeine, 10 mg/mL	Eisenberg and Kang[5]	82
Dexamethasone, 1 mg/mL	Nahata et al.[4]	353
Diazoxide, 10 mg/mL*	Jackson[6]	1695
Domperidone, 1 mg/mL	Ensom et al.[7]	1850
Hydrocortisone, 1 mg/mL	The Hospital for Sick Children[8]	1850
Levetiracetam, 50 mg/mL	Ensom et al.[9]	1855
Phytonadione, 1 mg/mL†	Compounded from injection†	25
Sildenafil, 2.5 mg/mL	Allen[10]	1690
Spironolactone-hydrochlorothiazide, 5 mg/mL each	Allen and Erickson[11]	1810
Trimethoprim, 10 mg/mL	The Hospital for Sick Children[8]	3000
Ursodiol, 50 mg/mL	The Hospital for Sick Children[8]	1530

*Made with 100-mg capsules and Ora-Blend vehicle (Medisca).

†Made by dilution of 10 mg/mL injection with sterile water, as used for in-house stability testing by the original manufacturer, Sabex, in 1993.

phytonadione and dexamethasone (both of which were injectable products that are given enterally in our setting), as well as caffeine (which is specifically compounded for preterm neonates). Compounds made from injection solutions or formulated specifically for neonates may have lower osmolalities than those made with sweetened and preserved diluents; however, this supposition would need confirmation through further osmolality measurements of multiple compounded oral liquid medications.

Our results demonstrate the lack of appropriate neonatal medication formulations available from manufacturers and a lack of appropriate compounding recipes for neonates.

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