New ways in dialysis

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Experience of the clinical application of dialysis for long term replacement of renal function now extends for two decades. The first decade was in general devoted to improving the design of existing equipment to make it safe and suitable for routine use, and the second to conceiving new ideas. However, so far most of the new ideas have found little routine clinical application and the old methods remain in general use although transformed by new industrial techniques to give greater efficiency.

IMPROVING BASIC CONCEPTS

Blood access

In an excellent historical review of dialysis¹ it can be seen that blood access is the Achilles' tendon of long term haemodialysis. The initial breakthrough came with the development of the Quinton-Scribner external arteriovenous shunt.² Unfortunately its use was complicated by infections and by clotting, resulting in eventual loss of access. The next and most valuable improvement came with the concept of the internal arteriovenous fistula, which when well fashioned and efficiently used gives permanent access. There are certain patients, some even before starting dialysis treatment, who have lost major veins through thrombosis, and these can be provided with bridged arteriovenous fistulae based on homologous³ or bovine heterologous vein grafts,^{4,5} and more recently on mandril-grown autografts⁶ or polytetra-fluoroethylene (PTFE) self-sealing conduits.

Dialysers

The desire to improve dialysers is as keen today as it was 20 years ago. Originally the aim was for efficiency and low resistance, small blood volume and easy reassembly without technical failure or rupture of membranes. Today it is taken for granted that rupture of membranes will not occur; that the dialyser will be extremely small but will give greater efficiency because of better thinner membranes, evenness of blood and dialysate flow patterns; and that reassembly is unnecessary as the dialysers are now disposable. However, in spite of the falling costs of dialysers due to bulk production, they are still expen-

sive and most centres in the UK do attempt to reuse by cleaning and resterilising as many as 12 times.

In spite of many attempts to produce new more efficient membranes from cross-linked water soluble polymers, polypeptides, block copolymers or polyacrylonitrile, membranes based on cellulose still remain the standard material. The cellulose membrane has improved by changing from cellophane to cuprophane, then to cellulose acetate, and finally to ultra-thin membranes of cellophane and cellulose acetate. Along with increased permeability to solutes there is an increase in ultrafiltration, which with some materials, such as polyacrylonitrile, is so great as to be dangerous without substantial modification of the dialysis equipment.⁷

Monitoring

Initially, safe dialysis was achieved by many medical and nursing staff supervising the patient and equipment. Today, although staff are required to prepare the equipment, little or no supervision is required during the dialysis procedure, as simple fail-safe monitoring already in use in the industrial world has been incorporated into artificial kidney machines.

Water treatment and dialysis fluid

Dialysing fluid was originally prepared in batches of 100 litres by dissolving salts in tap-water. The batch was discarded after 2 hours' use and a fresh batch substituted. Little attention was paid to the chemical and bacterial quality of the tap water although bacterial growth was reduced by cooling the dialysate. Apart from the risk of infection, such batches are inconvenient because of their bulk and the labour required to make them up.

Subsequently monitoring equipment permitted the development of proportional systems whereby a concentrated solution of salts was continuously mixed with water directly from the tap thereby eliminating storage and reducing infection.

The development of the concentrated salt solutions made it necessary to replace bicarbonate with acetate to prevent the precipitation of calcium and magnesium. Acetate also has the advantage of bacteriostatic and bacteriocidal properties.

It was soon found desirable to pretreat the tap-water, in particular to remove any excess calcium, by either cationic exchange resin or the commercial water softeners or deionisation using both anion and cation resin beds. Today there is increasing pressure to pretreat water by reverse osmosis to remove trace minerals, particularly aluminium which has been found responsible for major complications in dialysis-treated patients.⁸

The use of acetate instead of bicarbonate is now believed to account for some of the adverse symptoms seen during and after dialysis, probably due to a failure of some patients to convert acetate to bicarbonate quickly enough to prevent acetate overload. Acetate intolerance is seen most commonly in the very sick or elderly patient. The most recently developed equipment has an extra pump which allows the addition of bicarbonate to the mixed dialysis fluid from which the acetate can then be omitted.

NEW CONCEPTS

Ultrafiltration

Ultrafiltration to remove excess fluid accumulated by the patient between dialyses has always been part of a standard dialysis procedure. However, with improved polyacrylic membranes, ultrafiltration can be a major feature, permitting removal of as much as four litres within one hour. This property is particularly valuable for patients with massive fluid gains. It has been found that patients tolerate rapid ultrafiltration extremely well so that large volumes of excess fluid can be quickly removed without the development of hypovolaemia and its associated symptoms. After a period of ultrafiltration routine dialysis follows, the treatment being referred to as sequential filtration dialysis. This treatment is currently used by 10% of European patients approximately once in every 12 dialyses.⁹

