Correspondence

Treatment of renal failure in neonates

Sir,

Meeks and Sims describe their experiences of acute renal failure in a neonatal intensive care unit; data were abstracted retrospectively from the hospital records over a four and a half year period; and acute renal failure was defined as anuria of 24 hours’ duration or by a clinician about poor urine output together with a serum urea concentration exceeding 10 mmol/l or serum potassium exceeding 7.5 mmol/l.1 I would like to comment on some of the points raised in their paper.

Between February and December 1985 I carried out a prospective survey of acute renal failure in 388 consecutive admissions to a regional neonatal intensive care unit. The diagnosis was based on at least one of the following three criteria: a serum creatinine concentration persistently rising over a minimum of two days, oliguria (<1 ml/kg/hour) or anuria resistant to volume repletion and present for a minimum of eight hours, hyperkalaemia (confirmed on a repeat unhaemolised sample; potassium concentration >7.5 mmol/l) together with at least one of the following two criteria: otherwise unexplained metabolic acidosis (pH <7.25, base deficit >10 mmol/l) or haematuria.

Twenty four (6-2%) babies developed renal impairment suggestive of acute intrinsic renal failure; six infants (25%) survived, all of whom had been managed conservatively. Eleven babies presented anuric, 10 oliguric, and three were non-oliguric. Overwhelming sepsisemia was the commonest underlying associate, occurring in eight infants (33%), all of whom were of less than 1500 g birth weight. Four babies (17%) suffered severe perinatal asphyxia; all were over 35 weeks’ gestation and outborn.

Thirteen of the 24 infants had a plasma urea concentration within the normal range at the time of diagnosis. I would suggest that measurement of plasma urea is of little value in the newborn as it is influenced by numerous non-renal factors. Misleading rises in the presence of normal renal function may be seen in catabolic states such as trauma and sepsis and in the presence of sequestered blood; conversely, the higher anabolic state of the healthy newborn suggests that relatively smaller increments in serum urea may reflect renal impairment.

The usefulness of three biochemical indices, in the evaluation of the oliguric neonate, was assessed. A fractional sodium excretion exceeding 2.5%,2 urine to plasma creatinine ratio of less than 20, and urinary sodium concentration exceeding 40 mmol/l,3 have been described as suggestive of acute intrinsic renal failure. Only 57% of infants with volume repletion resistant oliguria had a fractional sodium excretion of greater than 2.5% however, and 43% a urine to plasma creatinine ratio of less than 20 (poor sensitivity). Although all these infants had a urinary sodium concentration exceeding 40 mmol/l (high sensitivity), the median urinary sodium concentration in infants less than 34 weeks’ gestation in the first week of life is around 88 mmol/l (poor specificity).4

Retrospective review can only be regarded as a poor index of significant oliguria or anuria. In addition to the possibility of prerenal oliguria, 7% of normal infants fail to void during the first 24 hours of life; neonates do not empty their bladders completely on voiding; sick infants may develop retention of urine. Furthermore the occurrence of non-oliguric renal failure in the neonate is a recognised entity.

Meeks and Sims describe 30 neonates with acute renal failure over a four and a half year period. Though they do not state the total number of admissions over this period, this is likely to be a considerable underestimate, despite their conviction to the contrary. Norman and Assadi reported a 6% incidence of acute renal failure in a series of 314 consecutive admissions to a neonatal intensive care unit5; this is a figure similar to ours.

The recognition of acute intrinsic renal failure in the neonate is difficult. Failure to consider the problem in an anticipatory manner, with careful monitoring of urine output and serial measurement of serum creatinine is likely to result in continued underdiagnosis.

References

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Drs Meeks and Sims comment:
We read with interest the letter from Dr Modi and would like to reply to some of her comments. Acute renal failure occurred in less than 2% of all admissions to the neonatal medical and surgical units during the study period. Although this figure is much lower than that of other reports,1 the incidence of acute renal failure depends on the diagnostic criteria used. We assumed oliguria of less than 24 hours’ duration to be a feature of hyaline membrane disease rather than acute renal failure.2 By taking oliguria present for more than eight hours as
significant, our incidence of acute renal failure would have been considerably higher, and the survival rate much more favourable.

