Increased Osmolality of Milk Feeds with Medications – Implications for the Premature Infant

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Introduction:

In preterm neonates, various additives are routinely added to expressed breast milk and preterm formula for therapeutic or nutritional benefit. The additives have the potential to increase osmolality of milk. Feeding the preterm infants with hyperosmolar feeds is thought to be associated with necrotising enterocolitis (NEC).[1-3] The concern of NEC led to the recommendations that enteral feeds for neonates should not have an osmolality above 450 mOsmol/kg and any additive increasing the osmolality of feeds further could be counterproductive.[4]

Aim:

1. **To determine the osmolality of 14 commonly used medications when administered with milk feeds.**
2. **To determine the optimal dilution of these medications, in 4 different diluents, to keep the osmolality within the safety threshold of ≤ 450 mOsmol/kg**

Methodology:

Osmolality of 14 neonatal medications, diluted using four different diluents (water, breast milk (EBM), breast milk with human milk fortifier (EBMF) and preterm formula (PTF)), were measured utilizing the Advanced TM Micro-osmometer Model 3300 based on freezing point depression. Highest osmolality measurable by this method is 2000 mOsmol/kg. Three separate readings within ± 2 mOsmol/kg were obtained for consistent results. The medications include caffeine citrate, multivitamin, iron hydroxide polymaltose complex, domperidone, omeperazole, folic acid, potassium phosphate, sodium phosphate, calcium glubionate, hydrochlorothiazide, Ibuprofen, phenobarbitone, 20% sodium chloride, and ursodeoxycholic acid. Dose-effect curves were plotted for each medication in each of the four diluents. The volume of each diluent that must be added to each medication to keep the osmolality ≤450mOsm/kg was then calculated. Data analysis was done using SPSS.

Results:

Among the diluents, osmolality of EBM, EBMF and PTF were observed to be 299 mOsmol/kg, 401 mOsmol/kg and 317mOsm/kg respectively. We could only determine the neat osmolality of 5 medications (Table 1). We postulate that the rest of the medications have osmolalities greater than 2000mOsmol/kg. Phenobarbitone and folic acid had osmolality lower than the diluents. For the remaining 12 medications, an indirect curvilinear relationship between increasing dilution and osmolality was observed and the optimal dilution to keep the drug/diluents osmolality was determined. Of the 12 medications iron and sodium phosphate required a lower dilution of 1:2 to 1:5 when EBM was used as diluent and sodium chloride needed a dilution of 1:50. When PTF was used as diluent all these 12 medications required minor increase in dilution where as with EBMF as diluent these drugs required 5 to 6 times more dilution to keep osmolality within the safe range. This was true especially for drugs like caffeine, multivitamin, iron and sodium/potassium phosphates, which are the most often used medications in the first 28 days of life in premies. Osmolality of the most often used 8 medications with the four diluents are shown in figures 1-4.

Conclusions:

It is imperative to know the osmolality of the feeds when additives and medications are added to the milk. Of all medications, only phenobarbitone and folic acid had osmolality lower than the diluents. Rest of the medications should not be given neat to premies. EBM alone was observed as the safest diluent, needing only lower dilutions whereas EBMF required very high dilutions which are impracticable when feeding extremely low birth weight babies. PTF also is a safer diluent and needed only minor increase in dilutions when compared with EBM. Ibuprofen, used for closure of ductus arteriosus, is known to cause gut perforation. When given orally it must be diluted adequately to ensure the osmolality is within the safe range. The clustered bar charts indicate the appropriate amount of diluent required to avoid hyperosmolality for 8 of the most often used medications. These observations provide information for optimizing and standardizing the dilution for medications used in neonatal feeding practice and thereby improves safety and minimizes the risk of NEC in preterm infants.

Table 1.

Medication	Neat Osmolality (mOsmol/kg)
Folic acid	2
Phenobarbitone	49
Iron Hydroxide	714
Potassium phosphate	1470
Omeperazole	1606

Figure 1.

