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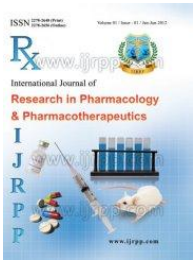

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Artificial kidney - review article

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ABSTRACT

The important factors for the treatment of both acute and chronic renal failure are the proper regulation of diet and maintenance of water and electrolyte balance. The presence of anuria or oliguria requires the administration of large quantities of fluid attempts to initiate diuresis, resulting in an overload of salt and water and the appearance of symptoms leads to renal failure. Where dietary treatment, including rigid control of water and electrolytes, has been ineffective the use of one of the following methods has to be considered: 1. artificial kidney, 2. peritoneal dialysis, 3. intestinal dialysis, 4. replacement transfusion. Treatment with an artificial kidney is the most widely applied therapy for kidney failure. Substantial improvements have been made in artificial kidney technology during the past decades, such as with regard to membrane technology, dialysate composition, and medication to address side effects.

INTRODUCTION

Kidneys regulate the concentrations of sodium, potassium, phosphorus and divalent cations, and the acid-base balance [1-3]**.** They control blood volume and pressure, and have important metabolic and endocrinologic functions [4, 5]. The hormones produced by the kidneys include erythropoietin, renin, prostaglandins and 1, 25-dihydroxy vitamin D3, which is also called calcitriol and is the most active form of vitamin D. The kidneys are also the major source of the growth factor bone morphogenetic protein (BMP)-7 in the adult body, which appears to be important for bone homeostasis [6-8]. Kidneys also can perform other function like immune modulation [9, 10].

Artificial kidney is the most widely applied therapy for the treatment of kidney failure. During the past decades, continuous improvements have been made in artificial kidney technology such as with regard to membrane technology, dialysate composition, and medication to adverse side effects. Despite of many improvements in the treatment, the high rates of mortality of critically ill patients with acute renal failure (ARF), ranging between 40-70%, did not change for several decades [11-15]. Also, the rates of morbidity and mortality of patients with end-stage renal disease (ESRD) receiving treatment with an artificial kidney remain high [16, 17], it is evident that the survival rate associated with renal transplantation is high [18-22]. Portable and wearable devices allow a more normal lifestyle to be achieved

and enable more frequent or continuous home-based therapies to be performed.

A portable device for home hemodialysis that also allows for travel is now available [23]. A wearable artificial kidney is being developed, and successful human pilot studies have been performed [24-26]. This is currently one of the most exciting and promising developments in the field. Portable artificial kidneys are already available [27-32], and clinical trials with wearable artificial kidneys are currently underway [33-43]. Thus, the engineering problems associated with miniaturization of cell-free artificial kidneys seem to be challenging but solvable.

