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The effect of intravenous carbohydrates on various parameters in blood

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With 4 tables

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Carbohydrates represent an essential component of the caloric intake in intravenous therapy. In general glucose, fructose and the two sugar alcohols xylitol and sorbitol are used. Various biochemical changes such as an increase in serum uric acid and serum bilirubin have been reported by us and by other workers following the infusion of fructose, sorbitol and xylitol (1, 2, 3, 4) and following their oral ingestion (5). *Schumer* (6) has confirmed the rise in serum uric acid concentration following the infusion of xylitol and has described certain other biochemical changes (rises in S.G.O.T., serum lactate, serum alkaline phosphatase and serum phosphate). He has collectively called these changes "adverse effects" and has suggested that xylitol is contraindicated for infusion purposes. As carbohydrates are essential in parenteral nutrition and as all the carbohydrates normally used cause biochemical changes in blood we have undertaken a comparative study and would clearly differentiate between biochemical findings and "adverse effects".

Material and Methods

Human and animal studies were undertaken.

In the human studies healthy male students aged 21–25 years, in a fasting state, were infused with 1.5 g of the appropriate carbohydrate/kg body weight as a 20 % solution in 20–25 minutes. Analyses of uric acid, bilirubin, GOT and GPT were carried out on serum from venous blood.

In the complementary animal studies male Sprague-Dawley rats of 280–350 g body weight were used. The rats were fasted for 12 hours and a silicone catheter was inserted under ether anaesthesia into the right jugular vein. 20 % carbohydrate solutions were then continuously infused for 68–72 hours using a continuous infusion pump (Perfusor, Braun-Melsungen) at a rate of 1.2 ml/hour. The rats received 28.8 ml fluid and 5.76 g of the appropriate sugar per 24 hours or about 18 g sugar/kg body weight in 24 hours. They were not fed during the infusion.

At the end of the infusion the animals were herparinised (250 U heparin) and plasma GOT, GPT and bilirubin were estimated. Liver glycogen was also measured.

The test for uric acid was carried out enzymatically with uricase. Boehringer-kits were used for all estimations, which were carried out in duplicate.

Table 1. Influence of sorbitol, xylitol and fructose infusions on various parameters (x ± S.D.). Rapid infusion in volunteer subjets (1.5 g/kg body weight in 20–25 min)

	uric acid (mg-%)			bilirubin (mg-%)		
	before infusion	60 min after infusion	180 min after infusion	before infusion	60 min after infusion	180 min after infusion
Sorbitol (n = 8)	4.4±1.0	6.2±1.1	6.3±1.1	0.54±0.25	0.80±0.35	0.91±0.36
Xylitol (n = 9)	4.8±0.6	6.2±0.7	5.9±0.5	0.61±0.18	0.81±0.18	0.84±0.17
Fructose (n = 8)	4.2±0.9	6.6±1.5	6.0±1.2	0.52±0.18	0.63±0.15	0.78±0.17
Glucose (n = 6)	4.7±0.6	4.4±0.8	4.6±0.8	0.58±0.22	0.71±0.20	0.82±0.23
Galactose (n = 9)	5.1±0.8	5.0±0.9	4.8±0.9	not determined		

	SGOT			SGPT		
	before infusion	60 min after infusion	180 min after infusion	before infusion	60 min after infusion	180 min after infusion
Sorbitol (n = 8)	7.2±3.0	6.8±2.0	6.0±2.8	4.8±1.5	5.0±1.4	5.0±1.5
Xylitol (n = 9)	10.0±3.4	9.6±2.5	9.2±2.0	5.0±1.3	6.2±2.0	5.2±1.0
Fructose (n = 8)	10.8±2.3	9.5±2.5	9.2±2.2	5.4±1.4	5.2±1.8	6.0±2.0
Glucose (n = 6)	10.2±3.7	9.9±3.3	9.0±2.7	5.5±1.8	5.0±1.5	5.0±1.8
Galactose (= 9)	not determined			not determined		

Results

The rapid infusion of fructose, xylitol and sorbitol (1.5 g/kg body weight) led to a significant increase in serum uric acid ($p < 0.01$) which was still present after 180 minutes (Table 1). Glucose and galactose infusion did not cause a similar rise.

Table 1 also shows that the infusion of fructose, sorbitol, xylitol and glucose also caused a significant rise in serum bilirubin concentrations. Unfortunately, the concentration of serum bilirubin was not estimated after the infusion of galactose. S.G.O.T. and S.G.P.T. were unaltered during the observation periods of 180 minutes.

Table 2. Blood lactate concentration after intravenous infusion of glucose, fructose, sorbitol or xylitol (1.5 g/kg body weight) in volunteer subjects (mg/100 ml ± S.D.)

	0 min	15 min	30 min	60 min
Glucose	11.7±1.2	16.6±1.8	15.7±2.3	13.2±1.7
Fructose	11.5±1.8	17.9±2.2	23.8±2.7	15.4±2.2
Sorbitol	9.6±2.1	17.3±2.4	17.9±3.2	13.2±2.1
Xylitol	10.3±1.4	12.8±2.1	10.5±2.1	9.0±1.8

Table 2 shows that blood lactate concentrations rose transiently but significantly after the infusion of glucose, fructose and sorbitol but not after xylitol. Fructose caused the greatest rise, but glucose and sorbitol were nearly as effective. The lactate concentrations had largely returned to normal after 180 minutes and therefore figures for 0, 15, 30 and 60 minutes only have been presented.