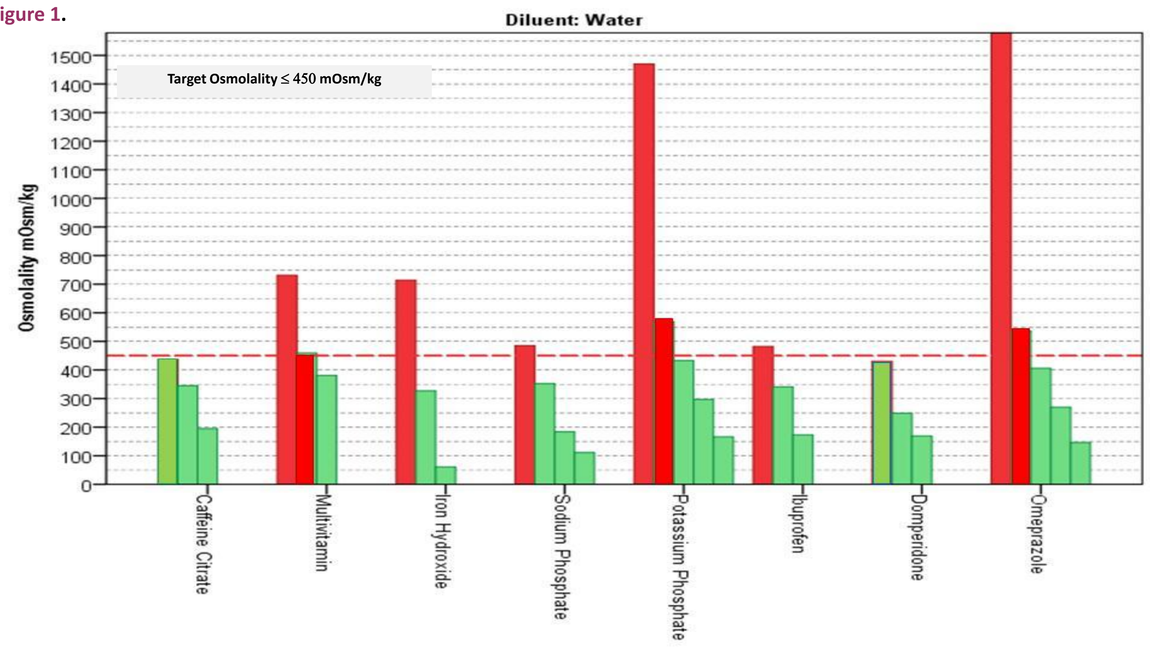


Figure 2.

