Electrocardiographic Changes during Hemodialysis with the Artificial Kidney

II. The Treatment of Digitalis Intoxication

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In a series of 63 hemodialyses with the artificial kidney, digitalis had been administered 30 times. The occurrence of digitalis intoxication is discussed and the results of treatment are analyzed.

In a previous communication we reported that hemodialysis with the artificial kidney consistently corrects acidosis, hyperkalemia, and hypocalcemia. We have observed, as have others, that the patient with heart disease receiving digitalis may manifest electrocardiographic changes of "digitalis effect" and toxicity during repair of fluid and electrolyte imbalance.

The management of digitalis toxicity often includes modification of plasma electrolyte concentrations. The administration of potassium salts or reduction of plasma calcium concentration by chelating agents is frequently successful. Clinical response and plasma electrolyte change, however, often fail to parallel each other. Therapeutic successes in the absence of demonstrable change in measurable plasma ionic constituents have been attributed to change in intracellular concentration, to altered ion gradients, or to altered rate of ion transfer at the cellular membrane. Lack of clinical response, despite demonstrated elevation of plasma potassium, has also been observed. Exact mechanisms for therapeutic success or failure are poorly understood.

We have previously reported an analysis of electrocardiographic changes in 33 hemodialyses and have correlated them with plasma electrolyte concentrations. Since then a larger series of patients has been observed. This report summarizes our experience with digitalis intoxication during 63 dialyses performed on 51 patients with acute and chronic renal disease. There were 25 patients with congestive heart failure in this group who were receiving maintenance doses of digitalis (digitoxin) up to the time of dialysis. They were treated with dialysis 30 times. Seven patients showed evidence of digitalis intoxication during 9 dialyses. Analysis of our data may better define the limitations of current therapy of digitalis intoxication during hemodialysis.

Criteria for Diagnosis of Digitalis Intoxication

The criteria for digitalis intoxication were limited to rigidly interpreted electrocardiographic manifestations. These included ectopic supraventricular tachycardia, atrioventricular block, or ventricular irritability occurring in a patient previously exhibiting normal sinus rhythm, in the absence of symptoms and signs of concomitant illness (pulmonary infarction, infection, etc.) that might induce or be associated with arrhythmia. Subjective manifestations of digitalis intoxication were rejected for 3 reasons. Each of these patients presented the uremic syndrome, so that anorexia, nausea, and vomiting were common without relation to medication. Secondly, antiemetics, which might have obscured such phenomena, had been administered to many patients and, finally, results could be evaluated better by objective measurements.

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Arrhythmias were uncommon in patients who had not received digitalis. Several patients had premature ventricular contractions without other arrhythmia or significant electrolyte change. Some severely ill patients developed atrial fibrillation with a rapid ventricular rate during hemodialysis. They were treated with digitalis and are not considered further in this report.

The technics employed for blood sampling and plasma analysis have been described previously.1

RESULTS

Digitalis intoxication was noted in 30 per cent of the dialyses of the patients receiving digitalis. In 26 patients treated by hemodialysis who had no prior digitalis therapy, there was no similar electrocardiographic change. In 2 patients whose dialysis was repeated, the signs of digitalis intoxication appeared on each occasion. Neither age nor sex seemed significant determinants. The cause of renal failure was varied and had no significant relationship to digitalis intoxication. Only 2 patients had had evidence of any cardiac alteration prior to the onset of renal failure. This consisted in the electrocardiographic pattern of left ventricular hypertrophy in each case.

In every instance the arrhythmia appeared during the correction of acidosis, hyperpotassemia, hypocalcemia, or combinations of these. The only treatment employed to correct the arrhythmia consisted in the addition of potassium chloride to the dialysis bath. Short case summaries follow. The serial electrocardiograms in cases 1, 2, and 3 have been published previously.1

Case 1. E. K., a 16-year-old girl suffering from chronic pyelonephritis, developed nodal rhythm during dialysis. Plasma potassium concentration which was 7.4 mEq./L initially measured 4.7 mEq./L at the onset of arrhythmia. Carbon dioxide combining power had risen from 10.8 to 17.2 mM/L. Thirty grams of potassium chloride were added to the dialysis bath and the rhythm soon changed to sinus tachycardia. At that time, plasma potassium concentration was 4.8 mEq./L.

Case 2. C. O., a 10-year-old girl with acute nephritis, developed nodal rhythm or atrioventricular dissociation during dialysis. Plasma potassium concentration was 7.4 mEq./L initially and 4.0 mEq./L at the onset of arrhythmia. Carbon dioxide combining power had risen from 8.4 to 18.8 mM/L. Twenty grams of potassium chloride were added to the dialysis bath, and the rhythm was converted to normal sinus mechanism. Plasma
potassium concentration at that time was 3.0 mEq./L.

During a second dialysis, paroxysmal atrial tachycardia with block was noted. Before this event plasma potassium concentration had changed from 7.4 to 3.6 mEq./L. and carbon dioxide combining power from 11.7 to 21.8 mM/L. After addition of 30 Gm. of potassium chloride to the dialysis bath, the plasma potassium was 4.1 mEq./L. and the rhythm was sinus tachycardia.

Case 3. R. F., a 42-year-old man considered to have subacute glomerulonephritis, manifested the electrocardiographic pattern of left ventricular hypertrophy. He developed premature ventricular contractions giving rise to quadrigeminy during dialysis. Subsequently he exhibited paroxysmal atrial tachycardia with block. During these intervals the serum calcium concentration had risen from 7.4 to 9.5 mg. per cent. There was no significant change in plasma concentrations of potassium or bicarbonate. No therapy was instituted and in a short period of time the rhythm changed to sinus tachycardia.

