Use of dialysis in the treatment of renal failure in liver disease

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Summary

Early and thorough peritoneal and haemodialysis has a part to play in the management of selected patients with hepato-renal failure. Patients with advanced irreversible hepatic damage due to cirrhosis, however, may have their prognosis shortened by dialysis, but there are many problems in these techniques in patients with multiple organ failure which still require investigation and solution.

Introduction

The objectives of dialysis in the treatment of patients suffering from hepatic and renal failure simultaneously are those which govern the use of dialysis in those patients who have renal failure alone, coupled with the extra demands of patients in hepatic failure. The main indications for dialysis in these patients involve the adjustment of the fluid balance in those who require room to receive infusions of clotting factors, and intravenous feeding, together with the correction of the toxic uraemic state with its effect on platelet function (Horowitz, Stein and Cohen, 1970) and liver regeneration (Chen and Leevy, 1973). The severity of the renal failure so far as toxins is concerned may be underestimated in the patient with hepatic failure since the urea : creatinine ratio is lower in this group of patients compared with those who do not have simultaneous hepatic failure (Fig. 1), the rule being 'dialyse earlier than the urea or creatinine would warrant'.

The indications for dialysis appear in Table 1. In addition, patients with hepatic failure suffer from a series of metabolic abnormalities, many of which can be treated with dialysis,

Sodium

The plasma sodium concentration is often depressed in hepatic failure. The most severe hyponatraemic states are seen in those patients with end-

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FIG. 1. The urea : creatinine ratio of a group of patients in acute renal failure with hepatic failure (liver) and in a group without signs of hepatic failure (other).

TABLE 1. Indications for dialysis of either type in patients with hepato-renal failure

- (a) Correction of fluid overload as shown by peripheral oedema, pulmonary oedema, heart failure and gross ascites.
- (b) Hyperkalaemia following massive transfusion and the use of diuretics with potassium supplements.
- (c) Rising blood urea and the presence of other toxic metabolites.
- (d) Severe acidosis, coma, encephalopathy.
- (e) Reduction of drug overload due to the onset of renal failure.

stage hepatic cirrhosis who carry a uniformly poor prognosis (Shear, Kleinerman and Gabuzda, 1965; Hecker and Sherlock, 1956) unless their future is considered together with hepatic replacement. Hyponatraemia can be controlled by the simultaneous use of full ultrafiltration at the usual dialysis concentration of sodium of 142 mEq/l, or by using hyperosmolar peritoneal dialysate (Ring-Larsen, Clausen and Ranek, 1972). Where the patient is particularly hypotensive the use of small infusions of 3 normal saline/l (2.7%) can be used to restore the blood pressure temporarily without bringing about excessive water loads (Leaf, 1970). Once the patient has had a period on dialysis, whether by peritoneal or haemodialysis, the hypoproteinaemia can be corrected by the infusion of fresh frozen plasma, stored albumin or ultrafiltrated ascitic fluid.

Calcium and magnesium

The treatment of hypocalcaemia (corrected for plasma protein concentration) is a difficult problem in these patients and extra calcium may have to be given intravenously during dialysis and we have repeatedly used dialysis against hard water containing 10 mg% of calcium in contrast to the normal dialysis concentration of 6.6 mg%. The correction of hypomagnesaemia, also a common finding in patients with hepatic failure (Fankushen *et al.*, 1964; Flink, 1956) is important, particularly when cardiac function is hazarded with high cardiac outputs secondary to anaemia, corrected by repeated blood transfusion containing large amounts of citrate or EDTA, which chelates both these ions effectively (Bajpai *et al.*, 1967; Young, 1964), and a check on calcium and magnesium concentrations at the end of dialysis is necessary. Magnesium depletion can prevent potassium correction in the plasma (Randal, Rossmeisl and Bleifer, 1959), and occasionally, following dialysis against conventional dialysis solutions, both ions are depleted and need replacement intravenously in the last hour.

