Haemodialysis and ultrafiltration in babies weighing under 1000 g

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Abstract
Until now it has not been feasible to haemodialyse babies with renal failure who weigh less than 1000 g. Three babies weighing 630, 808, and 1140 g are described. They had multiorgan failure and could not be peritoneally dialysed. They were treated with veno-venous ultrafiltration and haemodialysis using a manual syringe driven technique that required only simple equipment. This method is highly labour intensive, but can provide control of fluid volume and plasma biochemistry in these very sick infants. Their prognosis, however, is determined by the underlying cause of their renal failure, and remains poor.
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Acute renal failure is common in very small preterm babies, and is usually secondary to factors such as hypotension and hypoxia caused by medical or surgical conditions. The management of infants with oliguric renal failure that is unresponsive to a fluid challenge and frusemide is difficult; conservative treatment may provide only a temporary solution.

Although babies weighing below 1000 g with acute renal failure have a poor prognosis, if an infant was likely to survive undamaged but for its renal failure then dialysis could be considered. It has been argued that peritoneal dialysis is the method of choice in neonates,[1] and that haemodialysis and ultrafiltration cannot be considered for babies under 1000 g.[2] We describe three babies of 630, 808, and 1140 g where peritoneal dialysis failed but where we were able to haemodialyse and ultrafilter using venous access.

Methods
CASE REPORTS
Case 1
An 808 g, 25 week gestation, ventilated boy developed necrotising enterocolitis with an intestinal perforation which required laparotomy on day 29. The perforation site, however, could not be found. He developed anuria that was unresponsive to fluid and frusemide, and subsequently became oedematous and hyperkalaemic despite conservative measures. Peritoneal dialysis with a bicarbonate based dialysate was started,[2] and after the initial faecal contamination of the dialysis effluent cleared, his biochemistry corrected satisfactorily, but ultrafiltration could not be achieved.

Continuous arteriovenous haemofiltration

(CAVH) was not considered feasible because of technical problems with arterial access as a result of oedema. Spontaneous CAVH was also felt to be limited by relative hypotension, and pumped CAVH by the size of the extracorporal circuit relative to his blood volume. We therefore constructed a manually operated veno-venous syringe driven ultrafiltration (SDU) system with a small hollow fibre haemofilter, using his surgically placed right atrial line (0·5 mm internal diameter) for vascular access. Fluid (290 ml) were removed over the next 17 hours which substantially reduced his ventilation requirements. Every 12 hours for the next two days he had a three hour session of combined ultrafiltration and dialysis (SDUD), and his general condition and biochemistry further improved. He began to produce urine, dialysis was discontinued, and his plasma creatinine gradually fell to normal at 35 μmol/l. He then underwent a second laparotomy when an ileal perforation was found and an ileostomy created.

He remained well with normal renal function for a further six weeks, but then developed liver impairment, and subsequently died of liver failure aged 4 months. A post mortem examination showed diffuse hepatic parenchymal injury, but normal renal histology on light and electron microscopy.

Case 2
A 630 g girl was delivered by caesarean section at 27 weeks of gestation because of maternal hypertension. She needed ventilatory support from birth. On day 16 she developed necrotising enterocolitis and required an ileostomy because of a perforation; she developed renal failure unresponsive to a fluid challenge and frusemide. Two days later peritoneal dialysis was started because of severe oedema and abnormal biochemistry, but failed to produce any ultrafiltration. A right atrial catheter was therefore inserted surgically to provide vascular access for SDU, and 108 ml fluid was removed over eight hours. Despite this her general condition remained poor and she died 14 hours later.

Case 3
A 1140 g boy was delivered by caesarean section in a poor condition after spontaneous premature labour and compound presentation at 27 weeks of gestation. He was ventilated from birth and developed pulmonary interstitial emphysema and intraventricular haemorrhage with obstructive hydrocephalus. On day 33 he developed profound hypotension as a

