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Treatment of Diabetic Ketoacidosis with Low-Dose Insulin Perfusion*

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The occurrence of severe diabetic ketoacidosis has decreased because of early diagnosis and appropriate treatment of diabetes. In the treatment of diabetic ketoacidosis the severity of acidosis and initial blood glucose levels are considered important criteria for the initial insulin doses. In general, 2-4 U/Kg insulin is used for this condition, half of which is given intravenously and the other half subcutaneously. 1/5 to 1/2 of the initial insulin doses are repeated according to the patients' requirements after the initial doses. This classical treatment for diabetic ketoacidosis has not been changed considerably during the last 50 years since insulin became available to clinical application.

A few years ago insulin perfusion therapy was used in adult diabetics, but it has not been applied to childhood diabetes to the best of our knowledge. We employed perfusion therapy for the first time in a 13 year-old girl with uncontrolled diabetes, diabetic ketoacidosis and mucormycosis on October 20, 1974, when she needed sinus curettage. Since we have observed the successful balance in glucose homeostasis during the preoperative and postoperative period in this patient, we have used this method subsequently as the initial treatment of five children with diabetic ketoacidosis.

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Case Reports

Case 1: (S.B.) HCH: 640759. This 5 year-old girl was admitted to Hacettepe Children's Hospital in a diabetic ketoacidotic coma. Her diabetes had become clinically evident 15 days previously with polyuria and polydipsia. Twelve hours prior to admission she had become somnolent.

Physical examination at the time of admission revealed an undernourished girl (weight, 12 Kgs; height, 100 cms). Her pulse rate was 130/min, temperature, 36.5 C and blood pressure, 100/70 mm/Hg. She was unconscious, dehydrated and had acidotic breathing. Deep tendon reflexes were hypoactive but there was no evidence of stiff neck.

Since her serum electrolytes (CO_2: 4.9 mEq/lt, Na: 129 mEq/lt, K: 5.1 mEq/lt), blood sugar (630 mg/dl) serum acetone (positive) and urinalysis (sugar 4+, acetone 3+) indicated severe diabetic ketoacidosis, regular insulin perfusion (5 U/hr) was started. Intravenous fluid treatment was concomitantly begun from another vein. One hour after initiation of treatment blood sugar was 260 mg/dl, serum acetone disappeared and the patient became conscious. Since three hours later blood sugar was 200 mg/dl, insulin perfusion was stopped and four hours later blood sugar was 104 mg/dl. Fluid therapy was changed to saline, dextrose (1/2 Saline + 1/25 % Dextrose). This patient's ketoacidosis was treated in three hours with a total of 15 U regular insulin. Later she was maintained by regular insulin every 6 hours subcutaneously.

Case 2: (N.B.) HCH: 574373. This four-and-a-half-year old girl's diabetes was diagnosed at Hacettepe Children's Hospital and was under control with 14 U NPH + 6 U regular insulin. Four days before admission she was given Penicillin in a local hospital for a sore throat. Because of somnolence she was considered in diabetic ketoacidosis (blood sugar was 480 mg/d.) and regular insulin I U /Kg intravenously and I U/Kg subcutaneously was given and she was transferred to this hospital when her somnolence increased.

Physical examination: Weight, 17 Kgms; Height, 100 cms; temp, 37.3°C, blood pressure 120/70 mm/Hg. She was unconscious, cyanotic and had frequent seizures but no response to painful stimuli. At the time of admission she had hypoglycemia (blood sugar 16 mg/dl) although serum electrolytes (CO_2: 33 mEq/lt, Na: 140 mEq/lt, K: 4.7 mEq/lt, Ca: 8.4 mg/dl) were almost normal. Hypoglycemia was related to hyperinsulin application and with glucose she became conscious in 20 minutes. However, her blood sugar decreased to 32 mg/dl shortly after and

she had occasional seizures. Therefore, treatment for hypoglycemia was continued. Nine hours later the blood sugar was found to be 420 mg/dl and blood acetone was positive. Urinalysis revealed glucosuria (4+) and acetonuria (3+).