Haemofiltration

An extension of the use of the excellent filtration properties of the new dialysers is the process of haemofiltration. The patient's blood is diluted by an infusion of a physiological solution of electrolytes before or after ultrafiltration. A 20-litre exchange over 4-6 hours is the standard treatment. It simulates the nephron whereby blood is ultrafiltered and tubular reabsorption to maintain satisfactory blood volume and composition is replaced by infusion of the electrolyte mixture. It is an expensive treatment due to the additional cost of the 20 litres of intravenous infusion, and it has had only limited clinical application, approximately 1% of European dialysis patients.⁹ Patients treated

by this method are reported to have better control of hypertension and to suffer fewer side-effects.^{10 11}

Adsorbent haemoperfusion

The properties of activated charcoal have interested several research workers in the possibility of removing uraemic toxins by adsorption. Charcoal used alone led to embolisation of the charcoal and to platelet depletion, but it has been possible to avoid such effects by enclosing the charcoal in semi-permeable microcapsules. It is a complex system requiring urease and anion and cation exchange resins. In addition it has been found necessary to incorporate standard dialysis or ultrafiltration to maintain normal body weight. For renal failure patients it still remains a research procedure, which might prove more helpful for acute intoxication and hepatic failure.

Dialysate regeneration: the Redy System

Activated charcoal combined with urease, hydrous zirconium oxide and zirconium phosphate has found another clinical application. These substances can be assembled as layers in a cartridge which is able to regenerate dialysate after passage through the dialyser, so that a 5-litre pool of dialysis fluid can be used instead of the 200 litres used in the single pass of regular dialysis equipment. This equipment does not require permanent plumbing and is particularly valuable as portable equipment for use in other parts of the hospital, for holidays or in countries with limited water supply. However the cartridges are expensive compared with the cost of tap-water and salt concentrates¹² and their preparation is labour-intensive.

The new concepts discussed above have neither simplified the treatment nor reduced the cost and unless it can be proved that the patients treated by the new methods have substantial clinical advantages there is no great incentive to use them routinely.

CONTINUOUS AMBULATORY PERITONEAL DIALYSIS—CAPD

There is, however, one new concept which has simplified treatment and reduced cost, and this has occurred in the field of peritoneal dialysis. It is termed Continuous Ambulatory Peritoneal Dialysis or CAPD, the original method of intermittent peritoneal dialysis now being termed IPD.

The improvement and simplification of peritoneal dialysis came about by a very logical approach to the characteristics of peritoneal dialysis. Peritoneal dialysis has only 1/6th the efficiency of haemodialysis of similar duration, because the dialysate does not achieve anything like full equilibration with the patient's blood during the 10-40 minutes normally

allowed for dwell in the peritoneal cavity; 6-8 hours is a more realistic equilibration period. Attempts to improve efficiency by the use of drugs to increase peritoneal blood flow or permeability of the peritoneal membrane have had little success. Increasing the flow rate of dialysis fluid achieves only a slight increase in efficiency because the dialysate becomes even less equilibrated, and the cost of dialysis fluid is greatly increased for little gain. Hence the best way to increase efficiency is to prolong the period of equilibration between dialysate and blood, and this makes it possible to reduce the volume of dialysis fluid. This is the basis of CAPD.

Standard maintenance IPD, if it is to be as effective as haemodialysis, lasts 40 hours per week and uses 150-200 litres of dialysis fluid. CAPD achieves a similar effect operating 24 hours a day, 7 days a week, but using only 8 litres per day, a total of 56 litres per week. The system requires the average adult patient to instil the contents of a 2-litre dialysis fluid bag into the peritoneal cavity and to lodge the empty bag and attached line somewhere within his or her clothing. The patient remains ambulatory and can perform his or her usual daily activities. After 4-5 hours the peritoneal fluid is drained back into the empty bag and then exchanged for a new bag of peritoneal dialysate. The patient usually does 4 exchanges within 24 hours spaced as three periods of 5 hours during the day and one 8-hour period over-night. Most adults can easily accommodate 2 litres within their peritoneal cavity but for small patients and children, bags of different volumes appropriate to their size can be used. A great advantage of this treatment is the excellent control of blood biochemistry without the rapid changes in plasma composition or blood volume such as occur during haemodialysis. It is safe and free from symptoms. It avoids the regular blood loss of haemodialysis and patients maintain better haemoglobin concentrations. Plasma phosphate concentrations are better controlled. Patients are allowed a less restricted diet, especially in relation to potassium and protein, although they are still required to limit sodium and water intake. The procedure is simple to teach and patients appreciate the freedom from the anxiety associated with the use of haemodialysis equipment. However a major disadvantage is the risk of peritonitis which, although often mild and effectively treatable, is frequently associated with pain and general malaise. Experience has shown that peritonitis results from patient error or technical faults and that, if these can be

eliminated, patients do extremely well. This observation makes it apparent that although the treatment is simple it cannot be safely applied to all patients, as some are so poorly disciplined that patient error is inevitable and peritonitis and morbidity are frequent with eventual loss of effective peritoneal membrane. Hence, although this treatment has been in use for only four years, there has been a steady loss of patients from CAPD to haemodialysis and transplant. Technical improvements will occur and the failure rate will fall—but the final judgement of this treatment must be reserved.

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