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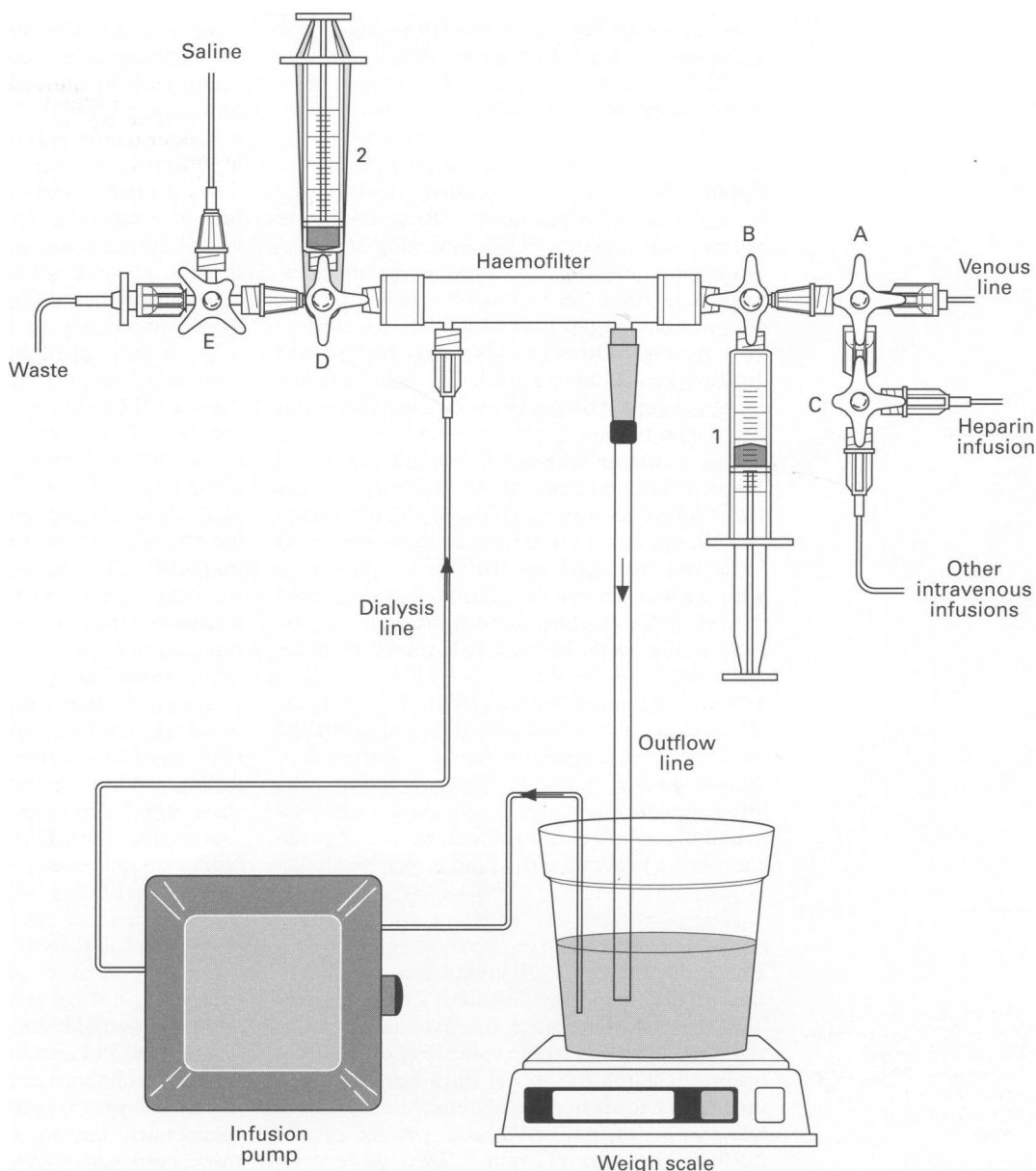J Sharp

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result of necrotising enterocolitis and a duodenal perforation which was oversewn after resuscitation. He subsequently had anuric renal failure resistant to fluid challenge and frusemide. Abdominal distension precluded peritoneal dialysis, and his platelet count was too low to attempt arterial puncture for CAVH, so a right atrial catheter was inserted surgically to permit SDU.

He had a daily five hour session of SDU which removed about 130 ml fluid, allowing intravenous nutrition and drugs to be administered and resulting in good biochemical control. Four days later he required extensive resection of necrotic ileum, and died 10 hours later. Renal histology at post mortem examination showed normal glomeruli and changes in the proximal tubules consistent with recovering acute tubular necrosis.

DIALYSIS TECHNIQUE; SDU(D)
A polysulphone hollow fibre haemofilter with a

blood priming volume of 6 ml and a membrane surface area of 0.015 m^2 was used initially (Minifilter; Amicon). Later, a filter was supplied by Amicon from their non-clinical product range which had the same priming volume but finer capillaries, giving a membrane surface area of 0.04 m^2.

The extra-corporeal circuit is constructed aseptically from five three-way taps and two syringes using Luer locks throughout (figure). Blood flow through the haemofilter is achieved manually between the two syringes. Blood is drawn from the baby into syringe 1, then pushed back and forth between the syringes until sufficient volume has been lost by ultrafiltration, and the remainder returned to the baby. Thus the blood flow rate through the filter is independent of the rate at which blood can be sampled from the venous access line. This allows SDU(D) to be applied when the flow from the vascular access is relatively slow, unlike other haemodialysis or filtration techniques. The total volume of the venous lines and taps is

Ultrafiltration and haemodialysis circuit for a very small infant. Note that the lower half of the figure is drawn to a smaller scale than the upper half.