One of us (AM) has also conducted a prospective study of renal function in babies requiring ventilatory support for four or more days during their first week of life. The study group of 22 babies, mean (SD) gestation 31 (4-3) weeks, represented about 10% of those admitted to the neonatal unit over a six month period and were typical of those requiring intensive care. Depending on the criteria used, the incidence of acute renal failure in the study group was between 5% (hyperkalaemia) and 82% (urinary sodium concentration exceeding 40 mmol/l for 48 hours).

Sick newborns are treated with many drugs having renal effects, such as in this study: frusemide (n=17), isoprenaline (n=6), tolazoline (n=4), epoprostenol (n=3), dopamine (n=2), and sodium nitroprusside (n=1). The natriuretic effect of frusemide, for example, may be delayed until beyond the third day after administration and its duration of action is variable,1 making interpretation of urinary sodium and fractional excretion of sodium impossible and invalidating their use as parameters for acute renal failure.

We agree that retrospective diagnosis of acute renal failure is far from ideal, but it should be appreciated that prospective recognition may also be difficult. Only by carefully monitoring urine output and critically assessing biochemical parameters will accuracy of diagnosis improve.

References

Thyroid function in children after treatment for acute lymphoblastic leukaemia

Sir,

It is known that cranial irradiation during central nervous system prophylaxis of acute lymphoblastic leukaemia can cause endocrine deficiencies, including thyroid dysfunction.1 Shalet et al showed that five out of 58 patients treated for acute lymphoblastic leukaemia had raised serum thyroid stimulating hormone concentrations after treatment with 2400 or 2500 cGy cranial irradiation,1 and Robison et al showed that 10% of long term survivors treated with 1800 or 2400 cGy cranial or craniospinal irradiation had thyroid abnormalities, which included primary hypothyroidism, compensated hypothyroidism, thyroid adenoma, and carcinoma.2

In an attempt to discover whether thyroid damage occurs with low dose cranial irradiation, we evaluated thyroid function by measuring concentrations of serum thyroxine and thyroid stimulating hormone in 64 out of 98 patients with acute lymphoblastic leukaemia. They were diagnosed between August 1981 and September 1985 and had received prophylactic treatment to their central nervous systems. The latter comprised 1800 cGy cranial irradiation in 10 fractions over 12 days which was given soon after achieving complete remission and intrathecal methotrexate. All patients were treated according to a protocol devised at this hospital3 or the UKALL X pilot protocol.4 The 30 girls and 34 boys were aged between 2 and 12 years (mean 6-2) at diagnosis. Thyroid status was evaluated between three and six years (mean 4-9) from diagnosis.

One out of the 64 children was found to have a mildly raised thyroid stimulating hormone concentration (6-4 mU/l) at three years from diagnosis but this returned to normal within four months. Serum thyroxine concentration was normal when tested on three occasions over this period. The remaining 63 children had normal thyroid function. No patient had clinical evidence of thyroid neoplasia.

A proportion of patients in the study of Robison et al received craniospinal irradiation that involved direct irradiation to the thyroid gland. Although they found no association between radiation dose or field and thyroid hypofunction, we surmise that direct irradiation of the thyroid, together with higher dose used in some patients, may account for the increased incidence of thyroid abnormality in their series. None of our patients received irradiation of the spine, and all were treated at the lower dose of 1800 cGy. The dose of scattered radiation received by the thyroid gland was assessed in 10 patients and was found to be between 2-5 and 4% of the total dose.

We conclude, therefore, that prophylactic irradiation confined to the cranium at the dose of 1800 cGy is not deleterious to the thyroid gland up to six years from diagnosis.

References

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