POTASSIUM
In the Treatment of Diabetic Coma

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Emphasis on early and adequate use of insulin and fluid therapy and the introduction of antibiotics have resulted in a marked reduction in the mortality from diabetic coma during recent years.[1, 2] Hope for further decrease has been stimulated by the demonstration of profound alterations in potassium metabolism and the response of these changes to appropriate therapy.

POTASSIUM METABOLISM IN ACIDOSIS

Atcheley and others[3] first demonstrated a markedly negative potassium and phosphorus balance during the development of diabetic coma with a corresponding positive balance during recovery. Holler[4] proved the clinical significance of potassium in diabetic coma in a patient who developed severe dyspnea due to almost complete paralysis of the respiratory muscles 21 hours after the initiation of therapy. The concentration of serum potassium was 2.5 mEq./L.; potassium chloride given intravenously produced a prompt and dramatic improvement. It was immediately suspected[5] that in many cases death attributed to respiratory failure or vascular collapse after apparent recovery from acidosis may have been, in fact, caused by hypopotassemia. That this suspicion was well-founded has been adequately proved.[5–7]

During diabetic acidosis, first there is increased glycogenolysis and gluconeogenesis resulting in a marked shift of potassium and phosphorus from the intracellular space; secondly, there is profound diuresis which washes out the intracellular ions thus mobilized; and thirdly, there may be terminal dehydration with contraction of the intracellular and extracellular spaces resulting in oliguria, prerenal azotemia and hyperpotassemia.[3, 8] A paradoxical condition of elevation of serum potassium and phosphorus despite a total body depletion of these elements is produced.[8–12]

During therapy, on the other hand, there are 1) rehydration with expansion of the extracellular space and resulting dilution of potassium; 2) re-establishment of urinary excretion with further loss of potassium; and 3) the movement of potassium into cells during glycogen storage and cellular rehydration. A moderate to marked fall in serum potassium results during the treatment of diabetic coma.[8–12] The fall in serum potassium, although significant, is not usually of a degree sufficient to produce untoward effects; nevertheless, the numerous demonstrated examples of morbidity or death due to hypopotassemia make mandatory the consideration of this possibility in all cases of diabetic coma.

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HYPOPOTASSEMIA

Symptoms of hypopotassemia encountered in the treatment of diabetic coma include: varying degrees of skeletal muscle paralysis with or without associated respiratory distress,[4, 5] vascular collapse[13] which responds to intravenous infusion of a solution containing potassium but not to blood transfusion, and intestinal ileus with increasing nausea and vomiting (see below).

Opinion varies as to the best method of prevention and treatment of hypopotassemia. Some authors[2, 14] feel that infusion of fluids containing potassium in low concentration should be stated routinely three to six hours after institution of therapy, providing the urinary output is adequate. Others[15] think that the requirements for potassium usually can be satisfied with early oral feedings if the initial dosage of insulin has been adequate, and if no intravenous glucose has been given early in therapy. The latter observers have reserved oral or intravenous potassium for the treatment of symptoms of hypopotassemia. We believe that prevention of hypopotassemia is more logical than treatment after symptoms have occurred. Since potassium can be given orally with safety in the presence of an adequate urinary excretion, we have administered it routinely except in mild cases. Such therapy prevents clinically significant hypopotassemia in virtually all instances; it obviates the necessity for determination of serum potassium in the majority of cases.

In the event of inability of the patient to ingest potassium, or if symptoms of hypopotassemia appear, additional potassium may be used intravenously. Study of the serum potassium with the flame photometer becomes valuable if the patient is not responding to therapy properly. In any case with vascular collapse and oliguria, the use of potassium intravenously would be hazardous in the absence of serum potassium determination.

PLAN OF TREATMENT

The patient is given an initial dose of insulin which must be based entirely on clinical evaluation. In adults this varies from 100 to 300 units. As soon as the blood sugar is determined, the initial dose is supplemented so that the total amount of insulin given in the first one or two hours in units is equal to half the admission value for blood sugar (Table I). These dosages are reduced in the young, the aged, or in any instance where insulin sensitivity is recognized or suspected. They are increased in the presence of known insulin resistance. We do not hesitate to give all or part of these amounts of insulin intravenously if vascular collapse is present or impending. Insulin is used in regular or crystalline form only during the first twenty-four hours.