Case 4. V. W., a 43-year-old man with extensive burns and acute renal failure, developed a supraventricular tachycardia, probably nodal in origin, during dialysis. Plasma potassium concentration, initially 6.3 mEq./L., was 3.9 mEq./L. at this time. Twenty grams of potassium chloride were added to the dialysis bath and the rhythm changed to sinus tachycardia. The plasma potassium was unchanged at a concentration of 3.9 mEq./L. (fig. 1).

Case 5. F. R., a 52-year-old woman with chronic glomerulonephritis, developed multifocal premature ventricular contractions during hemodialysis. Carbon dioxide combining power, which had been 12.3 mM/L. at the start of dialysis, was 16.3 mM/L. Plasma potassium concentration remained normal. Only 5 Gm. of potassium chloride were added to the dialysis bath and the premature ventricular contractions disappeared (fig. 2).

Case 6. J. R., a 57-year-old man with acute renal failure, was treated with hemodialysis on 2 occasions. The electrocardiographic pattern of left ventricular hypertrophy was present. During the initial dialysis, first-degree heart block was noted concomitant with reduction in plasma potassium from 5.5 to 3.4 mEq./L. and an elevation of carbon dioxide combining power from 22.2 to 27.5 mM/L. No treatment was directed toward the first-degree heart block, which persisted for 12 hours after completion of dialysis. During the second dialysis, first-degree heart block again appeared as plasma potassium changed from 5.1 to 3.9 mEq./L. On this occasion, 30 Gm. of potassium chloride were added to the dialysis bath and plasma potassium concentration rose to 4.8 mEq./L. First-degree heart block persisted, however, until after dialysis.

Case 7. M. P., a 52-year-old woman with chronic pyelonephritis, developed first- and second-degree heart block during dialysis. Plasma potassium had changed from 4.0 to 2.5 mEq./L. Ten grams of potassium chloride were added to the dialysis bath and plasma potassium rose to 3.9 mEq./L. Concurrently, the heart block disappeared (fig. 3).

Discussion

In all 9 instances in which the manifestations of digitalis intoxication occurred they were relatively benign, and idioventricular rhythm was not observed, suggesting that these more serious manifestations of digitalis intoxication are relatively rare during hemodialysis.

The management of digitalis-induced arrhythmias should include the addition of potassium chloride to the dialysis bath. The limitations of supplementary potassium chloride administration, however, are evident. In 6 of 9 instances, this treatment appeared effective but the plasma potassium concentration after the addition of potassium to the dialysis bath in 2 of these successful cases was the same as or lower than that at the time of toxicity. We have data to demonstrate an
alteration in cellular potassium concentration during hemodialysis, and have regarded an altered intracellular extracellular potassium gradient or potassium transfer rate across the cellular membrane as an important mechanism in these cases. An explanation is still lacking for the spontaneous reversion of the arrhythmia in case 3 and for the failure of potassium chloride administration (in the face of concomitant elevation of plasma potassium) in case 6.

Rapid elevation of serum calcium can play an important role in the development of digitalis toxicity, since calcium and digitalis have long been known to be synergistic in action. Case 3 may illustrate such mechanism.

The recent development by Wacker and Vallee of an accurate method of measuring serum magnesium concentration has allowed comparison of the similarities of electrocardiographic changes produced by hyperpotassemia and by hypermagnesemia. It is possible that a reduction of serum magnesium from elevated levels during hemodialysis may contribute to the defects of rhythm and conduction of digitalis intoxication.

Digitalis intoxication constitutes a hazard to many patients undergoing hemodialysis. It is impossible to predict its occurrence, and results of treatment are occasionally unsatisfactory. It appears advisable, therefore, to defer the administration of digitalis until after hemodialysis whenever possible. A more rational approach must await further clarification of the pathogenesis of digitalis toxicity during hemodialysis. In any case, during hemodialysis, frequent electrocardiographic observations are warranted for early detection of digitalis intoxication.

**Summary**

The appearance and management of digitalis intoxication during 63 hemodialyses with the artificial kidney have been analyzed. Digitalis had been administered in 30 instances. In 9 instances digitalis-induced arrhythmias were observed. Their occurrence had no relation to age, sex, or cause of renal insufficiency.

In all instances the arrhythmia was relatively benign, and idioventricular rhythm was not observed. The addition of potassium chloride to the dialysis bath was effective in 6 cases, although the mechanism of action appears obscure in 2 of these. In 1 patient, treatment failed, and in another spontaneous reversion to sinus rhythm was observed.

Continuous electrocardiographic monitoring is necessary during hemodialysis. It appears advisable to avoid treatment with digitalis before the procedure whenever possible or to remain alert to the problem of induced toxicity if digitalis administration is urgent.

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**Summario in Interlingua**

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Continue controlo electrocardiographic es necessari durante le hemodialyse. Il pare desirabile evitar tractamento a digitalis ante le manovra del hemodialyse artificial. Si le administration de digitalis es urgele, le problema de toxicitate require un semper-vigilante attention.
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J. ARTHUR THOMSON
British: professor of natural history, editor and author: 1861-1933

Many of the misunderstandings that have arisen in regard to "science and religion," "science and philosophy," and similar questions are due to a failure to recognize what science aims at—the formulation of things as they are and as they have come to be. The primary aim of science is not to "explain," except in the sense of saying, "this is the outcome of that." It does not inquire into the "why" of things, the purpose or significance of the cosmos.—The Outline of Science, Vol. 4, p. 1165. From Great Companions. Readings on the Meaning and Conduct of Life from Ancient and Modern Sources. Vol. I, Boston, The Beacon Press, 1952.
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