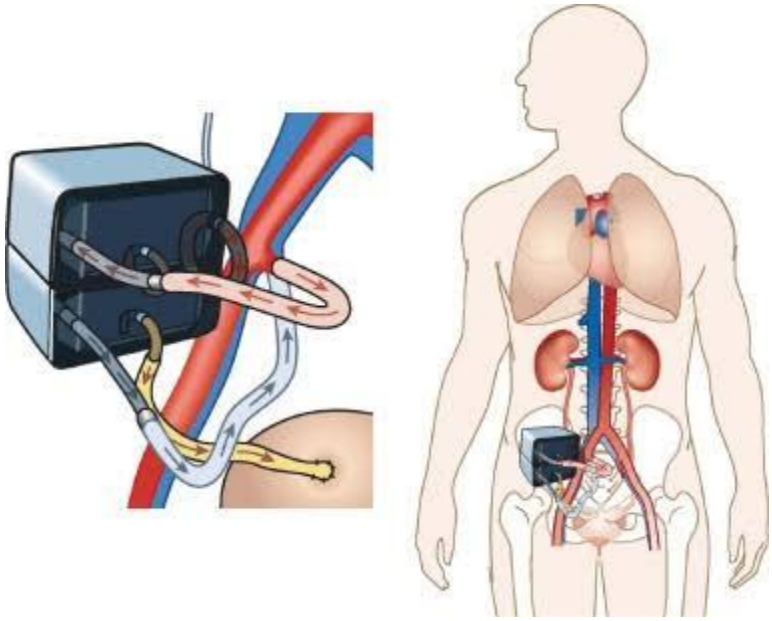

Fig 1: Artificial kidney

PRINCIPLES OF ARTIFICIAL KIDNEY

Regardless of the type of artificial kidney used the patient's blood must be rendered uncoagulable by the injection of heparin. The blood is then guided along a cellophane membrane on the other side of which is the rinsing fluid. By the process of dialysis, a large part of the abnormally retained products of metabolism —urea, uric acid, creatinine, substances giving the xanthoprotein reaction such as phenols, 58 indoxyl, etc. pass from the blood through the cellophane membrane into the rinsing fluid. They become so diluted that return dialysis is negligible. In addition to this process an exchange takes place between the necessary electrolytes of the blood plasma water and those in the rinsing fluid. Hence, if the patient's blood electrolyte pattern is abnormal before treatment, it will tend to be corrected as it approaches the composition of the rinsing fluid inasmuch as the fluid contains normal concentrations of these ions. Since water passes through the cellophane easily, careful attention must be given the osmotic pressure on the two sides of the membrane. On the inside the blood plasma protein tends to draw water from the rinsing fluid to the blood. This can-be prevented by making the rinsing fluid isotonic with the addition of glucose. If desired it can be made hypertonic and capable of withdrawing fluid from the patient.

Table 1: Statistical data of patients receiving traetment

S .No	Diagnosis	Hours of dialysis	Blood flow ml/min	Fall in blood urea mg/ml	Survival days
1	Bilateral hydronephrosis	1.0	10	470-?	3.0
2	Cortical necrosis(post-partum)	3.3	75	316-223	0.3

3	Post-traumatic anuria	4.1	86	390-211	-
4	Haemoglobin nephrosis	7.5	58	460-209	0.5
5	Acute glomerulonephritis	3.0	80	504-428	0.4
6	Chronic nephritis	1.0	72	750-?	0
7	Bilateral hydronephrosis	4.4	51	440-292	1.6
8	Post-operative anuria	4.1	76	424-264	-
9	Aspirin suicide	3.0	58	105-59	5.0
10	Acute glomerulonephritis	2.3	50	428-307	0.2
11	Chronic nephritis	3.7	70	400-238	0.4
12	Bilateral hydronephrosis	3.3	80	360-178	14.0

TYPES OF ARTIFICIAL KIDNEYS

Artificial Kidney Employing Dialysis

The rotating type of artificial kidney works purely by dialysis. A thin film of blood moves by gravity through a long cellophane tube wrapped spirally around a rotating drum which is partially immersed in rinsing fluid. The dialyzing capacity of this kidney in terms of clearance, 100 to 200 cc. per minute. While the original model was used by Mac Lean, de Leeuw, van Noorwijk, Palmer and Fishman, and details have been altered by others (Bywaters and Joekes, Vanatta, Merrill, Kearnsand Darmady) its main principle of a rotating drum has remained unchanged. This type of kidney has been used successfully on patients in Europe, Canada and the United States. It may be concluded that dialysis of the blood across a cellophane membrane removes adequately the waste products from the organism, and that death in uremia is a result of the accumulation of such waste products.

Artificial Kidneys Employing Filtration

It might be called an artificial glomerulus. The human kidneys need a filtrate of 150 liters per 24 hours to produce 1.5 liters of urine per day. In constructing an artificial kidney that works with filtration, one might have to reinfuse 148.5 liters of fluid per day.

Artificial Kidney Employing Dialysis and Filtration

Derot et al dipped a rat's small intestine in a 10 per cent formol solution for fixation and sterilization. It was then rinsed and one end connected to the radial artery of a patient and the other to a vein. This dialyzing membrane was immersed in rinsing fluid. The older artificial kidneys utilize collodion tubes or peritoneum; the newer types utilize cellophane tubes or chambers through which blood is forced under pressure while negative pressure is applied through the rinsing fluid. The most efficient is doubtless the Skeggs' and Leonards' model in which cellophane sheets are compressed between rubber plates; blood and rinsing fluid flow through grooves in the rubber on opposite sides of the cellophane.

