DIALYSIS IN ACUTE INTERMITTENT PORPHYRIA

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Acute intermittent porphyria is known as the most frequent congenital disturbance of porphyrin metabolism. The disease is characterized clinically by periodic attacks of intense abdominal colic, obstinate constipation, neurotic or even psychotic behaviour, and neuromuscular disturbances. The neurological manifestations are quite varied and may include neuritic pain of the extremities, areas of hypaesthesia and parasthesia and motor paralysis. Paraplegia or a complete flaccid quadriplegia may ensue and may be followed by bulbar paralysis and death. The mortality rate is very high.

During the attacks of the disease there is an increased formation of delta-amino-levulinic-acid and porphobilinogen in the liver. These metabolites of porphyrin synthesis are excreted by the kidneys. Both substances are non-toxic. However, the assumed toxic agents, which are responsible for the clinical manifestations, are not yet known.

To relieve the acute symptoms, different chemical substances are recommended, such as chlorpromazine, corticosteroids, BAL, and adenosine-monophosphoric acid.

In one of our patients with acute intermittent porphyria we had tried such medical treatment without any success. Since the patient was rapidly deteriorating, we decided to try treatment by the artificial kidney, assuming the causative toxic agent to be dialysable.

The figure illustrates the symptoms of the patient before, during, and after dialytic treatments.

The patient was a 29 year old woman, mother of a 3 year old child. Since 1962 she had complained of loss of weight, progressive weakness and intermittent colicky abdominal pains. In March 1963, the patient was admitted to our hospital because of severe abdominal colic with nausea and vomiting. She showed neurotic symptoms, a marked loss of weight and a tachycardia. The abdomen was distended and tender. The urine was of a dark red colour showing a positive Watson-Schwartz reaction.

In spite of the treatment with infusions of fructose, vitamins, and prednisone, the symptoms continually increased. On the 11th day after onset of the severe attack, a quadriplegia developed. Within hours the symptoms of bulbar paralysis appeared. In this desperate situation we decided to attempt treatment with the artificial kidney. After 4 hours of dialysis, the patient showed an astonishing reduction of all the symptoms. She stated that the abdominal pains had disappeared. The disphasia passed. The respiration became normal. After 6 hours the dialysis was stopped. At this time the other muscular paralysis was also markedly improved.

Six days after the first dialysis, the muscular paralysis and the severe respiratory disturbances occurred again. So the artificial kidney was used once more, which resulted in a normalisation of the breathing, appearing after three hours of treatment. The other symptoms showed an improvement as well, though not quite so impressive as at the time of the first treatment.

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Later on, the acute symptoms disappeared slowly. During the following months, the polyneuritic manifestations diminished gradually. The patient was discharged from the hospital. She felt quite well and kept on working as a housewife.

One year later, in May 1964, she was readmitted again with symptoms of acute intermittent porphyria. This time, she complained of severe abdominal as well as back pains. A treatment with fructose, ATP, and vitamins did not prevent a partial muscular paralysis of the extremities. She became depressive and somnolent. At this time a third treatment with the artificial kidney was tried and resulted in complete abolition of all her mental disturbances. The severe pains disappeared 5 hours after the treatment was begun. On the other hand the improvement of the muscular paralysis was only observed after some days. The patient was dismissed a fortnight later and until now she feels fairly well.

All three times we noticed a marked clinical improvement of the symptoms of acute intermittent porphyria during or after dialysis. Are these improvements the true effects of the treatment by the artificial kidney? Spontaneous remissions even of severe attacks of the disease have been reported.\(^1\) Some remissions may have been also accomplished by means of different chemical agents.\(^2\) But in all cases reported the earliest remission appeared not earlier than 4 days to several months. The clinical improvement by dialysis, however, was noticable in only 3 - 6 hours after the beginning of the treatment. This short interval of time makes it probable that the remissions are a true effect of haemodialysis. We were of the opinion, that such treatment had not previously been tried, but two weeks ago we learned that Last\(^3\) had also reported on 'Haemodialysis in acute porphyria'. There is another observation similar to ours. Deparis and co-workers\(^4\) described the disappearance of nausea and vomiting in a 41 year old woman with acute intermittent porphyria during an exchange transfusion of 6 litres. Two to six hours later the abdominal pains were also abolished. The paralysis of an arm was not influenced.

Toxic metabolites of porphyrin synthesis may be withdrawn from the organism by the exchange transfusion as well as by the treatments with the artificial kidney. Since these substances are still unknown, a chemical proof of such an effect is not possible. In comparison with the results obtained through exchange transfusion we feel that extracorporeal haemodialysis is probably more effective.

Therefore our observations encourage further attempts of dialytic treatment in severe attacks of acute intermittent porphyria.

REFERENCES
SYMPTOMS OF ACUTE INTERMITTENT PORPHYRIA INFLUENCED BY DIALYSIS

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Figure 1.
THE CHAIRMAN, W. J. KOLFF (Cleveland): I should like to compliment Dr. Jutzler on the very beautiful way in which he has shown his clinical results in the slides. It is one of the nicest ways I have ever seen it presented.

J. HESS THAYSEN (Copenhagen): In the acute attack of porphyria, toxic metabolites may be retained. We do not know anything about their nature, but it cannot be excluded that they may be dialysable, and that the clinical improvement, which you have observed with the use of the artificial kidney, may be due to this fact.

I should like to draw your attention to one other possibility, however. Recently I listened to a paper by Dr. Bent Nielsen and Dr. N. A. Thorn both of Copenhagen (Excess urinary excretion of antidiuretic material in acute intermittent porphyria with hyponatremia. Acta Neurol. Scand. (1964). 40, 186; to be published also in the Amer. J. Med.). These doctors showed that two patients with acute attacks of porphyria were severely hyponatre- mic and presented symptoms compatible with water intoxication (convulsions, coma). In one of them they demonstrated an increased excretion of antidiuretic material in the urine. Symptoms worsened when the patients were given free access to water and improved on water restriction and administration of hypertonic saline.

When you treat a patient with acute porphyria with dialysis you may thus be doing two things. You may - as you said - remove some hypothet- ical toxic agents. You may also correct overhydration and bring the serum sodium up.

I do not know whether antidiuresis is an obligatory concomitant of an attack of acute porphyria. Possibly it is not. However it appeared to me from your slides that the mental symptoms of your patients improved more rapidly than the polyneuritic symptoms following dialysis. I should therefore like to ask you whether serum sodium was measured before and after the dialytic treatment? Did you find very low values for serum sodium before dialysis and normal ones afterwards?

G. A. JUTZLER (Homburg): Our patients showed no disturbances in water and electrolyte metabolism. She was normally hydrated and had normal plasma sodium levels before, during, and after dialytic treatments.

A. PRINGLE (London): One of my colleagues recently dialyzed a patient with acute porphyria. She came with severe barbiturate poisoning, and it was only the fact that after dialysis she remained paralyzed that made us realise that she had acute porphyria in addition. The porphobilinogen in this particular patient's urine stayed only for a very short time. I cannot quote the number of hours that we dialyzed this patient, it was certainly over six, but I wondered whether, with your patient, there was any bar- biturate precipitation of the porphyria.

M. FARK (Homburg): I do not think she had any barbituric acid; she was not treated with barbituric acid at all because she was well known to have porphyria.