Phosphate

The existence of hypophosphataemia is also a feature of intravenous carbohydrate feeding, Gram-negative septicemia, endotoxaemia, and is also seen in patients on large doses of steroids and in those with dietary intakes of phosphate which have been extremely low for a period. The importance of the correction of hypophosphataemia is necessary because it affects oxygen transport in the red cell (Sheldon, 1973), the full functioning of the white blood cell (Craddock *et al.*, 1974) and also over a period of time hypophosphataemia leads to a serious myopathy which may hazard the rehabilitation of the patient (Yawata, Craddock and Hebbel, 1973). Unfortunately, dialysis solutions do not contain

phosphate and this will have to be given as a bolus of intravenous buffered phosphate calculated on theoretical ECF volumes from the body weight (Anderson and Parsons, 1963). Where the patient has simultaneous bone disease, the administration of large quantities of phosphate may also lead to healing, again lowering the serum calcium concentration, and this will have to be subsequently corrected as it is difficult to correct both simultaneously without precipitation of calcium phosphate in the dialysis lines.

Acid base balance

Patients with acute hepatic failure have a persistent alkalosis and, when dialysed against acetate or lactate containing dialysate, may develop an increasing alkalosis and we have back titrated the bath pH to 7.3 with hydrochloric acid to compensate for this, checking pH during and at the end of dialysis.

Calories and insulin

In addition to the administration of blood, fresh frozen plasma and albumin during dialysis, the physician will also be faced with the problem of intravenous feeding to counteract the catabolic situation, giving both intravenous fat emulsions (intra-lipid) and intravenous amino acids (Vamin). With their utilization in the liver hindered by hepatic disease, lipids may accumulate, thus interfering with biochemical estimations during the dialysis procedure. The use of high concentrations (25% or 30%) of glucose, dripped in simultaneously through the blood lines during dialysis, is a good source of calories, but insulin administration has to be monitored carefully, preferably by the use of a slow continuous infusion of insulin (Page *et al.*, 1974) rather than by the intramuscular injection of insulin into oedematous areas. The use of sorbitol has been advised but the utilization of sorbitol in a patient with hepatic disease may be diminished and problems of hyperosmolar coma have been recorded in the use of high sorbitol concentrations during peritoneal dialysis (Raja *et al.*, 1971). The use of intravenous amino-acid solutions, particularly those containing only L-amino acids may be contra-indicated in the patient with Grade III or IV hepatic coma in view of their already altered metabolism (Buxton *et al.*, 1974). The process of dialysis removes water-soluble vitamins (Mackenzie *et al.*, 1968) and it is advantageous to administer these at the end of dialysis.

Removal of toxins

Correction of some other abnormalities which occur during hepatic disease also takes place on dialysis. The blood ammonia concentration falls rapidly (Kiley *et al.*, 1958) and there may be an

improvement in the EEG pattern in those patients in coma. The complication of bleeding during dialysis may lead to a high concentration of blood in the gut leading to even further rises, albeit slowly, of the blood urea concentration.

Anticoagulants

The use of heparin during dialysis may be restricted to the dialysis machine by the use of regional heparinization of the coils involved (we are using two Ultra Flow II Coils in our series at the present time), or the patient may be tightly heparinized in view of the prolonged bleeding and clotting times that often occur, by the use of very low doses of heparin on the arterial side during haemodialysis, or routinely with the use of heparin 1000 u/l of peritoneal dialysate. In a proportion of our patients mild peritoneal blood oozing has occurred but this is not a contra-indication for carrying on the regime.

The correction of the raised blood urea which occurs in a proportion of these patients may also assist platelet function by the reduction of the concentration of guanidino succinic acid, one of the toxins that inhibit proper platelet function. Occasionally in the septicaemic patient diffuse intravascular coagulation may occur and this is an indication for continuing heparinization.