A perfusion of 5 U per hour of regular insulin was started. In two hours blood sugar was 267 mg/dl, and at the 4 th hour of perfusion it was 120 mg/dl; serum acetone was negative at this time. The diabetic ketoacidosis could be controlled by a total of 20 U regular insulin so perfusion therapy was discontinued.

Case 3: (N.D.) HCH: 607826. This 10 year old girl with a history of polyuria, polydypsia and polyphagia of 5 months duration, was admitted to Hacettepe Children's Hospital in a diabetic coma.

Physical examination: Weight, 25 Kg; height, 130 cms; pulse rate, 100/min; temp, 37.5°C; blood pressure, 110/70 mm/Hg. With the exception of mild dehydration her physical findings were not contributory. Laboratory findings revealed hyperglycemia (360 mg/dl) acetonemia (3+) with normal serum electrolytes (CO_2: 21 mEq/lt, K: 4.6 mEq/lt, Na: 140 mEq/lt). Urinalysis showed glycosuria (4+) and acetonuria (3+). While regular insulin perfusion was started (5 U/hr), ringer-lactate was employed from another vein. In two hours blood sugar was found to be 120 mg/dl, so the insulin perfusion was discontinued. In this case a total of 10 U regular insulin was enough to abolish acetonemia and acetonuria.

Case 4: (M.S.) HCH: 605395. This 7 year-old boy had a history of weight loss, polyuria and polydypsia for 2 months and mental confusion for 3 days. He was admitted to Hacettepe Children's Hospital with the diagnosis of diabetic ketoacidotic precoma.

Physical examination: Weight, 16 kg; height, 120 cms; pulse rate 92/min; temp, 36.5°C; blood pressure 105/70 mm/Hg. He was unconscious and markedly dehydrated, and responded to painful stimuli only. Blood sugar was 360 mg/dl, and acetone was positive. Serum electrolytes indicated metabolic acidosis (CO_2: 10.4 mEq/lt, Na: 130 mEq/lt, K: 3.6 mEq/lt). Urine sugar was (4+) and acetone (3+). Regular insulin perfusion (5 U/hr) was started and simultaneously 15 cc/kg of ringer-lactate was given I.V. within 45 minutes. Then 30 cc/kg ringer-lactate was infused in six hours.

The blood sugar decreased to 150 mg/dl and plasma acetone disappeared within 2 hours so the insulin perfusion was discontinued. At the 3rd hour of admission blood sugar became 75 mg/dl and fluid treatment was changed to saline and 5 % dextrose (half and half).

Case 5: (S.Y.) HCH: 597246. This was a 15 year-old boy who had been followed in Hacettepe Children's Hospital for 1 year with the diagnosis of diabetes mellitus. He was admitted to the hospital this time because of vomiting and malaise and it was learned that he had not received insulin during the last two days.

Physical examination: Weight, 55 kg; height, 178 cms; pulse rate, 88/min; temp, 36.5°C; blood pressure 120/60 mm/Hg. His general condition was fairly good although he appeared drowsy. The mucous membranes were very dry, turgor was decreased and his breath had an acetone odor. Blood sugar was 460 mg/dl, serum acetone was positive and urinalysis revealed glycosuria (4+) and acetonuria (3+). Serum electrolytes were normal (CO_2: 27.6 mEq/lt, Na/ 130 mEq/lt, K: 5.4 mEq/lt). Regular insulin perfusion was started and at the same time 15 cc/kg of saline solution was perfused within 45 minutes; this was followed by Ringer-lactate 30 cc/kg within 6 hours via another vein. During the first hour, blood sugar was 205 mg/dl and his consciousness cleared. At the 3rd hour of treatment blood sugar was 186 mg/dl, so the perfusion therapy was stopped. A total of 15 U regular insulin was given. Later regular insulin was started subcutaneously every 6 hours with oral feeding.