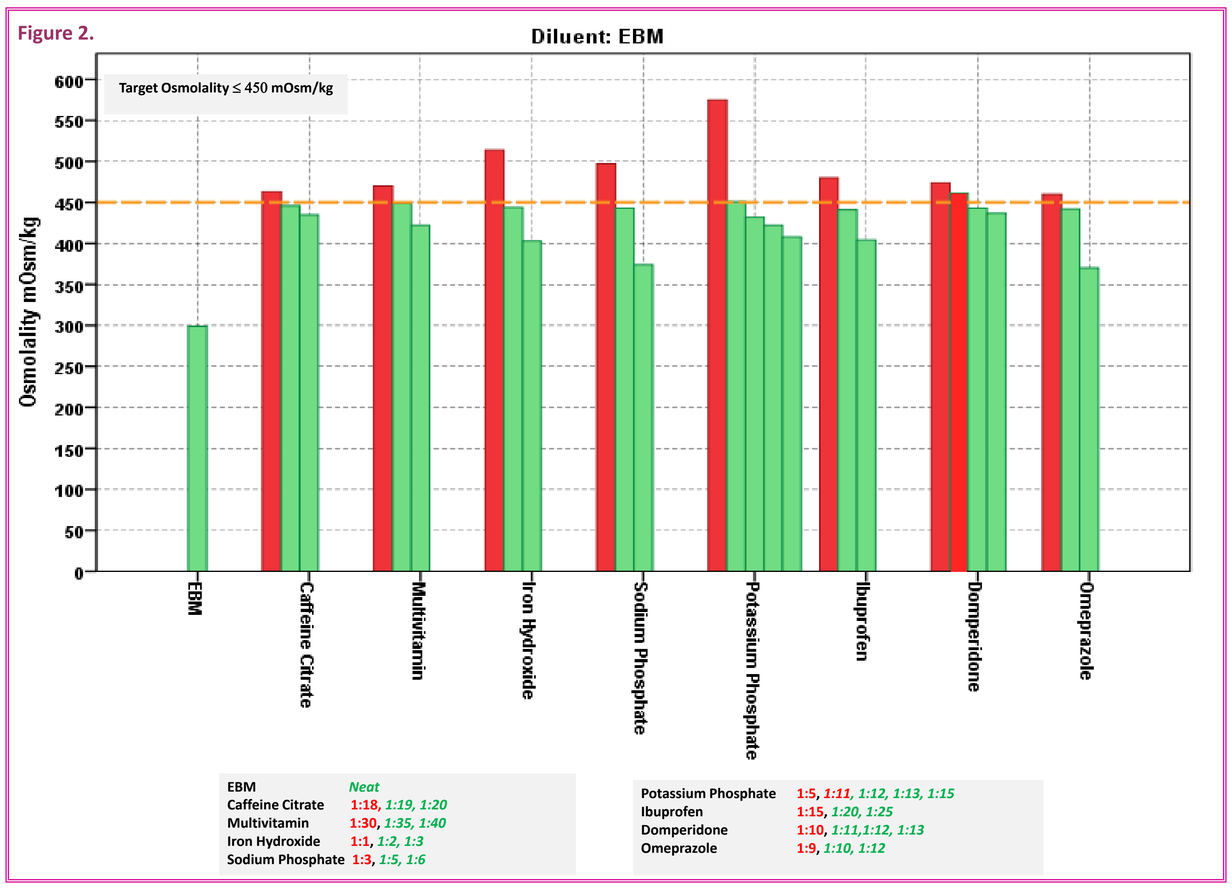


Figure 3.

