MECHANISM OF INSULIN COMA ARREST BY INTRAVENOUS GLUCOSE INJECTIONS

V. F. Vasil'eva, A. E. Lichko and M.M. Sokolova

From the I. M. Sechenov Institute of Evolutionary Physiology (Director — Academician L. A. Orbeli) AN SSSR, Leningrad

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Injection of 40 % glucose solution is the recognized method of treatment for insulin coma. In recent years it has been shown that glucose may be replaced by hypertonic solutions of inorganic substances such as sodium chloride, magnesium sulfate, etc.[5, 10].

It has been suggested that when injected as a 40% solution, glucose acts by raising the osmotic pressure and so causing cell dehydration. In this way the intracellular edema of the brain cells [2,3, 9] is overcome. This view has been supported by B. A. Tselibeev [5] who injected isotonic or hypotonic glucose solution. Instead of injecting 20 ml of 40% glucose, he gave 160 ml of 5% or 300 ml of 2.5 % solutions, and found that the effect was very much smaller, and often that the coma was not interrupted.

In spite of the general acceptance of the theory of the hyperosmotic action of glucose in insulin coma, no reports have been made on determinations of the osmotic pressure of the blood following the injections.

We have studied osmotic changes in the plasma following intravenous glucose injections during insulin coma in 8 patients suffering from schizophrenia or other psychoses who were undergoing insulin therapy.

METHOD

The injection was given into the vein of one arm, while samples of blood were withdrawn from a vein of the opposite limb; 1-2 ml samples of blood were taken at intervals during the insulin coma, before, during, and immediately after the injection of the 40% glucose solution, and subsequently after 2,5,10-15,and 20-30 min. Osmotic pressure was measured by determination of the freezing point, and the blood glucose by Hagedorn-Jensen's method.

RESULTS

It was found that intravenous injection of 20-40 ml of 40% glucose solution caused no change in the blood osmotic pressure.

Treatment of insulin coma using P. F. Malkin's method [1], by giving a large amount of glucose (80-100 ml of 40% solution), which caused a considerable hyperglycemia, did not change the osmotic pressure (Table 1). Similar results were obtained in 19 other tests.

In order to find by what means the osmotic pressure was maintained constant, the determination of the blood sodium was made in the same samples, by flame photometry. It was found that injection of 20 ml of 40% glucose solution causes no appreciable change in the sodium concentration. Some reduction in blood sodium is caused by injecting 40 ml of 40% glucose during the period of hyperglycemia, and a still greater change results from injecting 80-100 ml of this solution (Table 1).

TABLE 1

Osmotic Pressure and Blood Sodium in Treatment of Insulin Coma by Intravenous Injection of 80 ml 40% Glucose Solution

Time of determination	Osmotic pressure (in milliosmols), normal 300-330	Concentration in blood		Theoretically calculated value (in milliosmols)	
		Glucose (in mg %), normal 80-120	Sodium (in mequiv), normal 130-145	Increase in partial glucose osmotic pressure	Reduction of partial osmotic pressure of sodium
Insulin coma	322	26	142	—	—
During injection	322	556	138	+30	—7
At end of injection	328	385	127	+19	—21
After 2 minutes	322	310	131	+15	—11
After 5 minutes	328	304	123	+15	—34
After 20 minutes.	322	96	128	+3	—21
After 30 minutes.	328	81	130	+3	—21

TABLE 2

Blood Sodium, and Its Excretion in the Urine and into the Intestine during Insulin Coma Treatment by Injection of 40% Glucose

Time of determination	Concentration in blood		Urine			Amount in intestine			Total Na excreted (in mequiv per min)
	glucose (in mg %)	sodium (in mequiv per liter)	diuresis (in ml/ min)	Na concentration (in mequiv/liter)	excretion of Na (in μ equiv/min)	volume excreted (in ml/min)	Na concentration (in mequiv/liter)	Na excreted (in mequiv per min)	
Insulin coma	33	130	0,35	8	3	0,45	84	38	41
During injection	115	125	0,35	9	3	0,35	86	23	26
After injection	416	118	0,25	8	2	0,30	88	26	28
After 4 minutes	211	125	1,00	4	4	0,20	88	17	21
After 8 minutes	138	125	0,80	3	2	0,15	88	13	15
After 12 minutes.	129	126	0,50	4	2	0,12	88	11	13
After 20 minutes	107	128	0,20	7	1	0,07	86	6	7

It can be seen from the calculations in Table 1 that the extent of this reduction (or, more accurately, the reduction in the amount of sodium chloride) corresponds quite well to the increased glucose concentration.