For perfusion therapy 20 U regular insulin was added to 120 ml saline which was infused in four hours (5 U per hour). A scalp vein set was used for perfusion without albumin addition. Insulin solution was stopped when the blood sugar decreased to 200 mg/dl. Fluid therapy was maintained as 1/2 saline solution and 1/25 % dextrose. Urine sugar and acetone were tested within clintest and acetest tablets.

Discussion

Continuous infusion of insulin was first used in 1960 in the management of diabetic patients undergoing surgery.[1] However, it became popular in 1972 after Sonksen et al[2] used this method to study the responses to growth hormone and cortisol in diabetic patients. In these studies it was shown that low-dose insulin infusion (I.V.) was quite effective in correcting the metabolic derangements of severe diabetic ketosis. Mensel[3] also used this method with an apparatus which permitted continuous I.V. insulin infusion for 24 hours or more, in diabetic adults with complications. In these studies it was shown that insulin infusion up to 50 U could be used successfully in patients with insulin resistance.[5]

The purpose of continuous I.V. insulin infusion in patients with diabetes millitus is to stabilize the insulin at an effective level in the serum; thus, the insulin: glucagon (I/G) ratio reaches nearly normal levels

by stabilization of the blood sugar.[6] Christensen and Orskow[7] demonstrated that maximal glucose transport would occur at 20 to 200μU/ml of serum concentration of insulin. It is easily calculated that 2 to 4 U/kg insulin in the classic therapy of ketoasidosis would give a much higher level than that of 200 μ U/ml. This high dose of insulin was advocated in classical therapy since a relative resistance to insulin in acidosis is postulated. However very recently some important doubts have been expressed on this matter.[8, 9]

Five units of regular insulin per hour was used in the treatment of our five cases without considering the severity of ketosis and the size of the patients.[10] The blood glucose level fell below 200 mg/dl and the plasma acetone cleared in 2 patients with 10 U regular insulin in 3 hours. However, in one patient 20 U regular insulin was needed (Figure 1). All patients regained consciousness within 2 hours.