TABLE I. Total Amount of Insulin Given in the First Two Hours

ADMISSION BLOOD SUGAR, mg. per 100 cc.	INSULIN DURING FIRST 2 HRS., UNITS
300	150
400	200
500	250
600	300
700	350
800	400
900	450
1000	500

After the initial dose of insulin is administered, the other measures usually advocated in the treatment of diabetic coma are carried out. At first fluids are given intravenously in the form of physiological saline only. Glucose is never given until there has been demonstrated an adequate fall in blood sugar, or until the urine has become sugar free. Intravenous treatment with lactate is not given; sodium bicarbonate is used only in rare instances.

An indwelling catheter is always inserted into the bladder. One can then ascertain merely by a glance whether or not the urinary output is adequate.

After a period of four hours has elapsed, the contents of the stomach are aspirated; 80 cc. of 10 per cent solution of dibasic potassium phosphate diluted in 100 cc. of water are instilled into the stomach. This treatment is given only if it can be domonstrated that the rate of flow of urine from the catheter is adequate. The rate of flow (number of drops per minute) from the catheter should be approximately one-half that of the intravenous saline.

As soon thereafter as the patient is able to take fluids without nausea, he is given hourly feedings of 100 gm. of fruit juice, broth or milk, to which 10 to 20 cc. of dibasic potassium phosphate have been added. This regimen is usually continued for four to six hours.

The level of blood sugar and the carbon dioxide combining power of the plasma (and more recently the serum potassium) are determined at intervals of four hours until return to normal can be demonstrated. If the drop in the blood sugar at the fourth hour is not satisfactory, the initial dose of insulin is repeated in equal or increased amounts.

Intravenous treatment with potassium (in the form of one per cent potassium chloride in the water) is given only if: 1) the patient is unable to take potassium phosphate by mouth, 2) the urinary output is

adequate, 3) there is hypopotassemia as evidenced by vascular collapse, muscular weakness, respiratory distress, or actual measurement.

We have found it necessary to give intravenous potassium in only five instances.

RESULTS

In order to compare our results in the treatment of diabetic coma before and after the inauguration of supplemental potassium therapy in June, 1948, we have carefully reviewed all instances of coma treated by us over a ten year period. All cases of diabetic coma in which the carbon dioxide combining power was less than 10 mEq. are included. The group treated since the use of potassium was started included 11 cases with less serious coma in which food could be taken early and in which there was rapid improvement on therapy without potassium. These cases were not considered separately.

As will be seen in Table 2, the patients treated before and after potassium therapy form roughly comparable groups; the only significant difference being the longer duration of diabetes in the cases treated since the use of potassium was begun.

TABLE 2. Comparison of Cases Treated Before and After Potassium Therapy

	32 Cases Before Potassium Therapy		53 Cases After Potassium Therapy	
	Range	Mean	Range	Mean
Age in Years	3-72	30.8	5-65	31.5
Known duration of Diabetes in years	0-17	4.8	0-27	8.0
Admission Blood Sugar, mg. per 100 cc.	273-1396	592	203-1048	546
Admission Plasma CO_2, mEq/L	4.1-10	7.0	2.7-10	6.3

TABLE 3. Comparison of Insulin Dosage, Fluid Administration and Time Until Urine Free of Diacetic Acid, Before and After Potassium Therapy

	32 Cases Before Use of Potassium		53 Cases Since Use of Potassium	
	Range	Mean	Range	Mean
Insulin Dosage in two hours, units	28-380*	180*	10-700	237
Insulin Dosage in 24 hours, units	80-710*	355*	63-1090	445
Parenteral fluids given in 24 hrs., liters	1-7	4.1	0.5-10.8	5.2
Hours until diacetic acid absent from urine	5.5-21	11.1	2-31	11.3

*Eliminated from these figures is one case with extraordinary insulin resistance in which 440 units of insulin were given in the first 2 hours and 5,490 units within 24 hours after the onset of coma.

Table 3 shows that the administration of fluids and insulin has increased somewhat in the passing years. The average patient now receives almost 500 units of insulin within the first twenty-four hours after admission, and, nearly all of this is given within four to five hours after admission to hospital. It is interesting to note that in spite of the use of larger doses of insulin and increased amounts of fluids, the number of hours required for the disappearance of ketonuria is almost exactly the same in the two groups.

Table 4 shows the amount of potassium given in the 42 cases given this treatment. It will be noted that some patients received as high as 48 gm. of dibasic potassium phosphate (551 mEq. of K.). The average amount administered was 18.6 gm. (214 mEq. of K.).

