Effect of Intravenously Administered Fructose on Blood Acid-Base Balance in Patients with Pre-existing Acidosis

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Recently there has been a greatly increased use of fructose as a source of carbohydrate and calories in parenteral alimentation. Since it has been shown that metabolism of fructose in patients with diabetes mellitus proceeds readily even in the absence of insulin,[1,2] intravenous fructose is being employed as an adjunct in the treatment of diabetic acidosis and insulin-resistant diabetes.

The observation has been made that administration of fructose produces a greater increase in blood pyruvic and lactic acid levels than does administration of a comparable amount of glucose.[1-4] This effect has been noted in both normal and diabetic subjects. The question arises whether this increase in organic acids may become of sufficient magnitude to have an adverse effect in patients with pre-existing respiratory or metabolic acidosis.

Weichselbaum, Margraf and Elman[5] have reported minimal alterations in blood *p*H and plasma bicarbonate levels in normal individuals given a liter of 10 per cent fructose at a rapid rate; however, in two patients under anesthesia given similar quantities of fructose, an appreciable decrease in *p*H and bicarbonate values apparently ensued. Since acid-base changes known to occur as a result of anesthesia alone[6,7] were not controlled in Weichselbaum's experiments, we considered it important to re-examine these fructose-induced effects, not only in patients under anesthesia, but also in patients with pre-existing acid-base derangements associated with a variety of clinical states.

SUBJECTS AND PROCEDURE

Studies were performed on 20 patients. Of these, 8 were in normal acid-base balance, 9 were in metabolic acidosis in various stages of compensation, 2 were in respiratory acidosis induced by pentothal anesthesia, and 1 was in metabolic alkalosis due to vomiting. The metabolic acidosis group consisted of 6 normal subjects given ammonium chloride orally in a dose of 1.5 mEq./kg. of body weight per day for 3 to 10 days prior to the fructose infusion. There were also 3 patients studied who had chronic glomerulonephritis with reduced renal reserve. All subjects studied, with the exception of the 3 with glomerulonephritis, were free of respiratory, renal, or hepatic dysfunction.

The subjects ordinarily were given 1000 ml. (range 500 to 1600 ml.) of 10 per cent fructose in water (Levugen[R]) intravenously at rates varying between 0.36 and 1.23 gm. per kg. of body weight per hour. Blood samples were taken immediately before and after infusion (table 1). In some instances, samples also were taken frequently during infusion.

METHODS OF ANALYSIS

In the 2 anesthetized patients analyses were performed on specimens obtained by direct brachial artery puncture. All other analyses were performed on arterialized venous blood, which were drawn under oil from an antecubital vein by the method of Davenport.[8] All blood samples were promptly analyzed for *p*H level and carbon dioxide content. The *p*H was determined on whole blood at room temperature by means of a Beckman model G *p*H meter. Appropriate correction to body temperature was made by subtracting 0.014 *p*H units per centigrade degree difference between room and body temperatures. The carbon dioxide content of plasma was measured by the manometric method of Van Slyke and Neill.[9] Bicarbonate concentration was calculated according to the Henderson-Hasselbach equation. A *p*K of 6.1 was used for carbonic acid in this calculation.

RESULTS AND DISCUSSION

The blood *p*H and plasma bicarbonate values for each subject before and after fructose infusion are given in

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table 1. In almost every instance these values decreased slightly following fructose administration. At no time was any marked fall in *p*H or bicarbonate observed.

TABLE 1
Blood *p*H and plasma bicarbonate levels immediately prior to and at end of fructose infusion

Patient	*p*H*	HCO_3* mEq./L.	Fructose ml. 10% sol.	Infusion rate gm./kg./hr.	*p*H†	HCO_3† mEq./L.
			Normal			
P.A.	7.42	25.7	1,000	0.94	7.35	23.1
C.R.	7.40	22.1	1,000	1.01	7.35	19.4
D.I.	7.38	24.2	1,000	1.04	7.33	22.1
W.I.	7.36	26.1	1,000	1.21	7.32	23.3
G.R.	7.37	26.5	1,000	1.20	7.33	22.0
N.A.	7.41	24.8	1,000	1.05	7.36	20.3
K.E.	7.43	24.2	1,000	1.23	7.37	19.5
W.L.	7.39	24.4	1,000	1.15	7.37	22.1
Average	7.39	24.7			7.34	21.4
			Metabolic Acidosis			
H.A.	7.31	19.1	500	0.96	7.41	18.4
G.O.	7.41	29.8	1,000	1.23	7.25	26.2
L.I.	7.36	27.5	1,000	1.21	7.26	22.5
H.R.	7.33	18.6	1,000	1.06	7.28	19.4
W.S.	7.34	22.9	1,000	1.11	7.31	19.5
N.L.	7.37	22.0	1,000	1.18	7.34	17.6
L.O.	7.41	22.5	1,300	0.76	7.38	23.8
R.O.	7.43	25.1	1,300	0.46	7.36	21.0
R.D.	7.36	23.8	1,600	0.36	7.44	24.8
Average	7.36	23.5			7.34	21.5
			Anesthesia			
M.O.	7.29	22.9	1,000	0.91	7.24	18.9
F.T.	7.23	27.7	900	0.85	7.30	23.0
			Metabolic Alkalosis			
A.L.	7.40	31.4	1,000	0.92	7.35	29.5

*Before fructose administration.
†At the end of fructose infusion.