0·34 ml, giving a recirculation fraction of only 7% if 5 ml syringes are used for dialysis. This is similar to values achieved with standard single needle dialysis and conventional blood lines. The total blood prime volume is 6·34 ml plus the syringe stroke volume, so it may be as low as 8·3 ml in the smallest infants. Though this exceeds the recommended 8·5 ml/kg, our infants showed no acute signs of instability on starting treatment. At the end of an SDU(D) session all the priming blood is returned to the baby by rinsing with saline from syringe 2.

The transmembrane pressure (TMP) for ultrafiltration is generated by an elastic band stretched over notches cut in the plunger of syringe 2 (figure). Without the elastic band the TMP depends on the blood flow rate between the syringes, but with it in place TMP, and thus ultrafiltration, occurs throughout the time the plunger of syringe 1 is depressed. The elastic band tension also serves to return the blood from syringe 2 to 1, making the technique easier to perform. The TMP generated by the elastic band was about 400 cm of water and the maximum recommended for the filter is 500, though the safety margin is wide. The resistance of elastic bands that would generate significantly higher pressures also makes them very uncomfortable to use.

There was no evidence of haemolysis in the two babies in whom we measured free haemoglobin by a highly sensitive technique.[3] Haemolysis of fresh adult blood could be caused only by repeatedly syringing it vigorously and rapidly through a haemofilter. Anticoagulation is achieved with heparin infused through tap C at a mean hourly dose of 40 units/kg. Other fluids may be infused through tap A during SDU(D), except while blood is being syringed between the haemofilter and the baby.

The filtration achieved from each syringe of blood processed can be seen easily by the reduction in its volume. When using ultrafiltration alone, the cumulative filtrate volume is measured by attaching the outflow line to a burette. When using ultrafiltration with dialysis the cumulative filtrate volume cannot be measured directly because it is mixed with the dialysate.

By using a recirculating system, however, the ultrafiltrate volume can be deduced from the increase in total reservoir fluid, measured continuously on weigh scales (figure). Using a 2·5 litre reservoir, the dialysate volume is large relative to the baby's water volume, so loss of gradient is not a problem if the fluid is changed daily.

PLASMA CLEARANCES

The concentrations of creatinine, urea, and electrolytes were very similar in ultrafiltrate fluid and plasma; hence the plasma clearance achieved is similar to the volume of ultrafiltrate removed. Thus the initial fluid removal from case 1 was equivalent to a glomerular filtration rate (GFR) of 0·35 ml/minute per kg, or one third of the normal value.[4] Two three hour sessions of SDU per day using the standard Minifilter produced a clearance equivalent to

8% of normal GFR (similar to adult patients on regular peritoneal dialysis) and removed enough water to allow a daily fluid intake of 150 ml/kg. Using the filter with finer capillaries increased the ultrafiltration rate by about a half, and using the dialysis circuit increased urea clearance by a further 40%.

Discussion

Our infants are the smallest reported to have been treated by haemodialysis or ultrafiltration. Larger newborns have been treated by arteriovenous haemofiltration, with[5] or without[6] dialysis, and by pump driven venovenous methods.[7] However, the application of these standard techniques to babies of around 1000 g is limited severely by the need for vascular access that will allow sufficient flow for ultrafiltration, and the need for an extracorporeal circuit which is large relative to the baby's blood volume. Circuits for the smallest infants would have to be primed with blood. CAVH also requires sufficient arterial pressure to drive the blood through the circuit. This is unlikely to be achieved by a sick 1000 g baby considering that most larger infants need pump assistance.[8] CAVH also requires either umbilical arterial cannulation or arterial puncture with relatively large lines, carrying a risk of limb ischaemia.

By contrast, for SDU and SDUD the blood flow through the dialyser is independent of vascular access; it is determined not by the rate that blood can be drawn from the baby, but by the rate at which the syringes are operated. It is merely necessary to have venous access that will allow 5 ml of blood to be syringed out manually, with no limit on the speed of withdrawal. The fact that SDU(D) does not require the technology of pump driven haemodialysis circuits may be seen as an advantage for many neonatal intensive care units. However, it is very labour intensive and tedious to perform. It may be possible to automate SDU(D) in the future, but meanwhile the nursing time necessary to run it will remain a major drawback. Peritoneal dialysis still remains the treatment of choice for newborns whose renal failure cannot be managed conservatively.[1] When it is not possible to perform peritoneal dialysis, either because of abdominal surgical conditions, or other technical problems, including failure of ultrafiltration, then SDU or SDUD could be considered.

Most very small infants who develop renal failure do so because of other serious pathology, rather than because of a primary renal cause. All three babies that we treated had multisystem failure, and all three died. Their deaths were not caused by their renal failure; one died after recovering normal renal function for six weeks and had normal kidneys at post mortem examination, one had histological evidence of recovering acute tubular necrosis, and the baby that did not have a post mortem examination had good biochemical control at the time of death. For those babies in acute renal failure who cannot be peritoneally dialysed, SDU and SDUD provide potential therapeutic tools, but the

prognosis for survival remains poor, reflecting the prognosis of their underlying conditions, especially in those neonates with multisystem failure.

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