A POSSIBLE WAY OF PREVENTING HAEMOCHROMATOSIS IN PATIENTS UNDERGOING INTERMITTENT HAEMODIALYSIS

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Patients undergoing intermittent haemodialysis require 2-3 units of blood a month. It is true that Shaldon and his co-workers proposed to cut down this blood requirement to almost zero, but most dialysis units, including our own, do not find that feasible. The main reason may well be that in most hospital units some research project is going on, which requires repeated blood samples, and that most units feel that their patients are doing better if their haematocrit is kept between 20-25%. This means that the resulting iron overload reaches an estimated amount of 200-300 mg iron monthly, which is still further argumented by the probably increased iron absorption from the small intestine. Therefore, most patients undergoing intermittent haemodialysis manifest an increased level of serum iron with concomitant decrease in serum iron binding capacity.

Many researchers have contemplated therefore the use of iron-chelating agents, which should be able to bind the iron in a complex form. If this complex is dialysable, it could be dialysed out during regular haemodialysis. As far as we know, the search for a suitable chelating agent has not been successful because of one difficulty or another.

The prevention of post-transfusional iron overload and haemosiderosis (with the eventual iron deposition and damage to the parenchymal cells of the liver, heart and endocrine glands) has been made possible during the last decade with the chelating agent desferrioxamine (Desferal®). Desferrioxamine obtained from a metabolite of Streptomyces pilosus, exhibits a remarkably strong and specific affinity for iron ions; 100 parts of the drug bind 9.35 parts of iron to form water-soluble ferrioxamine, the renal clearance of which equals that of inulin.

The following report deals with preliminary studies to determine the dialysability of the iron complex (ferrioxamine) through artificial membranes and through the Kiil dialyser in vitro and during the actual conditions of haemodialysis.

Our results may be summarized as follows:
1. Heparinized blood was treated with desferrioxamine and dialysed for 8 hours against normal saline. Iron content of the blood dropped to 15% of the original value, while a control set-up under identical conditions, but without added desferrioxamine, showed no change in its iron content.

2. Radioactive iron labelled (Fe³⁺) ferrioxamine complex prepared by incubation of desferrioxamine with the radioactive iron sulphate was added to 2 litres of heparinized blood. This blood was recirculated at a rate of 60 ml/min. through a two-layer Kiil dialyser, regular dialysing fluid flowing in a single pass at 500 ml/min.

Blood samples were taken at 30 min. intervals and radioactivity determined. The decline of radioactivity in plasma could be represented by a straight semi-logarithmic line with a half-time of 100 minutes. Dialysance was calculated to be about 6.0 ml/min. Similar, somewhat higher, dialysance values could be obtained by injecting radioactive
ferrioxamine into a patient before the start of haemodialysis and following the declining radioactivity of consecutive blood samples during actual haemodialysis.

3. Dialysate was collected in hourly batches of 1 litre during the 12-hour period of the treatment and iron content was determined. While in control patients, who did not receive desferrioxamine prior to the start of the dialysis, no iron could be detected, a measurable amount was found in patients who received desferrioxamine. We calculated that during a 12-hour dialysis about 40 mg of iron could be removed by the administration of 500 mg of desferrioxamine. It still has to be determined whether administration of a larger amount of desferrioxamine will increase the amount of iron which can be removed by dialysis.

In summary it seems that desferrioxamine may be a useful agent to prevent, and maybe even to cure, haemochromatosis in patients on chronic haemodialysis.