Antibiotics

The administration of antibiotics, to treat septicaemia during dialysis, is best monitored by blood concentrations before dialysis and after the administration of sufficient antibiotics at the end of dialysis to achieve an adequate peak level, measured in the case of the rapidly eliminated antibiotic within half an hour of administration, and the more slowly eliminated antibiotics within four hours of the end of the dialysis (O'Grady, 1971). The administration of the appropriate antibiotic dose is then determined by body weight, losses in the urine, and dialysate from the peritoneum. To control sepsis within the peritoneum it may be necessary to give the antibiotics in the peritoneal dialysate, and a direct dilution may be made to achieve sufficient inhibitory concentrations in the peritoneal dialysate administered. The administration of every type of antibiotic is attended with the possibility of nephrotoxicity and this must be weighed against the indication for combating infection (Kleinknecht and Fillastre, 1973) with its effect of increased protein catabolism.

Type of dialysis to be used

The routine elective construction of a straight Ramirez-type shunt between peripheral artery and vein is indicated in all these patients both for the ease of blood sampling and for the early dialysis of patients who suddenly deteriorate. The choice of

peritoneal or haemodialysis is very often determined by circumstances and the staff available rather than by strict clinical indications. Those patients who are already suffering from severe cardiovascular problems may well benefit from peritoneal dialysis (PD) with its less stress on the cardiac output. Those patients where haemodialysis (HD) is urgently needed for the removal of excess fluid may well be dialysed with the arterial and venous shunt sites reversed so that the blood can be taken from the venous circuit, preferably using a long catheter in the femoral vein situated in the cava, and the blood then pumped back either into the vena cava or into a peripheral artery, in this sense not embarrassing the cardiac output. Patients who are already on a ventilator may be peritoneally dialysed as, with the diaphragmatic excursion incurred, the collection of fluid in the pleural and pulmonary spaces is probably cleared by positive pressure ventilation. Those patients who are already suffering from pulmonary complications, but not on a ventilator, are best haemodialysed in view of the effects of peritoneal dialysis on pulmonary function (Berlyne *et al.*, 1966). The choice of peritoneal dialysis in preference to haemodialysis for the removal of middle molecules, e.g. bile acids (Weston *et al.*, 1974) is a conjectural one at the moment, but it is our clinical impression that on occasions PD may remove more of these substances than would HD. Ascites is a common accompanying complication and, where this is a large collection, it may be concentrated and re-infused during HD. PD may then be used later if the collection is less than 3 l. It must be remembered that during PD between 30 and 40 g of proteins are lost during a day's dialysis and this must be replaced with plasma or albumin infusion in the patient who already has low circulating levels.

Pulmonary complications during dialysis

The measurement of pulmonary function in patients with renal failure has revealed a series of abnormalities, not only due to high output left ventricular failure and the collection of fluid in the pulmonary vessel bed, but also due to the collection of fluid and sodium in the interstitial tissues of the lung (Crosbie and Parsons, 1974). These abnormalities can be corrected by ventilation and by dialysis and the early use of ventilation in these patients is indicated although this carries a higher complication rate from pulmonary sepsis. There is a tendency among some nephrologists to regard ventilation as a very ominous sign of a poor prognosis, but this may stem from its being tried too late.

Cardiac complications during dialysis

The heart is already compromised in the uraemic state by the high output required to maintain oxy-

genation of peripheral tissue in the anaemic hypovolaemic state that many of these patients are faced with. Whether uraemia has a specific depressing effect on myocardial metabolism is difficult to establish, but analogies with skeletal uraemic myopathy may be drawn (Prosser and Parsons, 1975). Cardiac dilatation is common and small but possibly embarrassing pericardiac collections of fluid are often found. When haemodialysis takes place a variety of physiological and metabolic changes take place. Calcium concentration rises, potassium falls, magnesium falls slightly, phosphate falls and sodium may rise—all factors altering digitalis sensitivity, if it has been given. Coupled with these the cardiac output already is raised in a significant proportion of patients and dialysis may lead initially to a fall in cardiac output with profound hypotension making haemodialysis difficult. We encountered this repeatedly in the majority of patients in coma; there is evidence not only of the presence of endotoxins (Wilkinson *et al.*, 1974) but also of substances released from the ischaemic gut shunted past the failing liver (Glenn *et al.*, 1972; Haglund, 1973) which may be cardio-depressive. With careful use of (a) fluid replacement, preferably with colloid, (b) monitoring the CVP, (c) steroids, and (d) isoprenaline or angiotensin, a sufficient circulatory response can be achieved to continue with dialysis. Profound hypotension may also be due to occult haemorrhage into the gut and this may be difficult to estimate if melaema and blood in the gastric aspirate do not appear. Occasionally, bleeding from the peritoneal cavity may be excessive and although this has not been lethal in our experience it has been reported (Muhurkar, Arruda and Dunea, 1973).

