conclusion must be tempered by several methodological concerns. Multiple interventions were applied during the study, and the exact timing and interaction of these interventions are unclear. Some discussion of the background and expertise of the pharmacists participating in the intervention would have been valuable as neonatal expertise and experience are almost certainly important. Unfortunately, the authors expressed the major outcome measure as the absolute number of medication errors, rather than error rates per number of patient days or per number of orders written. We hope that these important denominators remained relatively stable during the study period. In addition, it is unclear to what extent the ascertainment methods used, which relied on voluntary reporting by clinicians, were accurate and unbiased. Voluntary reporting, although valuable on many levels, cannot be relied on to provide accurate incidence data. Finally, the authors provide no statistical measures of differences between the periods before and after intervention.

Implementation of CPOE in the NICU presents special challenges. Systems designed for use in older patients may not adequately address the unique aspects of NICU medication ordering. Unfortunately, development of systems appropriate for use in paediatric and neonatal patients has lagged. Industry must be challenged to provide software applications that are appropriate for NICUs. CPOE almost certainly will have to be integrated with other hospital clinical information systems to have maximum impact on error prevention. Adequate, built in decision support, using population specific knowledge bases, is essential for detecting drug interactions, out of range doses, and other prescribing problems. The LeapFrog Group,[15] a consortium of Fortune 500 companies, has urged hospitals in the United States to adopt CPOE. Given Leapfrog's leverage and influence, recognition of the unique needs of NICUs would be welcome.

Where CPOE is not available, attention to good prescribing practices and accurate communication are essential.[5 16] This is true not only for written orders, but verbal ones as well. The process for verbal orders should include a system of ''read back'' verification to ensure accuracy. Lacking CPOE, clinicians (doctors, nurses, and pharmacists) must implement unambiguous guidelines on appropriate dosing for NICU patients. Good communication and teamwork requires a blame free environment and a culture that places a high value on reporting and discussing patient safety concerns and systems problems.

Finally, NICU clinicians must remain aware of the advances in patient safety made in other industries. Crew Resource Management, which has been pivotal to improving the safety record of the aviation industry, may be particularly useful in helping teams communicate effectively and safely.[17] Translation of technologies from the retail sector, such as bar coding and radio frequency identification, may be helpful in preventing patient misidentification. When feasible, engineering approaches using affordances and reminders, forcing functions, and constraints may help staff to avoid errors due to human factors. Of course, these novel approaches to creating a safe care environment will have to be tailored to the very special and challenging environment of the NICU.

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Neonatal nutrition

Taurine in neonatal nutrition – revisited

W C Heird

Recommendations for no minimal taurine content of infant formulas should be reconsidered.

Taurine (2-aminoethanesulphonic acid) was isolated from ox (*Bos taurus*) bile in 1827[1] but, until the mid to late 1970s, it was thought to be merely a byproduct of sulphur amino acid metabolism. In 1975, it was noted that taurine deficiency in cats was associated with retinal degeneration, which was reversed by taurine supplementation.[2] This observation coupled with the high concentration of taurine in the developing brain[3] and mature retina[4] raised suspicion that taurine may play an important role in brain development. This was supported by observations that brain taurine concentration of several species decreased during the weaning period[3] and that taurine was the primary free amino acid in the milk of most mammals, including humans.[5] Moreover, labelled taurine injected intraperitoneally into lactating rats was found in the milk

of the dam as well as the brain of the suckling pups,[6] suggesting that adequate intake of taurine was important for maintaining brain taurine content.

Shortly after the observation that taurine deficiency in cats resulted in retinal degeneration, evidence that taurine may be a conditionally essential nutrient for the human infant began appearing. The first such evidence came from a study in Scandinavia showing that plasma and urinary taurine concentrations of formula fed infants were lower than those of infants fed human milk,[7] whereas the plasma and urinary concentrations of all other amino acids were higher in formula fed infants.[8 9] This was attributed to the presence of taurine in human milk but not formulas. Subsequently, it was shown that prolonged taurine-free parenteral nutrition resulted in retinal degeneration that was reversed with taurine supplementation.[10] Retinal abnormalities were also found in primates fed a taurine-free infant formula.[11]

On the basis of these findings, taurine was added to most infant formulas by the early to mid 1980s. The only randomised controlled trial of taurine supplementation was started before its routine addition to formulas but terminated for ethical reasons after 37 rather than the planned 50 infants were enrolled. Nonetheless, preterm infants assigned to the taurine supplemented formula had a more mature auditory brain stem evoked response than those assigned to the taurine-free formula.[12] However, no differences in electroretinograms or Brazelton scores were detected. Infants fed taurine supplemented formulas also have a bile salt conjugation pattern more like that of breast fed infants as well as a larger bile salt pool, but reported effects on fat absorption have been mixed.[13–15]

Owing to the relative lack of evidence that taurine supplementation of infant formulas has beneficial clinical effects, recent recommendations for the nutrient contents of term infant formulas do not include a minimum content of taurine.[16] However, as formulas have contained taurine for almost two decades and these seem to be well tolerated, a maximum amount (12 mg/100 kcal) is specified. This is near the maximum content observed in human milk and about 25% more than the content of modern formulas. A minimum content of taurine (5 mg/100 kcal) is specified for preterm infant formulas but without much enthusiasm.[17]

The findings of Wharton *et al*,[18] reported in this issue, suggest that the recommendations for taurine content of infant formulas should be reconsidered. These findings suggest that low plasma taurine concentration during the hospital stay may explain the paradox of higher developmental scores at 18 months[19] and 7 years of age[20] in preterm infants assigned to a nutrient enriched compared with a term formula during initial hospital admission but similar scores in infants assigned to banked human milk compared with the nutrient enriched formula despite the fact that the nutrient density of the banked human milk was even lower than that of the term formula.[21] Although the possibility that the paradoxical neurodevelopmental outcomes were related to taurine intake during infancy was suggested in reviews by Sturman and Chesney in 1995[22] and Chesney *et al* in 1998,[23] Wharton *et al*[18] provide the first indication that this explanation may be valid. They show that the Bayley mental developmental index at 18 months of age and the WISC-R arithmetic subtest score at 7 years of age are correlated with plasma taurine concentrations during infancy. They also report that the positive association of neurodevelopment with own mother' milk[24] was not significant after plasma taurine concentration had been allowed for. These findings are attributed to the presence of taurine in the preterm formula and human milk but not in the term formula.

As the authors emphasise, these findings are far from robust. Firstly, they are not derived from a randomised, controlled trial but, rather, from a retrospective analysis of existing data. Secondly, the strength of the reported relations is modest ($r = 0.28$ and 0.22). Nonetheless, they support the hypothesis that low neonatal taurine status adversely affects later neurodevelopment of preterm infants and that the neurodevelopmental advantage of human milk may be related to its taurine content. Thus the new data provide further support for the view that taurine is a conditionally essential nutrient for the preterm infant. They also provide an additional example of apparent long term effects of short term early differences in nutrient intake.

The findings of Wharton *et al* also present a quandary. Randomised, controlled trials of taurine supplementation for both preterm and term infants should clearly be the next step, but would either trial now be ethical? Like so many other issues in neonatal nutrition and, indeed, all of clinical medicine, it is unlikely that the role of taurine in infant nutrition will ever be evaluated in a randomised controlled trial.

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