Table 3. The lactate/pyruvate ratio in blood after intravenous infusion of glucose, fructose, sorbitol and xylitol (1.5 g/kg body weight) in volunteer subjects ($x \pm$ S.D.)

	0 min	15 min	30 min	60 min
Glucose	11.5±1.6	13.4±2.1	13.0±1.9	11.4±1.5
Fructose	12.1±1.4	14.2±2.2	15.4±2.3	13.2±1.8
Sorbitol	12.0±2.2	16.7±1.9	14.2±2.1	12.0±1.9
Xylitol	11.8±1.8	18.4±3.1	17.3±3.0	14.3±2.1

The lactate/pyruvate ratios rose transiently after the infusion of all carbohydrates, the rise being greatest after the infusion of xylitol. In the cases of glucose, fructose and sorbitol the rise in lactate/pyruvate ratio was due to the rise in lactate concentration whereas in the case of xylitol it was due to a fall in the blood pyruvate concentration.

In the continuous infusion studies in rats (Table 4) after three days infusion of fructose, sorbitol and xylitol there was a fall in the serum concentrations of bilirubin, G.O.T. and G.P.T. The liver glycogen was raised after infusion compared to that of starved rats. In rats starved for 72 hours we found values of 10 mg/g. The findings in the animal studies, and especially the high values for liver glycogen, are inconsistent with any degree of hepato-toxicity of the carbohydrates used.

Table 4. Continuous infusion studies in albino rats lasting 68–72 hours (about 18 g/kg body weight/day ($\bar{x} \pm$ S.D.)

	weight loss (g/72 h.)	liver weight (g)	bilirubin (mg%)	SGOT	SGOT	liver glycogen (mg/g)
Sorbitol (n=11)	30.1±4.4	11.6±1.6	0.20±0.06	32±12	3±2	26.4±13.1
Xylitol (n=17)	26.4±6.7	11.6±0.9	0.21±0.06	34±10	5±3	23.4±6.4
Fructose (n=8)	26.9±7.0	11.0±1.1	0.21±0.05	30±10	5±3	34.3±12.9
Control values (24 hours fasting rats)		(8.2±1.2)	(0.44±0.14)	(41±5)	(7±3)	(< 1 mg/g)

Discussion

The rise of serum uric acid following the intravenous infusion of xylitol, fructose and sorbitol is certainly due to an increase in purine synthesis. At the same time there is an increased excretion of uric acid in the urine

(6, 7). The xanthine oxidase inhibitor allopurinol (7, 8) and orotic acid (3) minimise the increase induced by carbohydrates. As an oral intake of saccharose in an amount which is nutritionally adequate also causes a rise in serum uric acid concentration (5, 9) it would appear that the increase in uric acid is of little importance. An increase in serum bilirubin levels occurs after glucose as well as other carbohydrates (4). *Schumer* only published bilirubin concentrations at the end of the period of infusion and as the initial values are unknown the degree of change cannot be estimated. The same may be said of the serum enzyme values which *Schumer* considered indicate liver damage (6). We do not have figures following continuous infusion in volunteer subjects but is seems unlikely that the infusion of 4.5 g/kg body weight over a period of 24 hours should give significantly different results to those obtained with a rapid infusion of 1.5 g/kg body weight. On the contrary, a slow infusion of fructose seemingly does not cause an increase in serum uric acid (9, 10). In the animal experiments reported here where high doses of carbohydrate (18 g/kg body weight/24 hours) were infused for 68–72 hours, there was no effect on S.G.O.T., S.G.P.T or serum bilirubin levels. These facts and the well maintained liver glycogen would seem to indicate that liver function was not significantly disturbed.

The alteration in lactate level and the lactate/pyruvate ratio are also not findings specific to xylitol as they are also seen in varying degree after fructose, sorbitol and glucose.

Somewhat unexpectedly the increase in lactate is significantly less following the rapid infusion of xylitol. This finding agrees well with the results following perfusion of isolated rat livers. In this case also there was a significantly higher rise in lactate concentration after fructose than after xylitol. Nevertheless, the lactate/pyruvate ratio after fructose perfusion of rat livers altered very little while there was a greater alteration after xylitol perfusion (11). In the perfusion experiments, xylitol gave the best glycogen deposition in the liver. The high lactate/pyruvate ratio after the infusion of xylitol would seem to have no significant effect on liver metabolism. Even the turnover of galactose which is considered a sensitive test of liver function (12) is hardly affected by the simultaneous infusion of xylitol (7). The greatly increased lactate concentration observed by *Schumer* are not explicable in the light of our findings. The increase in inorganic phosphate observed by this author is contrary to our findings (*Foerster*, unpublished) and to the findings of other authors (13). Apart from *Schumer* (6) – to our knowledge – an alteration of liver-specific serum enzyme activities after the infusion of carbohydrate has not been described.

Our results and the extensive literature especially concerning the use of fructose for infusion do not allow an interpretation of alterations in serum uric acid, serum bilirubin, serum lactate concentration and lactate/pyruvate ratio in blood as an "adverse reaction".

Summary

Carbohydrates are required in intravenous therapy yet biochemical changes in blood have from time to time been reported following their infusion. Suggestions have been made that these biochemical changes represent "adverse reactions"

and are contraindications for the use of one or other of the carbohydrates. Human and animal comparative studies of the commonly used carbohydrates show that they are safe to use and that biochemical changes are not synonymous with "adverse reactions". In particular xylitol causes fewer changes than fructose or sorbitol.

References

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