Intravenous Fructose Disappearance in Protein Calorie Malnutrition

D. J. BECKER, B. L. PIMSTONE

SUMMARY

The disappearance of intravenously administered fructose and glucose became more rapid after treatment in children with protein calorie malnutrition (PCM). Since fructose disposal is largely hepatic and is insulin-independent, the finding suggests a reversible disturbance of the appropriate hepatic enzymes in PCM. The impaired glucose disposal is unlikely to be caused solely by lack of insulin.

S. Afr. Med. J., **48**, 2243 (1974).

Although glucose intolerance is very common in protein calorie malnutrition (PCM),[1-5] the debate concerning its pathogenesis remains unresolved. An impaired secretion of insulin[6,7] is partly responsible, for there is a strong correlation between the low insulin response to glucose and glucose intolerance in untreated patients with PCM.[8] However, glucose tolerance does not improve at the same rate as insulin secretion during refeeding; the latter is sometimes normal within a few days of treatment in the face of abnormal glucose tolerance.[5,6,8] Furthermore, even in the untreated state, glucose tolerance may be abnormal in individual cases with adequate but sustained insulin levels,[9] and is not completely corrected by exogenous insulin,[10,11] suggesting insulin resistance. Thus factors other than insulin secretion appear to be important in carbohydrate homeostasis in PCM, with the possibility that the fatty liver might be unable to take up glucose normally[12] owing to mechanisms which are insulin-independent. Since the liver is the most important organ of fructose metabolism,[13-15] and since its uptake of fructose is uninfluenced by insulin,[16,17] it was thought worth while to investigate fructose tolerance before and after treatment in patients with PCM.

PATIENTS AND METHODS

Five patients suffering from kwashiorkor, aged 8 - 29 months, were admitted to the Metabolic Unit of the Red Cross Children's Hospital. All were hypo-albuminaemic (1,2 - 2,2 g/100 ml) with oedema and dermatosis, and had normal serum levels of bilirubin and hepatic transaminases. All patients were treated with antibiotics, vitamins and potassium chloride from the time of admission. They received a carbohydrate, protein-free diet (10 - 15 g/kg body weight) until tests were completed on the second day in hospital. Informed consent was obtained from a parent of each child.

Department of Medicine and of Paediatrics and Child Health, University of Cape Town
D. J. BECKER, M.B. CH.B., F.C.P. (S.A.)
B. L. PIMSTONE, M.D., F.R.C.P.

Date received: 14 August 1974.

Tests

On the second and third days in hospital, after an 8-hour overnight fast, an intravenous glucose or fructose load (1 g/kg body weight as a 25% solution over 2 - 3 minutes) was administered in random order. Side-effects, including hypoglycaemia, were not noted.

Venous blood was sampled at 0,5, 20, 45, 60 and 90 minutes, and analysed for glucose[18] after the glucose load, and for fructose[19,20] after the fructose load. Tests were repeated in all the patients after 3 - 5 weeks of feeding, when serum albumin levels had returned to normal.

The disappearance rate constants (K_t) for glucose and fructose were calculated after semilogarithmic plotting of total blood glucose and fructose values.[21]

RESULTS

Table I shows that in all 5 patients there was impaired intravenous glucose disappearance before treatment, returning to normal after feeding. Fructose disposal was more rapid than that of glucose, but also increased on recovery in each case.

TABLE I. GLUCOSE AND FRUCTOSE DISAPPEARANCE RATE CONSTANT IN 5 CHILDREN SUFFERING FROM PCM BEFORE AND AFTER TREATMENT

	Glucose K_t		Fructose K_t	
Patient	Before	After	Before	After
1	1,16	2,04	2,16	4,62
2	1,31	2,77	3,15	4,08
3	1,54	2,39	2,77	4,92
4	1,38	2,24	1,61	4,62
5	1,51	2,89	2,67	4,33