It appears that the reduction in the blood sodium is caused by its rapid excretion with the urine or by its passage into the intestine. This was confirmed by an experiment in which fistulas were established on a dog in the bladder and duodenum. Insulin shock was produced, during which 40 ml of 40% glucose solution was injected. The results of the experiment are shown in Table 2.

It can be seen from Table 2 that after the glucose injection there is a reduction in the urinary sodium. The sodium concentration in the intestine remains unchanged, but the amount of fluid obtained through the fistula is reduced. The excretion of sodium into the urine and intestine is therefore not increased, but actually decreased.

TABLE 3

Blood Changes Caused by Injecting 80 ml of 40 % Glucose Solution Intravenously as Insulin Coma Therapy

Time of determination	Osmotic pressure (in milliosmols)	Concentration in blood			Reduction of protein (in % of original value
		glucose (in mg%)	Na (in mequiv per liter)	Protein (in %)	
Insulin coma	338	28	131	7,35	—
During injection	333	205	128	7,35	0
At end of injection . . .	338	292	125	6,51	—11,5
After 2 minutes	333	319	123	6,51	—11,5
After 4 minutes	338	327	125	6,60	—10,2
After 6 minutes	328	350	122	6,71	—8,7
After 20 minutes	322	296	124	6,71	—8,7
After 30 minutes	338	202	125	6,90	—6,1

TABLE 4

Osmotic Pressure and Blood Sodium as Affected by Injection of 40 ml 10% Sodium Chloride Solution during Insulin Coma

Time of determination	Osmotic pressure (in milliosmols)	Blood sodium (in mequiv per liter)
Insulin coma	328	136
Immediately after injec.	381	175
After 2 minutes.	333	142
After 4 minutes.	328	132

It must be supposed that the osmotic pressure is maintained constant during glucose injections by a redistribution of water between the intra- and extracellular fluids, and that it is on this account that in hyperglycemia, the necessary amount of water flows from the cells into the tissue fluid and thence into the blood. The truth of this conclusion may be tested by determining the refractive index, which is a measure of the total protein content of the plasma. The following results were obtained.

After intravenous injection of glucose, at the period of maximum hyperglycemia , the total protein content in the plasma was noticeably reduced. The results of one of 12 such tests are shown in Table 3.

The observed reduction in blood sodium may be explained as being due to the reduced concentration resulting from the hydremia.

Having shown that the therapeutic action of glucose injection is not due to an increased osmotic pressure we decided to find the effect of an intravenous injection of 40 ml of a 10% sodium chloride solution. In contrast to the published reports, we found that not in one of the 7 subjects to whom the injection was given was there any therapeutic effect, or any noticeable reduction in the depth of the coma. At the same time, immediately after the injection there was a marked increase in the blood osmotic pressure, and an increased blood sodium. But even after 2-3 minutes, both of these quantities returned to their initial levels (Table 4).

Thus, injection of 20-100 ml of 40% glucose solution during insulin coma caused no change in osmotic pressure, despite the marked hyperglycemia. The pressure remained unchanged on account of the dilution of the blood which occurred simultaneously and which was demonstrated by the reduction in plasma protein.

It is probable that during the period of hyperglycemia, the hydremia is caused by passage of water from the cells into the tissue fluid. According to A. S. Troshina [4], dehydration of cells in glucose solutions is not caused by osmosis, but by the action of this substance on the sorptive properties of the protoplasm. From this point of view, the constancy of the osmotic pressure which we have demonstrated during the glucose injection agrees with the idea that the reason for the arrest of the insulin coma is the elimination of the hypoglycemic intracellular edema. The effect of the glucose injection may be due to its special dehydrating action on cells, including brain cells, which it exerts quite independently of its osmotic pressure.

The absence of any effect on injecting hypertonic sodium chloride solution, in spite of the increased osmotic pressure, affords yet further evidence for the truth of this view.

SUMMARY

Intravenous injection of 20-100 ml of a 40% glucose solution during insulin coma causes no change in the blood osmotic pressure, despite the considerable hyperglycemia. The osmotic pressure of the blood is maintained constant on account of a hydremia which develops simultaneously, as indicated by a decreased plasma protein. A short-lasting osmotic pressure rise resulting from the injection of 40 ml of 10% sodium chloride solution does not interrupt insulin coma. The arrest of the coma by glucose may be due to its specific action on the sorptive properties of the cellular colloids, an effect which is independent of osmotic pressure and which counteracts the hypoglycemic intracellular edema of the brain cells.

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