

A CONVENIENT HAEMOPERFUSION MICRO-APPARATUS OVER CHARCOAL FOR THE TREATMENT OF ENDOGENOUS AND EXOGENOUS INTOXICATIONS

ITS USE AS AN EFFECTIVE ARTIFICIAL KIDNEY

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It is the purpose of this paper to describe a new apparatus for the effective removal of certain substances (creatinine, uric acid, indican, phenolic compounds, guanidine bases, organic acids) directly from the circulating blood of uraemic patients by a simple and short (30-60 minutes) haemoperfusion over charcoal. Besides its verified usefulness as a practical and efficient artificial kidney for the management of renal insufficiency, this device may be used in the treatment of gouty arthritis, and barbiturate, salicylate and glutethimide poisoning, judging from observations made so far. The apparatus does not require priming blood and its cost does not exceed five dollars.

MATERIALS AND METHODS

The apparatus consists of a siliconized glass cylinder of 6 cm. internal diameter and 20 cm. length. The ends are designed to fit a system consisting of a 100 mesh filter cylinder, a rubber stopper and a nipple, which are closed with a screw to make the column air and water-tight (Figure 1. 1, 2). This filtering system is the same as that used by Baxter in their blood administration set No. 8. The cylinder is loosely packed with about 200 g. of active charcoal in a purified and granular form, well washed with deionized tap water. The charcoal prepared by Merck for gas chromatography (particle size 0.50-0.75 mm.) is suitable. The apparatus is assembled and is sterilized with the necessary siliconized tubing at 120°C for 2 hours.

The glass cylinder is connected with a container by tubes A and B and the column of charcoal is rinsed from below upwards with 2 of sterile physiological saline solution containing 100 mg. heparin/l. The apparatus is finally primed with about 200 ml. of the same solution (Figure 1, 3). The heparinised blood is perfused over the charcoal by connecting the rubber tubes A and C to previously cannulated vessels and is circulated in antigravity direction. In this way the particles of charcoal are able to float in the blood. Blood flow through the apparatus was measured with a simple flow meter (Usifroid, Paris) installed in place of the glass tubing; a flow of about 140 ml. per minute is achieved with arterial pressure alone, reflecting the low resistance of the apparatus. A pump attached to the proximal tubing A may augment the flow to any desired level (200- 400 ml. min.) and permits the use of veno-venous by-pass (Figure 1.1). At the end of the haemoperfusion the remaining blood in the apparatus is slowly returned to the patient.

If the column of charcoal is saturated and the severity of the biological abnormalities requires a second haemoperfusion (v. inf.) it is very

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easy to repeat it after a few hours or to prolong it by replacing rapidly with another column. The new column, primed with heparinised saline, is inserted into the extracorporeal circulation below the old column (at junction of glass tube and rubber tube B, Figure 1). Blood is allowed to flow again till 250-300 ml. have filled the new apparatus and displaced its saline content into the old column. The blood from the old column is by the same manoeuvre displaced into the patient. The old column is now removed. The manipulation is easy and takes only about 5 minutes; it minimises blood loss and prevents overhydration of the patient.

The blood samples (plasma or serum) collected from the systemic circulation and the proximal and distal tubes were analysed for urea⁽¹⁾, endogenous true creatinine⁽²⁾, uric acid⁽³⁾, indican⁽⁴⁾, phenolic compounds by the xanthoprotein reaction⁽⁵⁾, guanidine bases by a sensitive method⁽⁶⁾ using the Sakaguchi reaction for arginine, sodium and potassium by flame photometry, calcium and magnesium⁽⁷⁾, phosphates⁽⁸⁾, sulphates⁽⁹⁾, chloride⁽¹⁰⁾, organic acids⁽¹¹⁾, bicarbonate, protein, fibrinogen⁽¹²⁾, haematocrit, haemoglobin, plasma haemoglobin, red cells, white cells, differential count, platelets and sedimentation rate, using standard methods⁽¹³⁾. Blood pH was determined electrometrically at 37°C (pH meter, Methrom No. 322).

RESULTS AND DISCUSSION

Experimental data:

Five dogs weighing between 10 and 17 Kg. were anaesthetized with intravenous nembutal (25 mg./Kg.). The femoral artery and vein were cannulated and connected to the apparatus. The dogs received 1.5-2.5 mg. heparin per Kg. body wt. intravenously. The perfusion time was 10, 20, 30, 60 and 90 minutes with a flow rate of 50-100 ml./min.

All dogs withstood the perfusion very well, none presented any undesirable side effects and all were in full health the following day. The effects of haemoperfusion on blood elements, fibrinogen and proteins were estimated in blood samples from proximal and distal tubes every 10 or 20 minutes and 24 and 48 hours after the end of the procedure. No destructive effect on the blood elements was noted. The white cell count at the end of the procedure was 75-130% of the control value and the haematocrit and red cell count were 100-120% of control levels. The plasma haemoglobin level was always within normal limits. The platelets were unchanged in 3 animals but in the other 2 there were falls to 50 and 80% of the original level. A constant drop in plasma fibrinogen was noted, in some cases down to 40%, but it returned to pre-infusion levels within 24 to 48 hours. The sedimentation rate fell in parallel with the fibrinogen level. The plasma proteins were temporarily reduced by scarcely appreciable amounts (5%).

Clinical data:

Clinical experience comprises 20 haemoperfusions on patients with terminal chronic renal failure, who were heparinized with 2.5 mg./kg. body wt. aqueous heparin. Blood was perfused at a flow rate of 150-300 ml./min. for 30-90 mins. Arterial blood was sampled from the proximal tube before, and 2 hours after ending, the perfusion. Samples were also taken from the distal tubing 5 minutes after the start of the haemoperfusion.