DISCUSSION

Fructose disappearance is thought to be independent of insulin, and is normal in situations associated with severely

impaired glucose tolerance and insulinopenia, for example, in diabetes mellitus[16,22] and starvation.[23] Fructose tolerance is impaired only when there is a deficiency of the hepatic enzymes responsible for fructose metabolism, such as occur both in hereditary fructose intolerance[24] or fructosaemia, or in severe acquired liver disease with hepatocellular damage.[25] Fructose intolerance which responded to dietary refeeding in 5 children with PCM, might therefore suggest a reversible deficiency of one or more of the hepatic enzymes involved in fructose incorporation into intermediary pathways of carbohydrate metabolism. Evidence for an enzyme block beyond phosphofructokinase has been reported by Alleyne *et al.*[10] in association with decreased galactose clearance from the blood. A possible mechanism of such decreased enzyme activity could be the well-documented potassium depletion in PCM,[26,27] since potassium is necessary for the activation of several glycolytic enzymes.[28]

The finding of fructose intolerance in PCM therefore suggests hepatic disturbance of the enzymes concerned with its metabolism, and raises the possibility that the insulin-dependent component of the characteristic glucose intolerance in PCM might be associated with a similar hepatic mechanism.

This study was supported by grants from the South African Medical Research Council and the Wellcome Trust.

REFERENCES

1. Bose, J. P., De, V. N. and Mukerjee, P. (1946): Ind. J. Med. Res., **34**, 143.
2. Slone, D., Taitz, L. S. and Gilchrist, G. S. (1961): Brit. Med. J., **1**, 32.
3. Baig, H. A. and Edozien, J. C. (1965): Lancet, **2**, 662.
4. Hadden, D. R. (1967): *Ibid.*, **2**, 589.
5. Cook, G. C. (1967): Nature (Lond.), **215**, 1295.
6. Becker, D. J., Pimstone, B. L., Hansen, J. D. L. and Hendricks, S. (1971): Diabetes, **20**, 542.
7. Milner, R. D. G. (1971): Pediat. Res., **5**, 33.
8. Becker, D. J., Pimstone, B. L. and Hansen, J. D. L. (1974): *Ibid.* (in press).
9. Becker, D. J., Pimstone, B. L., Hansen, J. D. L., MacHutchon, B. and Drysdale, A. (1972): Amer. J. Clin. Nutr., **25**, 499.
10. Alleyne, G. A. O., Trust, P. M., Flores, H. and Robinson, H. (1972): Brit. J. Nutr., **27**, 585.
11. Bowie, M. D. (1964): S. Afr. Med. J., **38**, 328.
12. Holmes, E. G. and Trowell, H. C. (1948): Lancet, **1**, 395.
13. Mendeloff, A. I. and Weichselbaum, T. E. (1953): Metabolism, **2**, 450.
14. Weichselbaum, T. E. and Margraff, H. W. (1953): *Ibid.*, **2**, 434.
15. McIntyre, N., Turner, D. S. and Holdsworth, C. D. (1970): Diabetologia, **6**, 593.
16. Miller, M., Craig, J. W., Drucker, W. R. and Woodward, H. jun. (1956): Yale. J. Biol., **29**, 335.
17. Topping, D. L. and Mayes, P. A. (1972): Biochem. J., **126**, 295.
18. Somogyi, M. (1952): J. Biol. Chem., **195**, 19.
19. Roe, J. H. (1934): *Ibid.*, **107**, 15.
20. Roe, J. H., Epstein, J. H. and Goldstein, N. P. (1949): *Ibid.*, **178**, 839.
21. Ikkos, D. and Luft, R. (1957): Acta endocr., **25**, 312.
22. Miller, M., Drucker, W. P., Owens, J. E., Craig, J. W. and Woodward, H. jun. (1952): J. Clin. Invest., **31**, 115.
23. Craig, J. W., Drucker, W. P., Miller, M., Owens, J. E., Woodward, H., Brofman, B. and Pritchard, W. H. (1951): Proc. Soc. Exp. Biol. (N.Y.), **78**, 698.
24. Froesch, E. R. (1966): *The Metabolic Basis of Inherited Disease*, 2nd ed., p. 124. New York: McGraw-Hill.
25. Smith, L. H., Ettinger, R. H. and Seligson, D. A. (1953): J. Clin. Invest., **32**, 273.
26. Alleyne, G. A. O., Millward, D. J. and Scullard, G. N. (1970): J. Pediat., **76**, 75.
27. Hansen, J. D. L. (1956): S. Afr. J. Lab. Clin. Med., **2**, 206.
28. Svelter, C. H. (1970): Science, **168**, 789.