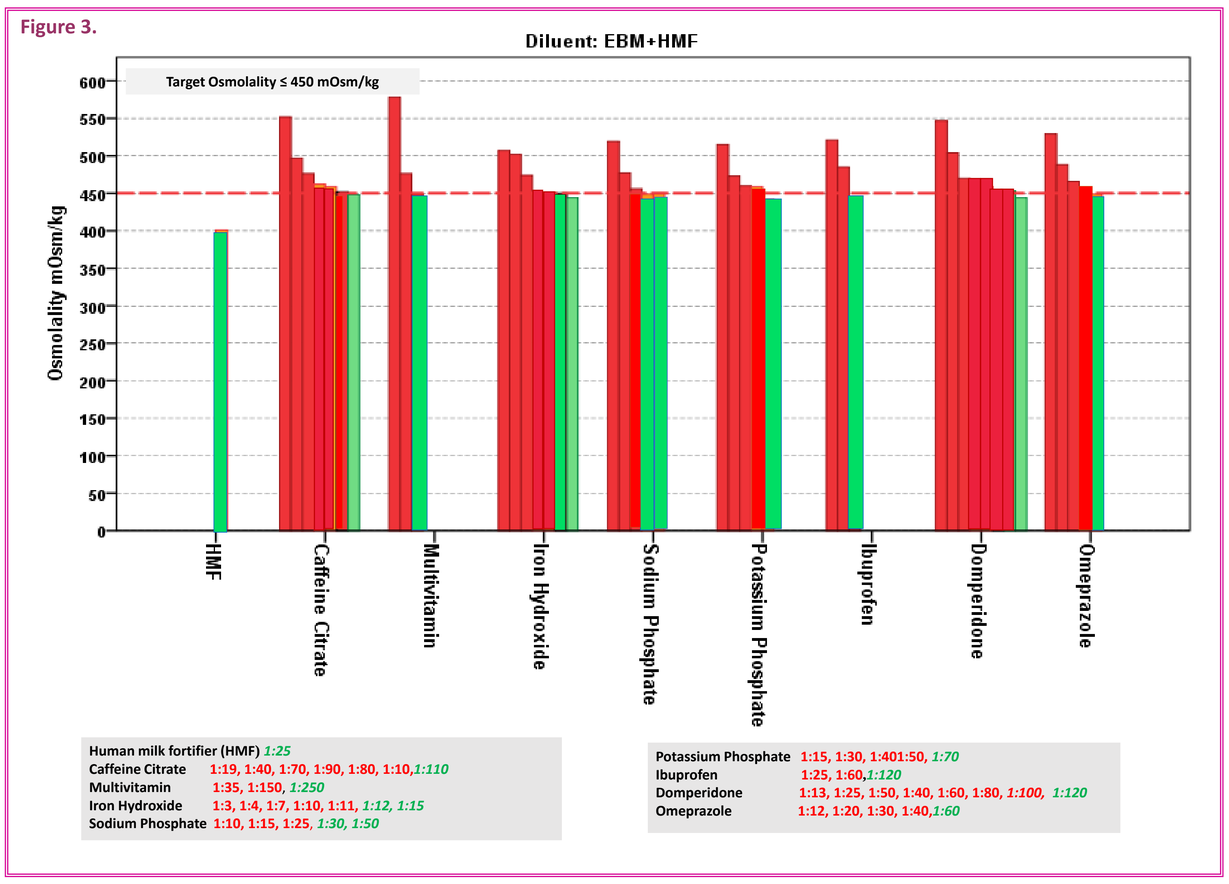
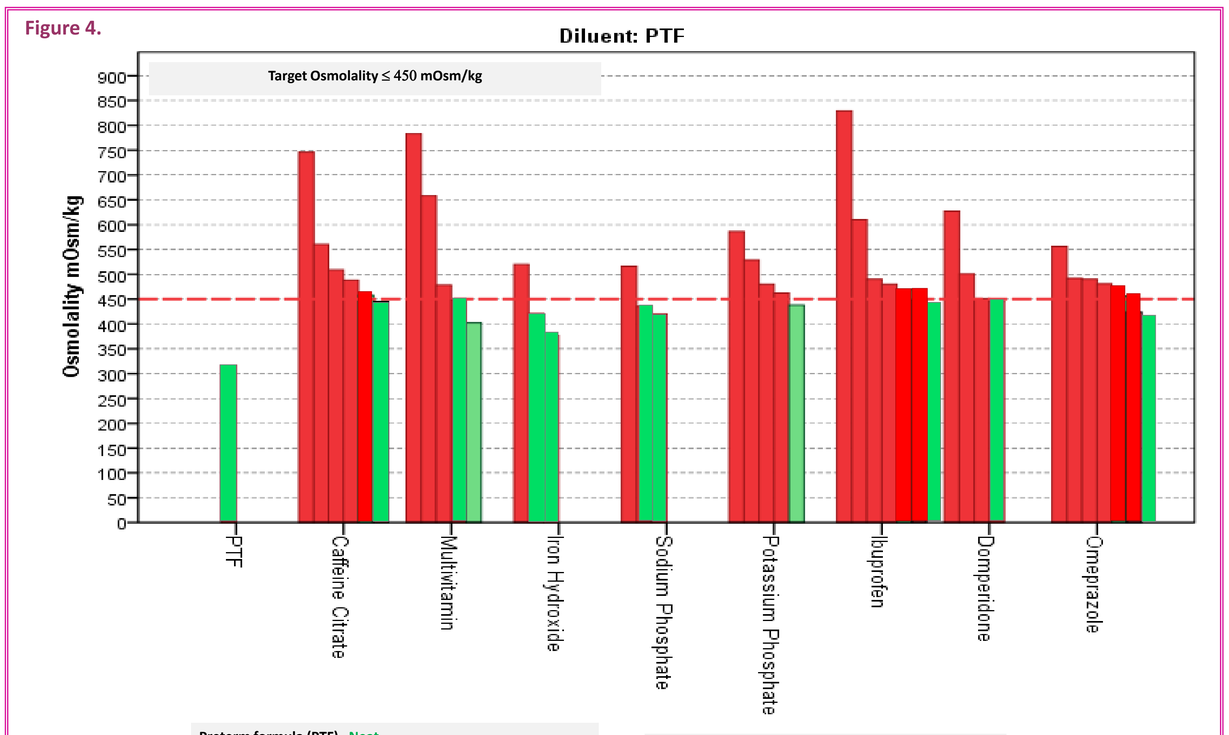


Figure 4.



Legend:
Figure 1 – 4 Clustered bar chart showing medications in X-axis and osmolality in Y-axis **dilution in which osmolality ≤ 450** **dilution in which osmolality > 450**

Reference:

1. Book LS, Herbst JJ, Atherton ST, et al. Necrotizing enterocolitis in low birth weight infants fed an elemental formula. J Pediatr 1975; 87:602–5.
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4. Pearson F, Johnson MJ, Leaf AA. Milk osmolality: does it matter? Arch Dis Child Fetal Neonatal Ed. 2013; 98(2):F166-9.

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