In all instances the procedure followed a normal course. Experience has shown that the above mentioned doses of heparin are ordinarily sufficient to prevent coagulation during a haemoperfusion of 60 minutes. The relatively high dose of heparin is not dangerous since the procedure is short and circulating heparin is neutralised with protamine or polybrene at the end. Regional heparinisation can be employed. In some cases there was an elevation of temperature (a pyrogenic reaction) at the end or after a few hours of perfusion. In most cases there was a drop in blood pressure during the first five minutes of haemoperfusion, but this was easily managed by drip administration of neosynephrine hydrochloride solution (25-50 mg./l.) into the distal tubing. No destructive effects of charcoal haemoperfusion on the formed elements of the blood were noted. The values of haematocrit, haemoglobin, red and white cell counts, platelet count, total proteins, fibrinogen and sedimentation rate fluctuated in the same way as in the dogs and the changes were not important. Haemolysis was consistently absent.

The improvement in some of the biochemical abnormalities during the 20 haemoperfusions in patients with chronic renal insufficiency was very impressive. The degree of correction varied with the original blood level, the volume of body fluids and the total absorbing capacity of the charcoal column. The last was studied more intensively in vitro, using different uraemic plasma, with the following results:-

True creatinine	800-850 mg.
Uric Acid	750-800 mg.
Indican	25-30 mg.
Phenolic compounds (as phenols)	150-175 mg.
Quanidine-bases	85-100 mg.
Organic acids	30-35 mEq.
Urea	3-4 g.
Phosphates, magnesium	traces
Sodium, calcium, chloride	nil
Sulfates, bicarbonates	nil

As representative cases, we tabulated the results in three patients under different conditions (Tables I, II and III). Charcoal can remove concurrently at the beginning (in one passage of the blood) almost the total quantity of plasma creatinine uric acid, indican, phenolic compounds, and quanidine bases, and reduces effectively the organic acids. Another important point is the correction of the low pH, the interpretation of which cannot be adequately determined. The final results are also very satisfactory. These laboratory results have been compared to those of 300 haemodialyses with a Kolff twin coil kidney, with reference to the above named substances. It is estimated that a 60 minute haemoperfusion over 2 or 3 charcoal columns has about the same efficiency as a haemodialysis of 4 to 6 hours duration. This new method has the advantage of being equally effective in patients with less marked biochemical abnormalities, since its effectiveness depends on the absolute absorbing capacity of charcoal and is not influenced by the blood level, as is haemodialysis, On the other hand haemoperfusion removes very little urea, magnesium and phosphate and no sulphate, potassium or water, and it cannot raise the lowered bicarbonate and calcium levels.

The notable correction of the biological abnormalities by haemoperfusion over charcoal coincides with an immediate clinical improvement. The general condition improves remarkably. The lethargy and the gastrointestinal symptoms (anorexia, nausea and vomiting) are decreased. On one occasion (Figure 3) we observed the disappearance of a loud pericardial friction rub twelve hours after haemoperfusion. In contrast to haemodialysis, which constantly produces an excessive oliguria for a two to three days period, the diuresis is not affected by haemoperfusion. The influence of haemoperfusion upon anaemia, high arterial pressure and the neurological disorders of chronic renal insufficiency are the principal object of our present studies.

A problem of great interest is the possible absorption by charcoal of some of the other constituents of blood. It has been demonstrated so far that charcoal does not absorb from the plasma; cholesterol, bilirubin, iron, pyruvic and oxaloacetic transaminases, mercury or phenylhydantoins. On the other hand charcoal absorbs very effectively the several pigments of normal urine (urochrome) and a large number of poisons. By repeated determination in vitro we observed that our charcoal column can absorb from plasma a considerable amount of barbiturates (15-2.0 g. of barbital, phenobarbitone, pentobarbitone), salicylates (2.5 g. of salicylic acid) and glutethimides (2.0 g. α -phenyl- α -ethyl-glutaric acid or Doriden)⁽¹⁴⁾.

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E.J.DORHOUT MEES (Utrecht): Peut-être vous l'avez mentionné, mais je n'ai pas compris, que les éléments sanguine ne changeaient pas. Qu'est-ce qui se passe avec les thrombocytes, parce que toujours dans ces séances avec les reins artificiels, on voit une chute et je pourrais imaginer que sur le charcoale il y avait une adhérence énorme.

H.YATZIDIS (Athens): Dans la moitié de nos cas il y a une diminution de thrombocytes de 10-20 pour cent, sans importance particulière à notre avis.

W.J.KOLFF (Cleveland): Ce sont des résultats très remarquables. Voulez-vous bien répéter les taux d'urée du sang et aussi, pour les mêmes cas, les quantités que vous avez éliminées.

H.YATZIDIS (Athens): La capacité totale de notre capsule envers l'urée est de l'ordre de 3-4 g. Il n'y a pas par conséquent une influence importante de l'hémo-perfusion sur l'urée plasmatique, contrairement en ce qu'on observe pour la plupart de substances urémiques.

S.T.BOEN (Seattle): I may have missed it but I should like to ask how you prevent charcoal from going into the patient. What kind of filter do you use?

H.YATZIDIS (Athens): Il s'agit d'un filtre métallique portant des trous de 0.15-0.20 mm. (100 mesh/inch). C'est le même filtre utilisé par Baxter pour son set de transfusion sanguine.