Artificial Kidney Employing Exchange Resins

The artificial kidney designed by Muirhead and Reid consists of a resin base composed of nine parts cation exchange resin and one part of anion exchange resin. Retention products are absorbed by these substances. Subsequently, a multicenter, randomized, controlled, open-label Phase II clinical trial was performed in 2004 and 2005, which enrolled 58 critically ill patients with ARF [44]. 18 patients received continuous renal replacement therapy (CRRT), whereas 40 patients were treated using continuous venovenous hemofiltration (CVVH) and received additional treatment with a RAD. Patients were treated for up to 72 h. The results showed effects on 28-day and 180-day survival, which were improved in patients receiving CVVH plus RAD treatment. Only the effects on long-term survival (180 days) were significant. This study was revolutionary but was also heavily criticized. It was pointed out that the study was severely underpowered [45].

CASE-STUDY

A female, aged 52, was admitted to St. John's Hospital, Lewisham, for removal of gall-stone examination.-B.P. 135/85. Urine: no albumin, sp. gr. 1020. Operation following myanesin injection, cholecystectomy was performed with the removal of a stone impacted at the junction of cystic and common duct. Appendix was removed and right

kidney felt to be normal. The blood urea rose and remained at a very high level despite a urine output of about a litre per day and some vomiting. Urine studies after operation showed albuminuria.

Post operative oliguria. 800 blood 400 urine urea

The data shows the following cholecystectom, dialysis removed 33 grams urea and blood urea fell from 424 to 264 mg%, with gradual recovery on a high fluid intake, and a later improvement of concentrating ability. Many granular casts, a specific gravity 1010-1014, chloride content (as NaCl) 200 mg. (third and fifteenth post-operative day), urea 600 mg.% (fifteenth day) and 100 mg. % (twenty-third day). Blood studies showed hemoglobin 10-2 grams %, plasma protein 5 grams% (sixth day), chloride as NaCl 370 mg%, CO2 (C.P.) 47-6 vols.% (seventeenth day), sodium 288 mg%, phosphate 10-2 mg. %, creatinine 10-7 mg.% (twenty-third dai). 1 Due probably to sulphate retention.

On admission to Hammersmith Hospital(twenty-sixth post-operative day)she was mentally confused, no oedema, no raised venous pressure, B.P. 155/90, CO2 (C.P.) 38 5 vols. Y., chloride as NaCl 468 mg %, blood urea 424 mg %, sodium 334 mg%, potassium 20'5 mg %. She was dialysed for 4-8 hours and given four bottles of blood, with the removal of 33 grams of urea and a reduction of blood urea to 264 mg%, rise of chloride to 548 mg% and of CO2 (C.P.) to 45 ml%. In the eight days following admission and dialysis almost anything given by mouth was vomited and despite a large parenteral intake blood urea rose and urine output remained stationary at about 1.2 to 1.5 litres/day. On the thirty-fifth post-operative day intravenous therapy started a gradual increase in output (which thereafter rose to 4 litres/day) and, as may be seen from the chart, a gradual rise in urine urea concentration occurred to 400 mg% despite this large diuresis and the continuously falling blood level, thus attesting a renal recovery. Follow-up studies have shown no abnormality by pyelography, and function has gradually returned towards normal.

Renal functional recovery days post-op. clearance figures

Glomerular filtration (mannitol)	: 4'2 ml./min.
Renal plasma flow (PAH)	: 10 4 ml./min.
Glomerular filtration (mannitol)	: 20-0 ml./min.
Renal plasma flow (PAH)	: 130-0 ml./min.
Urea clearance	: 26% of normal.
Creatinine clearance	: 20-0 ml./min.
Urea clearance	: 39 % of normal.
Creatinine clearance	: 168'0 ml./min.
Renal plasma flow	: 452 0 ml./min.

I.V.P. showed fairly good concentration both kidneys, with normal outline.

CONCLUSION

This was probably a case of pigment nephrosis due to myanesin haemolysis. The available data was insufficient to support this or any other etiological hypothesis. Of the remaining 8, all died at varying intervals, up to fourteen days. In some cases this was due to the inevitably fatal character of the disease, as in several with severe and advanced glomerulonephritis; in some, it was due to the dangerously labile cardiovascular state, and this was particularly noticeable in the cases with acute glomerulonephritis where it seemed very easy to overload. In one case where it seemed possible that we might be successful, in that the patient had a pigment nephrosis, conditions antecedent to his admission tipped the scales against his recovery.

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