THE EXCRETION OF SUGARS AFTER THE INTRAVENOUS ADMINISTRATION OF INVERT SUGAR

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Until recently glucose was the only sugar used for intravenous administration. Glucose was indeed the obvious choice, for it is constantly present in the blood and it also occupies a central position in carbohydrate metabolism.

The results obtained by the intravenous administration of glucose are satisfactory. However, if glucose in a higher concentration than 5% is used difficulties may ensue. The wall of the blood vessel is affected by the hypertonic glucose solution, with the result that in many cases thrombi develop, and continued administration in the same vessel becomes impossible. Moreover, the intravenous administration of large quantities of 10% glucose causes glycosuria and results in increased diuresis. Not only is part of the glucose again lost in this way, but also the patient loses more fluid than was administered. In many cases in which fluid is administered intravenously this is undesirable. Other nutrients were therefore sought from which to prepare a liquid of high caloric value for intravenous administration.

As long as intravenous administration of fat is still in the experimental stage, only carbohydrates and amino-acids should be considered as sources of calories. The highest concentration of amino-acids which can be given intravenously in larger quantities is about 5%. If amino-acids are given fairly rapidly in higher concentration, nausea and vomiting will soon occur so that any increase in the caloric value of the infusion liquid must be by increasing the carbohydrate content. An infusion liquid containing 10% carbohydrate and 5% amino-acid has a nutrient value of 600 calories per litre. With such a liquid it is possible, provided the excretion of sugar and amino-acids in the urine is small, to meet to a great extent the caloric need of a patient. Weichselbaum, Elman and Lund (1950) suggested giving invert sugar instead of glucose. They observed that if 10% invert sugar and 10% glucose were administered at the same rate, the amount of carbohydrate

in the urine after administration of glucose was about twice as great as after giving invert sugar.

Although fructose is less readily reabsorbed by the kidney than glucose, the rate of utilization of fructose in the body is so high that the fructose level of the blood remains low. The result is that excretion of fructose hardly takes place. This is due to the fact that fructose is absorbed more rapidly by the cells and phosphorylated than is the case with glucose (Cori, 1926). The phosphorylated product is then easily broken down by the organism into pyruvic acid, while at the same time glycogen may be formed (Soskin and Levine, 1952). There are signs which show that for carbohydrate metabolism liver tissue prefers fructose to glucose (Vestling, Mylroie, Irish and Grant, 1950). In some more recent reports the original observations by Elman are corroborated. It is a remarkable fact that the reaction of the vascular wall to 10% glucose is greater than to 10% invert sugar.

Lawton, Curreri and Gale (1951) on the other hand consider the advantages of invert sugar less important. The excretion during administration of 10% glucose is, according to them, not so great that the use of invert sugar is a marked caloric improvement. A secondary advantage is reduced diuresis after the administration of invert sugar.

The above-mentioned authors all carried out their observations on adults. However, the problem is also of importance in children, for it is desirable to have an infusion liquid available which will provide by intravenous alimentation not only sufficient fluid but also enough calories. Even more than in adults it is important in the growing child to maintain a caloric balance during acute disorders. For this reason we have studied the retention of intravenously administered invert sugar in children.

In connexion with the investigations by Elman we studied first the excretion of fluid and carbohydrates in a number of children who for 24 hours received either 10% glucose or 10% invert sugar. These children had been admitted to hospital for

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TABLE 1

THE URINE OUTPUT AND CARBOHYDRATE EXCRETION AFTER INTRAVENOUS DRIP OF 10% GLUCOSE AND 10% INVERT SUGAR FOR 24 HOURS

Patient	Volume (ml.)	Carbohydrate (gr.)		Weight (kg.)		Urine Output (ml.)	Carbohydrate Excretion	
		Glucose	Fructose	Before	After		Glucose (gr.)	Fructose (gr.)
10% Glucose								
1	1,950	195	—	13.8	13.7	1,325	2.8	—
2	2,000	200	—	17.2	16.8	1,860	2.0	—
3	1,370	137	—	12.3	12.7	560	0.5	—
Mean	1,775	177.5	—	14.4	14.4	1,245	1.8	—
10% Invert Sugar								
1	1,200	60	60	10.6	11.5	770	0.7	1.3
2	2,000	100	100	16.5	17.5	1,300	3.4	1.0
3	2,000	100	100	17.2	17.2	1,200	2.6	0.6
Mean	1,735	87	87	14.8	15.4	1,090	3.3	1.0

some acute infectious disease, and, as they showed signs of shock, they were given an intravenous infusion. During the last 24 hours the infusion liquid was replaced by either 10% glucose or 10% invert sugar. In that period the urine was collected and the urinary glucose and fructose were determined by titration. The results are given in Table 1. None of the children who had been given 10% glucose by intravenous drip for 24 hours showed an appreciable excretion of glucose. Only 1.4%, 1.0% and 0.4% of the administered glucose was eliminated.

For the patients who had been given invert sugar the percentages for total sugar excretion were: 1.7%, 2.2% and 1.6%. The sugar excreted by these patients was partly glucose and partly fructose. The glucose excretion amounted to 0.6%, 1.7% and 1.3% respectively of the total quantity of administered sugar. The fructose excretion was small, only 1.1%, 0.5% and 0.3% of the total quantity of administered carbohydrates.

The total sugar excretion of the children who were given 10% glucose was even lower than in the other

group. Calorically, however, the loss in both groups is insignificant. In this respect and under these conditions invert sugar does not produce an improvement.

