Editorial

LOWDOSE INSULIN THERAPY IN DIABETIC KETOACIDOSIS

Diabetic Ketoacidosis, a metabolic catastrophe is treated successfully by following the guidelines indicating effective doses of insulin along-with correction of hydration and electrolytes. Until a few years back the dose of insulin used in this condition depended on the level of hyperglycaemia and was thus fairly large. In 1973 papers were published describing the therapeutic effectiveness of small doses of insulin given either as a continous intravenous infusion or intramuscularly in diabetic ketoacidosis (Genuth, 1973; Alberti et al., 1973; Semple et al., 1974). A comparison of low and high dose insulin regimens has also been made showing both to be equally effective (Alberti et al. 1973). All this work gave a conclusion that low-dose insulin was as effective as high-dose insulin in reducing the blood glucose concenteration and correcting the acidosis and was not associated with side effects. Hypoglycaemia and hypokalaemia was encountered exclusively in patients receiving high-dose insulin (Kitabchi et al., 1976). The low-dose intravenous and intramuscular regimens have been equally effective in correcting hyperglycaemia and acidosis. The intramuscular route is not advisable for patients with severe dehydrated acidosis because absorption will be uncertain and irregular. A comparative study of low-dose insulin administered by a continuos intravenous infusion or after an initial primary dose intravenously followed by intramuscular and subcutaneous routes, elicited that the initial decline in the first two hours was more rapid in patients on the intravenous infusion. Later the rate of fall of plasma glucose and ketones was the same (Fisher et al., 1977).

The reason behind the success of the low insulin dosage regime has been explained on some limited observations. The maximum biologic effect of insulin is expected with a plasma insulin concenteration of 20-200 U/ml (Chirstensen & Orskov, 1968; Shade et al., 1977; Guerra and Kitabchi, 1976). Continuous intravenous infusions of regular insulin at 2-10 U/hour elevate the plasma insulin level to 83-150 U/ml (Page et al., 1974; Kidson et al., 1974; Semple et al., 1974). Whereas regular insulin given intramuscularly in the dose of 5-10 U/hour produced concenerations of 100 μU/ml (Kitabchi et al., 1976). Large doses of insulin produce very high plasma insulin concentrations which exceede the ceiling for maximum biologic activity which may not be metabolically more effective.

The production of hypoglycaemia with large doses of insulin could be attributed to the high plasma concentrations in the range of 500 to 1000 μU/ml maintained as such for a long period of four to six hours. Even after cessation of insulin administration this elevated level persists and hypoglycaemia ensues. With the low dose programme the plasma insulin concentration lies in a physiologic range and declines to baseline values in twenty minutes after withdrawal of insulin administration (Kidson et al., 1974), thus avoiding hypoglycaemia. These observations show that most patients with diabetic ketoacidosis will respond to low dose insulin therapy. But it should be kept in mind that because insulin sensitivity or resistance cannot be ascertained immediately, the effectiveness of this method cannot be predicted. Thus all patients should be kept in close supervision and when indicated the dose of insulin should be increased.

Along-with the correction of hypoglycaemia a prompt therapy for the hydration and electrolyte disturbances present in the diabetic ketoacidosis patients is equally inportant. Large quantities of fluid administration intravenously combat dehydration. The first two liters may be run in within an hour unless the patient is in heart failure in which case the rate is reduced to one liter in one to two hours. After about two hours when 2 to 3 liters have been given the rate is slowed. A total of 6 to 12 liters may be required. The fluid safely used is isotonic sodium chloride.

The most vital electrolyte disturbance is the development of hypokalaemia. The initial potassium estimation may give a normal value due to the dehydration and acidosis which causes a shift of the potassium to the extracellular spaces. With initiation of therapy the plasma potassium level falls reaching the maximum in one to four hours. This is due to haemodilution secondary to a rehydration, continued potassium loss in the urine after volume expansion and increased sodium delivery to distal tubule, re-entery of potassium to the inter cellular compartment by correction of acidosis and increased uptake of potassium by the cells as a result of insulin therapy. Potassium administration should be started from the outset or one hour after initiation of therapy. During treatment 20-50% of the administered potassium is excreted in the urine, (Martin et al., 1956.; Soler et al., 1972), thus raising the potassium requirement to 4-20 Gm of the chloride salt.

With emphasis on the low dose insulin regime, a new approach to the treatment of diabetic ketoacidosis has been achieved, which is thus strongly recommended due to the high efficacy and fewer associated complications of hypoglycaemia and hypokalaemia.

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