TABLE 4. Summary of Potassium Administered in 42 Cases

	Range	Mean
Grams K_2HPO_4 Given	4-48	18.6
mEq. K^+ Given	46-551	214
Hours before potassium started	1-12	5.1

After starting this plan of therapy, we had the good fortune to obtain a Weichselbaum-Varney flame photometer. Serial determinations of serum potassium with this instrument have given further proof of the profound changes in serum potassium and of the efficacy of this new plan of therapy.

ILLUSTRATIVE CASE HISTORIES

CASE 1. An eight-year-old, white boy without previous history of diabetes was semistuporous on admission. The level of blood sugar (Figure 1) was 432 mg. per

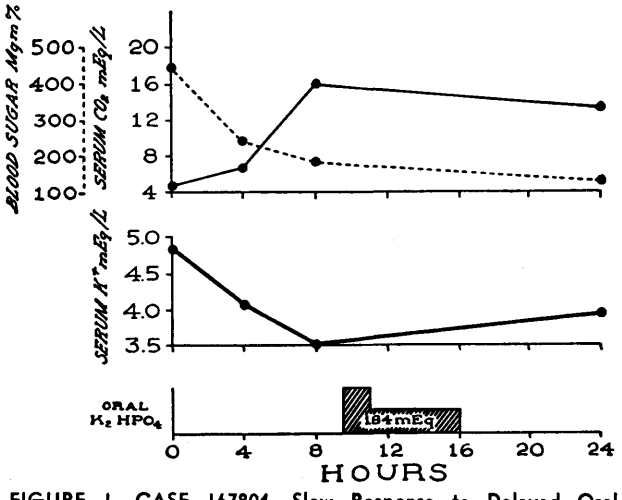

FIGURE 1. CASE 167804. Slow Response to Delayed Oral Potassium Therapy

100 cc. and the carbon dioxide combining power 4.7 mEq. He responded satisfactorily to treatment with 50 units of crystalline insulin and saline given intravenously; the test for diacetic acid in the urine became negative in 11 hours. The serum potassium was 4.7 mEq. on admission and fell to 3.5 mEq. in 8 hours. A total of 16 gm. of dibasic potassium phosphate (184 mEq. of K.) was given by mouth beginning nine and one-half hours after admission. The serum potassium concentration rose to 3.9 mEq. at the twenty-fourth hour. No symptoms due to hypopotassemia were noted.

CASE 2. A white man, aged 21 years, who had known diabetes for 14 years was admitted with moderate dyspnea and an odor of acetone on his breath. The blood sugar was 604 and the carbon dioxide combining power 9.4 mEq. (Figure 2). The response to an initial dose of 200 units of insulin and intravenous infusion of fluids was satisfactory. No further difficulties were encountered. The serum potassium was 6.2 mEq. on admission and fell to 4.3 mEq. in four hours. Twenty gm. of dibasic potassium phosphate (230 mEq.) were given by mouth beginning at the fourth hour. It is seen that the serum potassium concentration rose as a result, and that a normal serum potassium was maintained.