It is remarkable that although both groups eliminated an almost equal amount of sugar the output of urine differed. After administration of glucose the urine output averaged 1,245 ml. After administration of invert sugar this figure was 1,090 ml. The body weight of the children before and after infusion was in agreement with these figures. In the group given invert sugar there was an average increase of 0.6 kg.

In order to obtain a better insight into the differences in excretion during intravenous administration of glucose and fructose, we gave for a short time a larger quantity of 10% glucose and 10% invert sugar to some of the children (Table 2).

Table 2 shows that the urinary glucose output at this rate of infusion for the 10% glucose solution has become considerable, averaging 17.8% of the administered amount. For the 5% glucose solution the loss amounts to 6.4% of the quantity given.

TABLE 2

URINE OUTPUT AND CARBOHYDRATE EXCRETION AFTER INTRAVENOUS ADMINISTRATION OF 5% AND 10% GLUCOSE AND 10% INVERT SUGAR

Patient	Time (min.)	Weight (kg.)	Volume (ml.)	Urine Output (ml./9 hr.)	Carbohydrate (g.)	Carbohydrate Excretion (g./9 hr.)	
						Glucose	Fructose
5% Glucose							
1	60	21.6	1,000	1,002	50	2.0	—
2	60	22	1,000	926	50	6.0	—
3	110	43.7	1,000	1,448	50	2.2	—
4	60	20.7	1,000	765	50	2.5	—
Mean	72.5	27	1,000	1,037	50	3.2	—
10% Glucose							
1	60	28.4	1,000	1,080	100	15.9	—
2	80	43.6	1,000	1,008	100	13.1	—
3	90	24	1,000	1,183	100	15.8	—
4	60	21.2	1,000	1,230	100	26.4	—
Mean	72.5	29.3	1,000	1,125	100	17.8	—
10% Invert Sugar							
1	60	30.6	1,000	960	100	12.0	1.00
2	60	30.3	1,000	740	100	7.5	1.00
3	60	31	1,000	418	100	3.0	0.40
4	90	45.7	1,000	953	100	2.4	0.60
Mean	67.5	34.4	1,000	768	100	6.25	0.75

The losses of invert sugar are 12.5% of the glucose given and 1.5% of the fructose. This shows that the loss of fructose is very small. It is remarkable that fructose increases the loss of glucose. Whereas during administration of 5% glucose the loss amounted to 6.4%, this rose after the addition of 5% fructose to 12.5%, double the amount.

utilization of fructose the tissues have less need of glucose, so that the glucose in the blood rises to a higher level than is the case during administration of 5% glucose only.

Also remarkable is the small output of urine after the administration of invert sugar, viz. 768 ml. as against 1,127 ml. after the administration of 10% glucose.

FIG. 1.—The relation between urine output, carbohydrate excretion and time. A shows carbohydrate excretion: (1) during infusion (average duration approximately 70 min.); (2) in the first three hours after the end of the infusion; (3) from the fourth to tenth hour after the end of infusion. B shows the urine output under the same conditions. □ glucose output. ■ fructose output.

Nevertheless, the total loss remains considerably smaller than after the administration of 10% glucose; in that case the loss is 17.8 g. as against a total of 7 g. after the administration of invert sugar.

It is possible that fructose renders the reabsorption of glucose in the kidneys less complete. However, this is not likely, considering the low blood level which is in agreement with the urinary fructose output found. It is more likely that owing to

Apparently fructose in some way or other retains fluid. This shows that the metabolism of fructose is not altogether similar to that of glucose. Since patients who need intravenous alimentation generally suffer from dehydration, this tendency of invert sugar to reduce diuresis is of practical importance. How this fluid retention is brought about is not certain.

In view of the low fructose level in the blood found

after intravenous administration, it is unlikely that the quantity of extracellular fluid has increased.

In this connexion there is a striking difference in the time in which the largest quantity of urine is produced. Fig. 1B shows that in the case of the 5% glucose solution the largest of urine output is after all the fluid has been administered. For the 10% glucose solution this appears not to be so, while for a 10% invert sugar solution the urine output is at first the same as that after the use of 5% glucose but in the period after intravenous administration it is markedly smaller. This finding is the more remarkable as such differences are not found in the excretion of carbohydrates (Fig. 1A).

Discussion

Albanese, Felch, Higgons, Vestal and Stephanson (1952) demonstrated that fructose more than glucose stimulates the protein synthesis in the growing baby. Fructose might be called the sugar of the young foetus during intra-uterine life. The seminal vesicle as well as the endometrium contains fructose (Mann, 1949). The placenta is capable of converting glucose into fructose.

In many animal species the blood sugar of the foetus is largely fructose (Huggett, 1952). In these animals the amniotic fluid contains fructose (Okamura, 1938). In women fructose has disappeared from the blood in the second half of pregnancy. The placenta in women, however, also contains an

enzyme capable of converting glucose into fructose. Administration of fructose to young children is therefore indicated in view of their embryonic development. By stimulating protein synthesis fructose will at the same time promote water retention. During a short period of administration such as we have adopted it is unlikely that the cause of fluid retention will be found in accelerated protein anabolism. It seems more plausible that an accumulation of intermediate products from sugar metabolism has a water-retaining effect.

In view of the tendency to reduce diuresis and the rapid utilization of fructose by the cell, invert sugar is more suitable for intravenous administration than glucose of the same concentration, particularly if the concentration exceeds 5%.

The smaller loss of sugar during administration of invert sugar described by Elman *et al.* is important only if large quantities are given in a relatively short period of time.

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