EFFECT OF MAGNESIUM SULFATE ON BLOOD SUGAR LEVELS OF DIABETIC CHILDREN

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Although insulin is still the drug of choice in the treatment of diabetes in children, oral hypoglycemic drugs have been widely used in the control of adult diabetes. Rubenstein, et al. have recently reported on the hypoglycemic affect of manganese in a child with an unusual form of diabetes of seven years duration.[1] Since magnesium is known to be necessary in several pathways of carbohydrate metabolism and is closely related chemically to manganese, magnesium sulfate infusion was given to three diabetic children who were on insulin treatment at Hacettepe Children's Hospital. Although Rubenstein et al. used very small amounts (5 mg) of manganese by mouth, we gave large amounts of magnesium sulfate infusions (150 mg/Kg) intravenously. This is equal to 20 mg/Kg of magnesium.

The ages of the diabetic children were from 5 to 14 years. Two of them were admitted for the first time to the hospital for treatment of their initial diabetic acidosis. The third child (5 years old) had been followed in this hospital for more than three years for diabetes. The acidosis was treated according to Dr. Hartmann's method[2] and magnesium sulfate infusions were given after the diabetes was under moderate control, i.e., when total urinary sugar output was around five per cent of total available glucose.

For three consecutive days prior to magnesium sulfate infusion, fasting blood sugar levels were determined at 8 a.m. Then the daily insulin requirement was given in the form of a mixture of crystalline and NPH insulin, after which the patients had breakfast. Blood was drawn for blood sugar determinations again at 8:30, 9:00 and 9:30 a.m. This procedure was followed on the fourth day, with the addition of a 3 per cent solution of magnesium sulfate (150 mg/Kg) given intravenously while the patient breakfasted. The magnesium sulfate

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was given as rapidly as possible, within a period of 20 to 30 minutes. Blood was obtained again at 8:30, 9:00, and 9:30 a.m. During these four days, the patients' diets and insulin amounts were not changed. Blood sugar determinations were done by the Folin-Wu method[3] and the results are summarized in Table 1.

TABLE 1

BLOOD SUGAR LEVELS OF THREE DIABETIC CHILDREN ON THREE CONTROL DAYS AND AFTER INTRAVENOUS MAGNESIUM SULFATE INFUSIONS

	Fasting Blood Sugar 8:00 AM	Blood Sugar 8:30 AM	Blood Sugar 9:00 AM	Blood Sugar 9:30 AM
I.Y.				
Ist day	155 mg %	160 mg %	122 mg %	170 mg %
2nd day	262 mg %	258 mg %	222 mg %	190 mg %
3rd day	219 mg %	254 mg %	272 mg %	282 mg %
4th day*	226 mg %	169 mg %	127 mg %	111 mg %
M.S.				
Ist day	338 mg %	282 mg %	242 mg %	295 mg %
2nd day	448 mg %	434 mg %	414 mg %	tube broken
3rd day	400 mg %	416 mg %	432 mg %	390 mg %
4th day*	392 mg %	208 mg %	197 mg %	230 mg %
İ.B.				
Ist day	174 mg %	225 mg %	316 mg %	—
2nd day	64 mg %	200 mg %	308 mg %	310 mg %
3rd day	406 mg %	420 mg %	—	385 mg %
4th day*	550 mg %	432 mg %	410 mg %	316 mg %

* The day that magnesium sulfate infusion was given.

Magnesium sulfate infusions were given to three patients without diabetes as a control measure. These patients had urinary tract infection, iron deficiency anemia, and ecchynococcus of the lungs, respectively. Family history of diabetes was not obtained for any of the control cases. Blood sugar determinations of the control group were done at the same hours as the diabetic patients and the same procedure was used in administering the magnesium sulfate solution on the fourth day. The results of the blood sugar determinations for this group are given in Table 2.

TABLE 2

BLOOD SUGAR LEVELS OF CONTROL CASES PRIOR TO AND ON THE DAY MAGNESIUM SULFATE WAS INFUSED (IN MILLIGRAMS %)

Patient	Fasting Blood Sugar 8:00 AM	Blood Sugar 8:30 AM	Blood Sugar 9:00 AM	Blood Sugar 9:30 AM
M.Y.				
Ist day	70	92	87	92
2nd day	89	92	92	77
3rd day	83	77	91	85
4th day*	83	97	105	tube broken
H.E.D.				
Ist day	88	110	108	99
2nd day	98	82	95	98
3rd day	82	110	102	110
4th day*	90	99	103	91
T.Y.				
Ist day	112	111	118	108
2nd day	100	105	90	108
3rd day	87	110	120	103
4th day*	95	107	118	133

* The day that magnesium sulfate infusion was given.