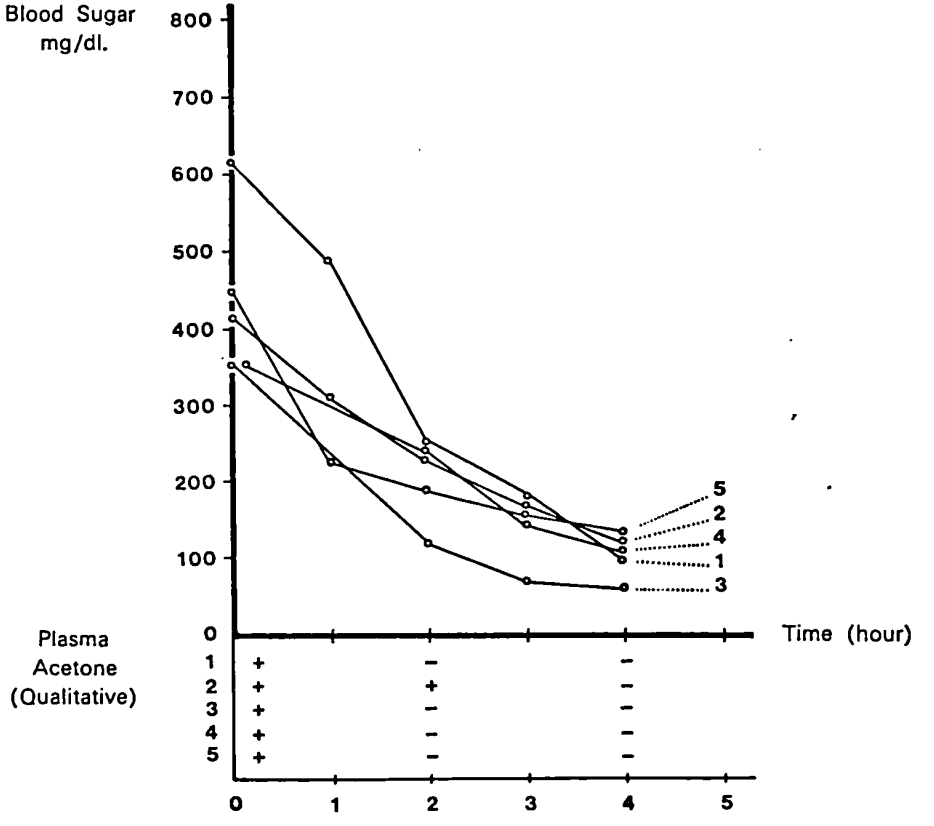

Figure 1

The diagram of the cases showing blood sugar and plasma acetone changes during insulin perfusion.
(The numbers on the diagram indicate the patients)

The advantages of continuous I.V. insulin infusion as supported by our results are:

a) The time for correcting metabolic derangements is markedly shorter, i.e. 2 to 4 hours in our patients.

b) The doses of insulin are low, e.g. maximal 20 U of regular insulin was used in this study.

c) Hypoglycemia can easily be overcome by discontinuing the infusion, because the half-life of insulin is 3 to 5 mins.[11]

d) Maximal glucose transport will be obtained by continuous I.V. insulin since the normal I/G ratio is easily established.

e) The incidence of hypokalemia is minimal.[11]

f) Although the occurrence of cerebral edema is minimal in the classical treatment of diabetic ketosis[12] it has not been recorded in adults with the new method.

For the above reasons we recommend the use of continuous I.V. insulin infusion as a practical, uncomplicated and safe method in the treatment of diabetic ketoacidosis.

Summary

Continuous I.V. insulin infusion therapy was successfully used for the treatment of 5 diabetic children with ketosis and the literature on this subject is reviewed.

REFERENCES

1. Galloway, J.A. and Shuman, C.R.: Diabetes and Surgery. Am.J.Med. 34: 177, 1963.
2. Sonksen, P.H., Srivastana, M.C., Tompkins, C.V., and Naborro, J.D.N.: Growth hormone and cortisol responses to insulin infusion in patients with diabetes mellitus. Lancet. 2: 155, 1972.
3. Mensel, R.: Insuline infusion in diabetic coma. Lancet. 1: 830, 1973.
4. Gerard Slame, M.D., Michel Hautecou verture, M.D., Roger Assan, M.D. and Georges Techobroutsky, M.D., Paris, France. One to five days of continuous intravenous insulin infusion on seven diabetic patients. Diabetes. 23: 732, 1974.
5. Genuth, S.M.: Constant intravenous insulin infusion in diabetic ketoacidosis. JAMA. 233: 1348, 1973.
6. Noel, K., Maclaren, M.D., Marvin Cornblath, M.D.: Insulin. Am.J.Dis.Child. 128: 610, 1974.
7. Christensen, N.J. and Orskov, H.: The relationship between endogenous serum insulin concentration and glucose uptake in the forearm muscle of non-diabetics. J.Clin.Invest. 47: 1261, 1968.

8. Hockaday, T.D., and Alberti, K.G.: Diabetic coma. Clin. Endocrinol. Metab. 1: 751, 1972.
9. Alberti, K., Hockaday, T.D., and Turner, R.C.: Small doses of intramuscular insulin in the treatment of diabetic coma. Lancet. 1: 5.5, 1973.
10. Page, M.McB., Alberti, K., Greenwood, R. et.al.: Treatment of diabetic coma with continuous low dose infusion of insulin. British.Med.lJ. 2: 687, 1974.
11. Turner, R.C. et al, Measurement of the insulin delivery rate in man. Journal of Clin. Endocrin. Metob. 33: 279, 1971.
12. Clements, R.S., Prockop, L.D., and Winegrad, A.I.: Acute cerebral edema during treatment of hyperglycemia. Lancet. 2: 384, 1968.