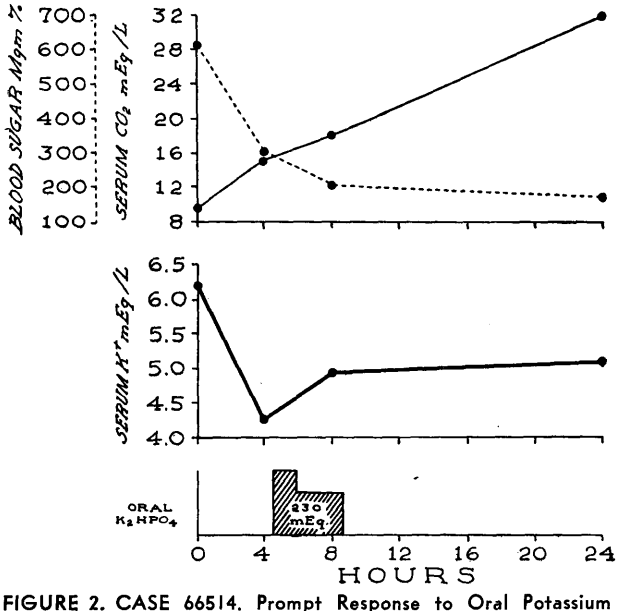

FIGURE 2. CASE 66514. Prompt Response to Oral Potassium Therapy

CASE 3. A white woman with a 13-year history of diabetes was admitted in diabetic coma with marked dehydration, Kussmaul respiration and an odor of acetone on her breath. The blood sugar was 448 and the carbon dioxide combining power 4.8 mEq., (Figure 3). A total of 250 units of crystalline insulin was given during the first two hours, and 6,500 cc. of fluid were given intravenously during the first 24 hours. The response to therapy was satisfactory; ketonuria disappeared in 8 hours. Oral treatment with potassium was started at the fourth hour; however, nausea began to recur at the sixth hour, and made it necessary to discontinue attempts to give oral feedings and potassium two hours later. The nausea subsided somewhat after the subcutaneous administration of atropine. Oral treatment with potassium and fluids was resumed at the 14th hour; however, the nausea began to increase. At this time the result of the determination of serum potassium at the eighth hour became available; it was 2.9 mEq. Since ketonuria had been absent for six hours, it was thought that the increasing nausea might be a symptom of the hypopotassemia. Potassium was administered intravenously using a solution containing 0.4 per cent potassium chloride and 5 per cent glucose. The nausea disappeared in 15 to 30 minutes and the subsequent course was uneventful. This was the only case in the series in which there were symptoms apparently related to hypopotassemia.

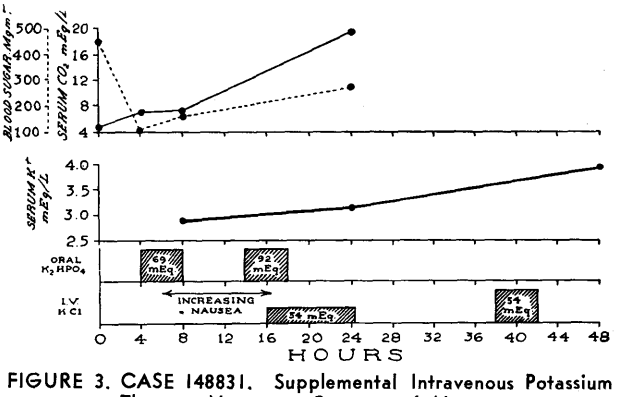

FIGURE 3. CASE 148831. Supplemental Intravenous Potassium Therapy Necessary Because of Nausea

COMMENT

Cases 1 and 2 both demonstrated a satisfactory rise in the serum concentration of potassium following oral potassium. Case 2, in contrast to Case 1, illustrates the importance of beginning the treatment with potassium early; it should usually be started at the fourth hour in order to prevent an abnormally low serum potassium level. Case 3, is an example of the occasional case in which there is not sufficient absorption of potassium from the intestinal tract and supplementary potassium must be given intravenously.

Final proof of the efficacy of any plan of therapy of diabetic coma must lie in the number of patients surviving the episode. That our plan of therapy is efficacious, we believe is shown in Table 5. No fatalities were encountered in a series of 53 cases of coma when the treatment included the use of potassium as compared with 3 deaths in the series of 32 cases treated before the use of potassium.

TABLE 5. Mortality Before and After Use of Potassium in Treatment of Coma

	Patients Before Use of Potassium	Patients After Use of Potassium
Number of Patients	32	53
Deaths due to coma	3	0
Percentage mortality	9.4%	0.0%

We will be the first to admit that there are a number of factors in this achievement, not the least of which are an awareness of the problem and a will to attain the ideal. However, we do feel that the free use of potassium salts has been a significant factor in the absence of mortality reported here.

SUMMARY

In this treatment of diabetic coma, up to 700 or more units of insulin are given during the first two hours; the dose determined by clinical evaluation of the case and the initial blood sugar level. Rehydration is accomplished with saline solution given intravenously.

Additional insulin is given at the fourth hour if the blood sugar has not fallen to one-half of the original level.

If the urinary output is adequate, dibasic potassium phosphate is given by stomach tube and in fluids given orally beginning at the fourth hour. Potassium is given intravenously only if the patient is unable to retain it when given by mouth or if symptoms of hypopotassemia occur.

No fatalities were encountered in a total of 53 cases of diabetic coma so treated in contrast to three deaths in a similar group of 32 cases treated prior to the oral use of potassium.

We believe that our series of 53 consecutive instances of diabetic coma without a death demonstrates the efficacy of the plan of treatment described.