In the normal subjects, the average fall in *p*H was 0.05 units. In the same group, the average fall in bicarbonate was 3.3 mEq./L. In the patients with metabolic acidosis, the average fall in *p*H was 0.02 units .The average decrease in bicarbonate concentration was 2 mEq./L.

The patients with uncompensated metabolic acidosis did not exhibit changes in *p*H and bicarbonate greater than those observed in the compensated group. Similar minor decreases in *p*H and bicarbonate after fructose administration were seen in the two patients under anesthesia and also in the single patient with metabolic alkalosis.

There was no evidence that the slight degree of acidosis which occurred as a result of fructose administration produced any of the manifestations ordinarily associated with clinical acidosis. Accordingly, we consider these slight changes to be of no clinical significance.

In figure 1 are shown serial blood *p*H and plasma bicarbonate values during the entire course of an infusion of fructose given rapidly to a patient under anesthesia. Control samples prior to fructose administration were taken after anesthesia had begun because of the known effect of induction of anesthesia alone on acid-base balance.[6, 7] It was hoped that in this way a distinction could be made between anesthesia-induced acidosis and any additional effect that fructose itself might have had on acid-base balance during the course of anesthesia.

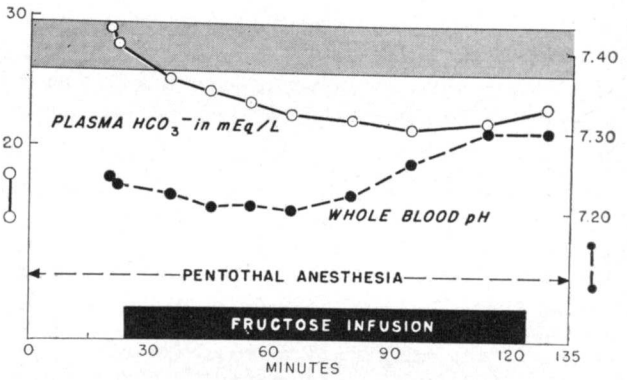

FIG. 1. Patient F. T. Effect of 900 cc. of 10 per cent fructose administered intravenously at the rate of 0.85 gm. per kg. per hr. on blood pH and plasma bicarbonate in an anesthetized patient. (Shaded area represents approximate normal range of pH and bicarbonate in unanesthetized persons. Slight rise in pH after 60 minutes was associated with improved ventilation; high values for bicarbonate early in anesthesia were associated with restricted ventilation.)

It is apparent that the control *p*H and bicarbonate values twenty minutes after induction of anesthesia were definitely low, indicating an acute respiratory acidosis due to anesthesia alone. Subsequent administration of 90 gm. of fructose did not appear to increase the severity of the acidosis.

Taken as a whole, the findings indicate that infusions providing 50 to 160 gm. of fructose at rates ranging from 0.36 to 1.23 gm. per kg. of body weight per hour induce small but consistent decreases in blood *p*H levels and plasma bicarbonate concentrations. It seems reasonable to attribute such changes to the increased production of organic acids which accompanies fructose catabolism.

These changes in acid-base balance do not appear to be of clinical significance, either in the normal individual or in patients with pre-existing acidosis.

SUMMARY

1. The effect of intravenously administered fructose on blood *p*H and plasma bicarbonate levels was determined in normal subjects, patients with ammonium chloride-induced acidosis, patients with metabolic acidosis associated with chronic renal insufficiency, and patients with respiratory acidosis induced by anesthesia.

2. Fifty to 160 gm. of fructose in water given at rates varying between 0.36 and 1.23 gm. per kg. of body weight per hour produced small but consistent decreases in blood *p*H and plasma bicarbonate levels in most of the subjects studied.

3. These minor chemical changes were unaccompanied by clinical manifestations of acidosis.

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SUMMARIO IN INTERLINGUA

Le Effecto de Fructosa, Administrate per Via Intravenose, Super le Balancia de Acido e Base in le Sanguine de Patientes con Pre-existente Acidosis

1. Le effecto de fructosa, administrate per via intravenose, super le nivellos de *p*H del sanguine e de bicarbonato del plasma esseva determinate in (a) subjectos normal, (b) patientes con acidosis inducite per chlorido de ammonium, (c) patientes con acidosis metabolic associate con chronic insufficientia renal, e (d) patientes con acidosis respiratori inducite per anesthesia.

2. Inter 50 e 160 g fructosa in aqua, administrate in ratas variante inter 0,36 e 1,23 g per kg peso corporee per hora, produceva in le majoritate del subjectos studiate un leve sed consequente reduction del nivellos de *p*H del sanguine e de bicarbonato del plasma.

3. Iste minor cambiamentos chimic non esseva accompaniate de manifestationes clinic de acidosis.