Dialysis results

The prevalence of the patients with hepato-renal failure in age cohorts is shown in Fig. 2. Two peaks are shown which coincide with a younger group suffering from acute hepatic failure, poisoning and pregnancy complications, the second due to advanced cirrhosis and hepatic dysfunction secondary to biliary

FIG. 2. The prevalence over 10 years of acute renal failure according to disease and age group, presenting in the King's College Hospital Renal Unit. (a) Hepato-renal failure; (b) cardiac and aortic surgery; (c) abdominal operations; (d) septicaemia/drugs/toxins; (e) obstetrics and gynaecology.

tract disease coinciding with other aetiologies of renal failure requiring dialysis.

Turning now to the results of dialysis in the various groups of patients with hepato-renal failure as shown in Table 2, it can be seen that the severe mortality associated with end-stage liver failure due to cirrhosis is confirmed. Those with a varied cause of hepato-cellular failure of acute onset regarded as fulminant hepatic failure also carry a poor prognosis whether given HD or PD, but some survivors particularly among those who have also received charcoal haemoperfusion (Gazzard *et al.*, 1974) and dialysis are encouraging.

We have had experience of five patients with severe hyperbilirubinaemia due to obstruction of the biliary tree with oliguric or anuric renal failure. Although the bilirubin concentration had taken several weeks to fall renal function eventually returned and all have survived after prolonged periods on dialysis, both using HD and PD for up to 6 weeks. It is in these patients that renal biopsy, when bleeding and clotting times are in the normal range,

TABLE 2. To show the treatment given to fifty-five patients with combined hepatic and renal failure according to type, and the outcome by method of dialysis (HD = haemodialysis alone, PD = peritoneal dialysis alone and HD + PD = combination of both). Survivors are shown as the first figure out of the total, the second figure in each column

Disease type	HD	PD	HD + PD	Total	Mortality (%)
Cirrhosis	0/5	0/7	0/2	14	100
Fulminant-hepatic failure	0/4	3/15	2/3	22	78
Biliary tract obstruction	2/2	2/2	1/1	5	0
Others	2/5	5/9	0/0	14	50
Totals	4/16	8/33	3/6	15/55	
Mortality (%)	75	76	50	73	

has shown the tubular damage accompanying pigment deposition and extensive ischaemic vascular damage.

There are no other large series of the use of dialysis for the treatment of renal failure specifically associated with liver disease, but Ring-Larsen *et al.* (1972) have used it to treat hyponatraemia. Although hyponatraemia was corrected, PD did not alter mortality.

There are several reports of clinical improvement in hepatic coma following peritoneal dialysis although often combined with exchange transfusion and steroids (Maxwell *et al.*, 1959; Krebs and Flynn, 1967; York, Grieve and Mienx, 1973; Neienhuis, Mulmed and Kelly, 1963; Conn, 1973).

We feel that dialysis should be reserved for the correction of fluid and electrolyte problems in those with obstructive jaundice or those whose hepatic failure has some chance of recovery or who are awaiting hepatic transplantation. In our series (Wilkinson *et al.*, in preparation) severe gastrointestinal haemorrhage and hypotension have been frequent complications where the evidence is such that the diagnosis is end-stage cirrhosis with hyponatraemia, hypoproteinaemia and a deficiency of clotting factors; dialysis is contraindicated and will probably hasten death.

Acknowledgments

We are grateful to Mr John Dawson, Dr Roger Williams, Mr Hedley Berry, Dr A. Eddlestone and Dr I. Murray-Lyon for their overall care of these patients. We are indebted to Dr N. White, Dr J. Wass and Dr J. Dufton (Renal Registrars) for their expert help in the management of these patients and to the nurses of the Renal and Liver Units for their devoted care.

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