Correspondence

Apnoea of immaturity

Sir,

We fully appreciate the difficulties encountered by Jones¹ when conducting a randomised trial in a busy neonatal care unit. We also recognise the need for proper evaluations of different treatments. However, the conclusion that ‘CPAP was less effective than theophylline’ is not fully proved from the data, though it may well be the case.

Dr Jones admits that the continuous positive airways pressure (CPAP) group had suffered significantly more peri-natal complications than the infants in the theophylline group. Obviously this is a weak point in her study, but a more serious one is the dependency on nursing observations of apnoea in the majority of her cases. Stein and Shannon² have pointed out the dangers of such dependence. To use such subjective records in statistical analyses is potentially misleading. In summary we do not think that the evidence reported substantiates her conclusions.

References


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Dr Jones comments:

It was indeed unfortunate that despite randomisation, the infants in the CPAP group had significantly more peri-natal complications than those in the theophylline group. Nevertheless, I found no correlation between the peri-natal complication score and the response to treatment, and as described in my paper, multiple co-variance analysis showed a significant treatment effect even after any effect of pre-treatment rates of apnoea and peri-natal complications had been removed.

Stothers and van Someren also question the validity of using nursing observations which are known to be inaccurate. The greater reduction in bradycardias for infants given theophylline rather than CPAP was confirmed, however, by the continuous recordings in the latter part of the study. In these later infants, I compared the continuous recordings directly with the nurses’ observations and found, as have many other authors, that nurses underestimated the number of attacks, but there was no significant difference in the degree of underestimation between infants on theophylline and those on CPAP. Ideally all infants would have had continuous recordings, but I do not consider that lack of these negates the overall conclusion that in very immature infants theophylline is more effective than CPAP in the treatment of apnoea.

Estimation of glomerular filtration rate from height/plasma creatinine ratio

Sir,

In the August issue, two papers discuss the reliability of the height/plasma creatinine (Ht/PCr) ratio as an estimate of glomerular filtration rate (GFR). Both studies used the plasma disappearance curve of ⁶⁷ Cr-EDTA as a reference for the estimation of GFR, and reached contradictory conclusions. While Morris et al.¹ found the Ht/PCr ratio ‘a clinically useful aid to the estimation of renal function,’ Davies et al.² by contrast, concluded that ‘the prediction of GFR in children from single Ht and PCr measurements was of limited value in clinical practice’.

In a commentary to these findings, Dr Barratt discusses the drawbacks of the estimation of GFR by the analysis of the plasma disappearance on a single compartmental model and emphasises that it is ‘somewhat hazardous to assess other methods of estimating GFR by comparing them with the plasma clearance of ⁶⁷ Cr-EDTA. From Dr Barratt’s assertion that ‘the clearance of inulin remains the definitive estimate of GFR’, it can be inferred that other methods for the estimation of GFR should preferably be compared to the standard inulin clearance.

This is precisely what we did in a retrospective analysis of 500 inulin clearance studies in children older than one year.³ All tests were performed during the years 1972 to 1979 and included routinely the assessment of inulin, para-amino-hippuric acid, creatinine, and urea clearances. Each clearance was expressed as the mean of 4 to 5 consecutive clearance periods obtained over 3 hours.

Seventy-two out of the 500 children were selected according to their standard inulin clearance, in order to obtain a group of patients whose inulin clearance values were uniformly distributed throughout the range from 5 to 160 ml/min per 1·73 m².

The Figure shows the correlation that we observed between inulin clearances and the Ht/PCr ratios. The slope of the regression line was significantly different from that of the line of identity (P<0·001). Calculated values using the expression 0·55 Ht/PCr underestimated inulin clearance values at GFR above 80 ml/min per 1·73 m², and overestimated them below 80. In addition, dispersion of the individual points around the regression line was substantial. We thus found little merit in the use of Ht/PCr ratios as an estimate of GFR.

233
Figure. Relationship between standard inulin clearance and the formula $0.55 \times \text{height/plasma creatinine}$ concentration in 72 children older than one year of age ($Y = 23.6 + 0.7 \times X, r = 0.82$). The slope of the regression line is significantly different from that of the line of identity ($P < 0.001$). The shaded area represents the 95% confidence limits of the regression line.

More promising were the results obtained by studying the combined creatinine and urea clearances. This method was used in adults by Lavender et al. who demonstrated a good correlation and minimal variability between the clearance of inulin and a value calculated as the sum of the clearance of creatinine and that of urea, divided by 2. We also found a good correlation between these parameters. The best correlation, however, was found between the clearance of inulin and a value calculated as the sum of twice the creatinine clearance and the urea clearance, all divided by three, $2 \times \text{Creat} + 1 \times \text{Urea}/3$. The regression line ($Y = 14.3 + 0.8 X, r = 0.93$, where $X$ represented the inulin clearance) was statistically indistinguishable from the line of identity. The scatter of points around the regression line was less pronounced but still appreciable.

From this study we concluded that the method of combining the 3 hours clearance of creatinine and urea was the best alternative to the complicated measurements of standard inulin clearance when precise values of GFR are not needed, and that the $Ht/PCr$ ratio could not be taken reliably as an estimate of GFR. This latter conclusion is confirmed by the studies of Davies et al.

Oral rehydration salts have a shorter shelf life with sodium acetate than with sodium bicarbonate

Sir,

We have read the interesting report of Patra et al., showing that sodium acetate can successfully replace sodium bicarbonate in the oral rehydration solution currently used for the treatment of infants suffering from diarrhoea and acidosis.

Since bicarbonate reacts with glucose to form furfural compounds leading to brown discoloration of the salt packets, the conclusion of the authors is that although there is slight increase in the cost of the packets in which bicarbonate is replaced by acetate, the 'longer shelf life, ease of packaging, and tablet making should more than compensate for it'. We will not argue about ease of packaging and tablet making, but in connection with shelf life of sodium acetate, the opposite is true: the shelf life of sodium acetate is shorter than that of sodium bicarbonate as it is highly hygroscopic.

We compared in triplicate, two mixtures of salts, identical with those used by the authors. One was prepared according to the formula recommended by the WHO and the other contained acetate instead of bicarbonate in an isosmolar quantity. Both were immediately sealed with heat into plastic bags. After about 72 hours at room temperature, most of the sodium acetate containing package, turned to a jelly or gum like material. At $37^\circ C$ the change was observed within 12 hours, and was, of course, more apparent by this time, if 0.1 ml of water had been added to the salt mixture. No change was observed in the sodium bicarbonate containing package, however, either in 72 hours at room temperature, or in 12 hours at $37^\circ C$. If 0.1 ml water was added at $37^\circ C$, the brown discoloration of bicarbonate was observed within 12 hours. The results of a typical experiment, are shown in the Figure.

References


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