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DISCUSSION

DR. CLIFFORD F. GASTINEAU, (*Rochester, Minn.*): Dr. Crampton has presented an enviable record: no deaths in 53 cases of diabetic coma. It is difficult, by the use of mortality rates, to evaluate the efficacy of potassium in this study, since the mortality rate of 9.4 per cent among the patients who received no potassium is itself an excellent record. Moreover, as Dr. Crampton has pointed out, other factors, such as the amounts of insulin and fluids administered, were different in the two series. Nevertheless, this report is important because it presents a scheme by means of which potassium can be administered safely and in quantities that will correct hypopotassemia.

I was particularly interested in Dr. Crampton's third case, in which he observed nausea associated with hypopotassemia, and found that there was a response to intravenously, but not to orally, administered potassium. The observation that gastrointestinal absorption of potassium occasionally may be inadequate in diabetic acidosis is a valuable one.

In view of the current interest in potassium metabolism, it is surprising how seldom we observe symptoms in the treatment of diabetic acidosis which may be attributed to hypopotassemia. Our arguments for the use of potassium would be weakened if we expected only to prevent the symptoms of hypopotassemia. It seems likely that much more is accomplished by the use of potassium in the treatment of diabetic acidosis than just the prevention of the symptoms of hypopotassemia. It is reasonable to presume that significant deficiencies of potassium and phosphate may occur without manifesting any symptom by which they may be identified, and it is probable that such deficiencies cause a general interference with cellular metabolism, thereby increasing the possibility of a fatal outcome. These presumptions, and Dr. Crampton's demonstration that potassium and phosphate can be administered safely and easily, seem ample justication for the use of these ions in the treatment of diabetic acidosis.

DR. FRED W. S. MODERN (*Long Beach, Cal.*): On my service at the Los Angeles General Hospital, we administer potassium chloride routinely in all cases of diabetic coma in which there is normal urinary excretion. The dosage is 3 gm., given 4 hours, 8 hours and 24 hours after starting treatment.

The first dose is routinely given intravenously, the second and third doses intravenously or orally, depending on the patient's state of consciousness.

The serum potassium is determined before the 4-hour and sometimes before the 8-hour and 24-hour doses. We find the electrocardiogram to be a poor index of hyperpotassemia or hypopotassemia—normal electrocardiograms with the serum potassium as low as 2 mEq. have been found.

We observed two cases of potassium resistance in which death occurred with hypopotassemia despite the administration of large amounts of potassium (close to 20 grams). In both of these cases there was pancreatitis. One patient had coma as the first symptom of his diabetes. As far as we could ascertain, the onset of coma was simultaneous with the onset of the pancreatitis. He died with a blood potassium level of 2 mg. in spite of the fact that within the 20 hours before death he had received about 18 gm. of potassium chloride.

DR. DAVID ADLERSBERG (*New York*): I was particularly interested in the observations of Dr. Crampton concerning the relationship between nausea and hypopotassemia. Another instance of nausea related to hypopotassemia has been recently reported in connection with intolerance to digitalis.

In metabolic balance studies it was found that early symptoms of digitalis intoxication were associated with negative potassium balance and hypopotassemia and that the tolerance of these persons to digitalis was decidedly increased by administration of potassium salts.

I would like to ask whether Dr. Crampton can offer an explanation for the impaired intestinal absorption of potassium salts in diabetic acidosis.

DR. JOSEPH H. CRAMPTON (*closing*): A comment is in order about the phosphate these patients were given. Just as there is a striking fall in the serum potassium with therapy, so is there a similar decline in the serum phosphorus. The oral administration of potassium phosphate rather than potassium chloride helps to compensate for both deficits. However, in spite of the oral administration of phosphate, there still is a marked decline in serum phosphate. This has been the experience of Franks et al who gave large amounts of phosphate intravenously.

I believe changes in the electrocardiogram are an extraordinarily poor index of the serum potassium. It has been postulated that they are an index of changes in cellular potassium. Having had difficulty with hypopotassemia in only one instance, we are not in a position to evaluate this point. However, it is our impression that many of the inconsistencies originally noted in this field may have been the result of technical difficulties in potassium determinations with the flame photometer.

With regard to the question as to impaired intestinal absorption, I have no direct explanation for the impairment except to say that the absorption is related to serum electrolyte concentration. In our instance, the explanation is simple. The patient was unable to retain any potassium by mouth, therefore none was absorbed.