Results

As can be seen in the tables, magnesium sulfate infusion did not have any effect on normal blood sugar levels in the control cases. However, blood sugar levels of all three diabetic patients dropped considerably (116 mg %, 195 mg %, and 234 mg %, respectively) within one hour following magnesium sulfate infusion. It seems that the higher the blood sugar level, the greater the effect of magnesium sulfate in decreasing blood sugar.

Discussion

Magnesium is second in abundance only to potassium as an intracellular cation known to be an activator in several pathways of carbohydrate metabolism.

The pathways in which the magnesium ion has some role, Embden-Meyerhof, glucose storage, and pentose shunt, are indicated in Figure 1. The magnesium ion is also required in the citric acid cycle (succinyl CoA $\xrightarrow{Mg^{++}}$ succinate). The magnesium ion is known to be necessary

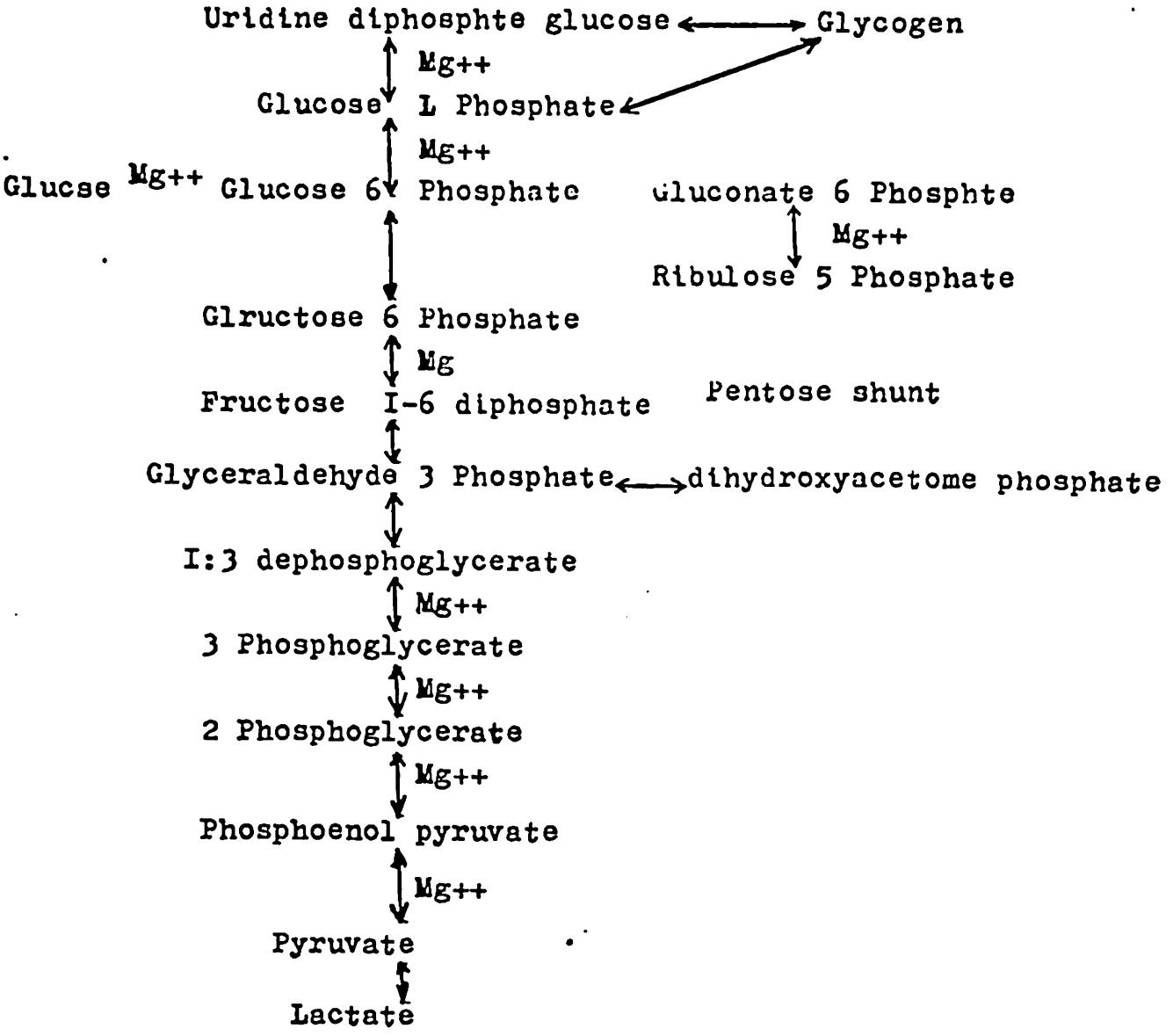

Figure 1. Pathways of glucose metabolism in which magnesium ion is the activator.

