enlarged and diffusely echogenic. Juvenile familial nephronophthisis may also show increased echo formation, particularly around the periphery of the medullary pyramids and associated with microcyst formation. Some larger cysts may also be visible.

Unlike Seyberth et al we found no abnormalities in tests of tubular function. Microscopic haematuria has been seen in infants with nephrocalcinosis who are given frusemide, but it does not seem to be associated specifically with nephrocalcinosis.

The combined use of chlorothiazide with frusemide has been advocated as a means of preventing hypercalciuria. It also aids the dissolution of nephrocalcinosis and any stones that may be present. We have shown that nephrocalcinosis can disappear without using chlorothiazide over a period of 16 months after stopping the frusemide. The most valuable use of chlorothiazide may be in those infants who have developed kidney stones and in those with osteopenia of prematurity. The volume of fluid tolerated by the infant receiving frusemide seems to be important in the development of nephrocalcinosis.

The long term effects of medullary nephrocalcinosis are unknown, but may be related to the density of calcium present and the underlying cause. The absence of tubular abnormalities in our group at 12 months suggests that they did not have any ill effects.

We thank Miss Gail Simons and Mrs Meg Hogg for typing the manuscript.

References


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Ranitidine in the newborn

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SUMMARY An infusion of ranitidine 0.2 mg/kg/hour abruptly halted a life threatening gastrointestinal haemorrhage in an anuric infant of 30 weeks' gestation.

We report the successful use of intravenous ranitidine in an extremely sick preterm neonate with severe acute gastrointestinal blood loss.

She was born at 30 weeks' gestation with a birth weight of 1700 g to a healthy primigravida. She required brief initial resuscitation with endotracheal intubation and assisted ventilation in addition to naloxone. Vitamin K was given intramuscularly. The infant developed respiratory distress and collapsed when 5 hours old with a generalised convulsion that required further intubation and assisted ventilation. She remained hypoxic despite vigorous ventilation, with the fractional inspired oxygen concentration being raised to 95%, and persistent fetal circulation was diagnosed. A bolus dose of tolazoline 2 mg/kg was given followed by an infusion at 2 mg/kg/hour, which produced a good initial response. She was transferred to the regional neonatal intensive care unit at the age of 12 hours.

Chest x ray pictures showed severe hyaline membrane disease and the baby continued to shunt with a PaO2 of only 5-33 kPa despite ventilation with 95% oxygen and infusions of tolazoline and dopamine (5 μg/kg/minute). At 40 hours of age she developed a loud murmur consistent with a persistent ductus arteriosus; this responded within nine hours to indomethacin 0.2 mg/kg and three doses were given 12 hourly intravenously.

On the third day she became anuric; renal ultrasound scan suggested acute tubular necrosis, and she required peritoneal dialysis for 36 hours for...
Within two mg/kg/hour which did aspirated during blood severity of the treated Her formed. Clinical no fresh fluid retention further 41 ml of infusion of 8*6 mmol/l. She developed ventricular rhythm indicated of 28 g/dl, ranitidine was chosen for the anuric neonate reported here because a greater proportion of ranitidine than cimetidine is excreted through the liver and because of the possibility of cerebral toxicity induced by cimetidine.

The ranitidine infusion controlled the gastrointestinal haemorrhage within two hours, the likely cause of which was the combination of tolazoline and indomethacin treatment.

Ranitidine reduces gastric acid secretion by histamine H2 antagonism. Release of histamine is thought to be both the mechanism of action of tolazoline in treating pulmonary hypertension and the cause of the gastrointestinal bleeding that complicates tolazoline treatment. Such bleeding has been reported in up to 55% of neonates receiving tolazoline and 7% were severely affected.

The theoretical risk of histamine antagonism by ranitidine leading to a recurrence of pulmonary hypertension was possible, but did not develop.

Extracranial haemorrhage has been reported in 22% of neonates given indomethacin for persistent ductus arteriosus. This may be due either to a prolongation of the bleeding time, which is still considerably increased 48 hours after course of indomethacin treatment, or to a direct effect on the stomach, or both.

Our patient had a high plasma concentration of ranitidine at 24 hours and it accumulated thereafter. The infusion of 0-2 mg/kg/hour was effective though excessive in treating life threatening haemorrhage in an anuric preterm infant.

We thank Dr DG Sims for allowing us to report this patient and Glaxo PLC for measuring ranitidine concentrations in serum and urine.

### References


### Discussion

There have been few reports of the use of histamine H2 receptor antagonists in preterm neonates. Although the successful use of cimetidine (4 mg/kg 12 hourly intravenously) has been reported in a preterm neonate with gastrointestinal bleeding and a creatinine of 20 mg/dl, ranitidine was chosen for the anuric neonate reported here because a greater proportion of ranitidine than cimetidine is excreted through the liver and because of the possibility of cerebral toxicity induced by cimetidine.

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### Table

<table>
<thead>
<tr>
<th>Time</th>
<th>Ranitidine concentrations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Plasma (ng/ml)</td>
</tr>
<tr>
<td>After 24 hours of infusion</td>
<td>789</td>
</tr>
<tr>
<td>After 36 hours of infusion</td>
<td>Not done</td>
</tr>
<tr>
<td>7 Hours after end of infusion</td>
<td>1390</td>
</tr>
<tr>
<td>24 Hours after end of infusion</td>
<td>Not done</td>
</tr>
<tr>
<td>36 Hours after end of infusion</td>
<td>375</td>
</tr>
<tr>
<td>48 Hours after end of infusion</td>
<td>Not done</td>
</tr>
</tbody>
</table>

Plasma level which results in acid suppression in 50% of adults=100 ng/ml.
Ranitidine in the newborn.

M Rosenthal and P W Miller

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