LETTERS TO THE EDITOR

Randomised trial of early tapping in neonatal post haemorrhagic ventricular dilatation: results at 30 months

EDITOR,—In reporting the results of follow up from questionnaires to the clinicians involved in the care of children randomised after the official end of this multicentre trial, Johnson et al have highlighted an important issue.1 Major functional loss can be identified at the age of 30 months by questionnaire, particularly when there is an unbiased comparison group. The primary question, however, is whether early tapping carried an advantage over conservative treatment in the prevention of major functional loss in the first 2 years of life. What may be missed, however, is impairment which, at that age, may not be perceived as major deviations from the norm. Abnormalities and asymmetries of tone may escape notice in a routine examination and become obvious only at a later stage. It is therefore not surprising that there are large differences between the proportions of children reported as being ‘normal’ and those having neuromotor impairment without functional loss, in children randomised before 31 January 1987 compared with those randomised after this date.

There may also be difficulties in categorising children as multiply or singly impaired without more formal testing. Silence or poor expression of language at this age is not attributed to shyness—particularly in the unfamiliar context of a short clinic visit.

However, for secondary questions concerning the refinement of the questionnaire, which is to be used in a multicentre trial, the present sample size will not allow this. Johnson et al suggest that the questionnaire will have to be revised in order to be more reliable and feasible in detecting major functional loss in large groups of geographically scattered children. The resulting increase in statistical power may then offset the gains in accuracy which are made by using a more sensitive test. It is hoped that this sort of issue is being explored in our research assessing the advantages and disadvantages of questionnaires completed by paediatricians in clinics, health visitors, GPs and parents (and teachers for school age children).

Pro-or antioxidant activity of vitamin C in preterm infants?

EDITOR,—It is with great interest that we read the paper by Silvers et al 1 describing plasma ascorbic acid concentrations and plasma antioxidant activity in premature infants at birth, and potential implications for reactive oxygen species induced injury. The antioxidant activity of plasma was by measuring plasma lipid peroxidation in rat brain homogenate, expressed as Dₘₐₓ (plasma volume in μl required for maximum inhibition of auto-oxidation). In this vitro system, as mentioned by the authors, 1 high peroxidation concentration of lipid peroxidation is therefore not surprising that plasma with low concentrations of ceruloplasmin (which has ferroxidase activity) and high concentrations of ascorbic acid (which can reduce free iron and initiate the formation of hydroxyl radicals through Fenton chemistry) has a low Dₘₐₓ. 1 Although ascorbic acid can act as a pro-oxidant in the presence of free transition metal ions, it is a potent antioxidant under other oxidative stress conditions. 2 Ascorbic acid scavenges directly a variety of reactive oxygen species, including superoxide and hydroxyl radicals suppresses the inactivation of antioxidants by oxygen generated by the myeloperoxidase-halide system, neutralises oxidants released from stimulated neutrophils in a dose dependent manner, and can regenerate membrane bound vitamin E. 3, 4 Ascorbic acid also has important metabolic roles—for example, in the biosynthesis of collagen, carnitine, and catecholamines.

The question, therefore, is whether in vitro observations such as the ones made by Silvers and colleagues 1 are relevant to the in vivo situation. The detection of non-transferrin bound iron in plasma of preterm and term infants 4 seems to support the authors’ concerns regarding a potential pro-oxidant role of ascorbic acid in vivo. 1 However, the various antioxidant and metabolic properties of ascorbic acid also have to be considered, and the integrated effect of high plasma ascorbic acid concentrations on the health status of premature infants is unknown. Therefore, we caution readers not to conclude that ascorbic acid is harmful to premature infants and that ascorbic acid intake needs to be restricted in these infants. Only carefully designed and performed future studies of vitamin C depletion or supplementation will be able to answer these important questions.

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1 Silvers RM, Gibson AT, Powers HJ. High plasma vitamin C concentrations at birth associated with low antioxidant status and poor outcome in premature infants. Arch Dis Child Fetal Neonatal Ed: first published as 10.1136/fn.72.3.F211 on 1 May 1995. Downloaded from http://fn.bmj.com/ on September 14, 2023 by guest. Protected by copyright.


Dr Powers et al comment: There is no doubt that ascorbic acid has several important biochemical functions in the body, including, under most physiological conditions, that of antioxidant. Under the particular conditions associated with premature birth, however, which include a low plasma concentration of plasma transferrin and ceruloplasmin, and possibly the presence of non-transferring bound iron, ascorbic acid present at high concentration would be expected to act as a pro-oxidant. Our published data suggest that this is indeed the case and that high plasma vitamin C concentration at birth is associated with poor outcome. As further support for this argument we have recently demonstrated that at ratios of vitamin C:ceruloplasmin which we observe in premature babies at birth, vitamin C strongly inhibits the ferroxidase activity of ceruloplasmin. 1 We have not suggested that vitamin C per se is harmful to premature babies, but it is difficult to ignore the fact that vitamin C concentrations in infant formula are higher than those measured in human milk, and that formulas for premature babies are even more generous. The argument we presented was that premature babies need high intakes of vitamin C to catabolise tyrosine completely, but our stable isotope studies of tyrosine metabolism in preterm infants support this. We do not think that there is no good evidence that high vitamin C intakes are beneficial, there are indications that they may be harmful. We would therefore advocate a thorough re-evaluation of vitamin C recommendations for premature infants rather than a reassurance that current intakes are appropriate.