for the activation of phosphoralase, phosphatase, enolase, peptidase, decarboxilase, and those enzymes which require ATP. Thus it has not been possible to prove an absolute requirement for this ion, and, on this basis, a definitive physiologic role for magnesium cannot be assigned.[4]

Normal serum magnesium levels have been determined for children and newborns.[5,6] Lower than normal levels have been observed in malnutrition,[6,7] hyper and hypoparathyroidism,[8] hyperaldosteron-

ism,[9] celiac disease,[10] malabsorption syndrome,[11] and following treatment for diabetic acidosis.[12,13]

Magnesium is absorbed from the small intestine and, as for calcium, increased phosphate intake and magnesium soap decrease magnesium absorption. Vitamin D however has no effect on the absorption of magnesium.[4] Fifty per cent of the body's magnesium is stored in the bones, and most of the remainder is intracellular.[14] Thirty-five per cent of the magnesium in plasma is bound to protein, and a small amount is bound to citrate.[4] The largest proportion of magnesium in plasma is in its ionized form. Excretion of magnesium occurs through the kidneys. Lactate decreases magnesium re-absorption through the proximal convoluted tubules, which is one cause of magnesium deficiency during the treatment of diabetic acidosis if lactate is used. Although Diamox[R] (Acetazolamide; 2-acetylamino-1,3,4,-thiadiazole-5-sulfonamide) increases calcium excretion through the kidneys, it decreases magnesium excretion. Parathormone effect on magnesium metabolism is similar to that on calcium metabolism. Magnesium has a pharmacologic effect on the cardio-respiratory system, the central nervous and the myoneural junctions of the muscles.[15] Eosinophilia and proximal tubular changes due to magnesium deficiency is reported in rats.[16,17]

Since manganese proved to be effective in controlling blood sugar levels of at least one diabetic patient, and since the effect of magnesium on carbohydrate metabolism can be partially replaced by manganese, and the mean serum magnesium concentration of patients with controlled diabetes receiving insulin is said to be low,[12] magnesium sulfate infusions were given to those diabetic children with high blood sugar levels. Although the data are not sufficient to support a definitive conclusion, it seems that magnesium sulfate is effective in decreasing high blood sugar levels.

Rubenstein and his colleagues[1] gave magnesium to their manganese-sensitive diabetic patient in order to ascertain whether the patient's response to manganese was specific, without any effect on his blood sugar level. The magnesium was given orally and the dose was not specified. Although Garby and de Verdier[18] did not show the effect of various concentration of magnesium on erythrocyte glucose consumption *in vitro*, it has been shown that glucose uptake by isolated rat diaphragm is increased in the absence of, but more so in the presence of, insulin.[19] Rubenstein et al postulated that manganese might act in one of two ways:

1. It may act peripherally, and may accelerate cellular glucose uptake or utilization either directly or by potentiating insulin action; or it may interfere with the action of glucagon in forming glucose from stored glycogen in the liver.
2. Manganese may act on the pancreas by accelerating the release of stored insulin into the bloodstream, or by inhibiting the release of glucagon.

In explaining the effect of manganese on their patient, they favored inhibition of the release of glucagon.

When blood glucose levels of diabetic children are in reasonably good control, glucagon produces a hyperglycemic effect as in a normal person. However, when the blood sugar is markedly elevated, the effect of glucagon is less predictable and might depress blood sugar levels.[20] For that reason, without further evidence, it seems more reasonable to suppose that the glucose uptake and storage in the cells is increased by magnesium infusion. Unfortunately, magnesium levels could not be measured in our cases. In one of these (I.Y) magnesium sulfate was given orally (0.5 gm) twice a day, b.i.d. with some decrease in his insulin requirement (about 10 units) at the beginning. Since we do not see many diabetic children in Turkey, more data could not be collected on this subject. We thought it worth publishing this preliminary data with the hope that it would interest other investigators.

Summary

The effect of magnesium sulfate on the blood sugar levels of three moderately well-regulated diabetic children is reported. With magnesium sulfate infusion in all these cases initial high blood sugar levels decreased considerably. Magnesium sulfate was not effective at all in three children with normal blood sugar levels.

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