Z. Ernährungswiss. **20**, 223–228 (1981)

ISSN 0044-264 X

*Faculty of Medicine, Pediatric Department, El-Mansoura University, El-Mansoura, Egypt National Research Centre, Dokki, Cairo (Egypt)**)*

The effect of L-tryptophan loading on glucose tolerance in kwashiorkor children

*El-M. M. El-Bassousy, F. A. El-Shobaki**),* and *Sh. M. El-Sallab*

(Received April 14, 1981)

Tryptophan is known to have many pharmacological effects on carbohydrate metabolism. Glucose intolerance in kwashiorkor children has been previously reported. The effect of L-tryptophan loading on glucose tolerance in kwashiorkor children was investigated. Results showed that rates of removal of given i.v. glucose in percentage of excess glucose removed per minute is lower than normal in kwashiorkor children. L-tryptophan loading improved glucose tolerance as manifested by increased percentage removal of excess glucose. These results were interpreted with reference to related research work in this field and the possibility of giving L-tryptophan during treatment of kwashiorkor children was discussed.

L-tryptophan is of particular interest among other essential amino acids since it has a diversity of functions other than its necessity for proper performance of cell organelle for protein synthesis (1). It is the precursor of the neurotransmitter serotonin (2) and supplies the body with its nutritional requirements of niacin (3).

Tryptophan is known to have many pharmacological effects on carbohydrate metabolism. It is among the amino acids reported to stimulate insulin secretion (4). Acute doses of nicotinic acid, a metabolite of tryptophan, can increase tolerance to a glucose load, while administration of L-tryptophan in doses approximating the amount found in a daily food ration inhibits gluconeogenesis in fasting rats (5).

Glucose intolerance as manifest by an abnormal glucose disappearance rate has been previously reported (6, 7) in children suffering from protein malnutrition. A characteristic feature of such cases is the state of hypoaminoacidemia (8), affecting in particular the essential amino acids including tryptophan (9).

According to the previous information it seems of value to investigate any beneficial effect of tryptophan-loading on glucose tolerance in malnourished children.

Materials and methods

The material of this study were 17 kwashiorkor cases with different degrees of severity. Their age ranged from 9 to 24 months and comprised both sexes. Besides, 5 healthy children of more or less similar age range and socioeconomic standard were

investigated to serve as controls. Patients and control subjects were selected among those attending the Paediatric department, El-Mansoura Faculty of Medicine, seeking medical treatment, or their relatives.

After clinical examination, cases showing any infection or other ailment than malnutrition were excluded. The selected cases were fasted overnight, and early in the morning they were intravenously injected with 0.5 g/kg body weight of 50 % sterile glucose solution, adjusting the rate of flow to require 5 min for its administration (10).

Blood glucose level was determined in a fasting blood sample, at half and at one hour after glucose injection. 11 cases were given high protein diet for 3 days together with a loading dose of L-tryptophan equivalent to 100 mg daily. Afterwards, the glucose tolerance test was repeated on the same individuals to reveal any difference in glucose tolerance after such treatment. Another group of 6 kwashiorkor children were investigated in the same way as the previous group before and after high protein diet, but with no L-tryptophan loading to reveal the effect of L-tryptophan alone. The 5 control subjects were subjected to glucose tolerance test for matching. Rate of removal of excess glucose removed per minute (%K) was calculated from the formula:

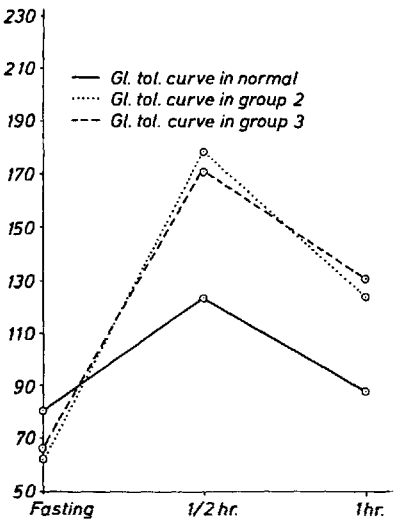
$$\% K = \left(\frac{2.3}{T_2 - T_1}\right) \left(\log \cdot \frac{C_1}{C_2}\right) \times 100$$

Where C_1, C_2 are mg/100 ml excess glucose at times T_1 and T_2 in minutes after the intravenous administration of glucose (11).

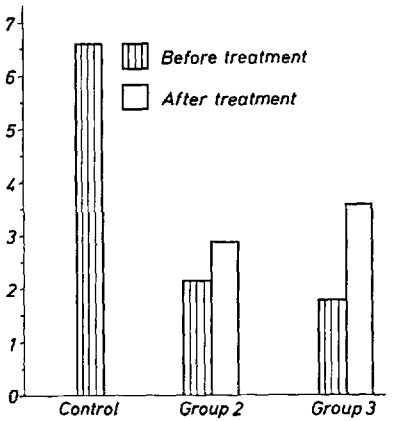
Blood glucose was determined by the method of Feteris (12).

Results

Table 1 shows the pattern obtained for the fasting blood glucose level and the values at ½ and 1 hour after intravenous injection of glucose in normal children. The %K is also given. As shown, a maximum value was



Glucose tolerance curve in normal and K.W.O. patients



% K in control and K.W.O. patients

Table 1. Glucose tolerance test in control group 1 (mg %).

	Fasting	½ hour	1 hour	% K
1	83	138	97	4.5
2	75	86	76	7.9
3	88	111	90	8.1
4	85	115	88	7.6
5	73	114	80	4.9
Range	73–88	86–138	76–97	4.5–8.1
Mean	80.8	112.8	86.2	6.6
S.D ±	6.49	18.4	8.3	1.75

reached half an hour after injection reaching a mean value of 112.8 ± 18.4, and the level returned back to more or less the normal value after one hour. The % K was found to be 6.6 ± 1.75.

Table 2 shows similar pattern for kwashiorkor children before and after 3 days of treatment with high protein diet with no tryptophan loading. As shown in the table, the mean fasting blood sugar level in such children was significantly lower than normal (63.0 ± 9.5 mg/100 ml). After glucose infusion, blood glucose rose to abnormally high level (178.0 ± 27.96 mg/100 ml) in half an hour and returned back slowly, so that after one hour blood glucose value was significantly higher than controls, and the % K (2.13 ± 0.32) was significantly lower, indicating a state of glucose intolerance in kwashiorkor cases.

Table 2. Glucose tolerance test before and after dietetic treatment without tryptophan (group 2) in mg%.

	Before dietetic treatment				After dietetic treatment			
	Fasting	½ h	1 h	% K	Fasting	½ h	1 h	% K
1	54	198	134	1.78	63	202	122	2.82
2	68	179	120	2.31	73	163	108	3.10
3	50	190	124	2.10	65	180	112	2.91
4	62	200	136	2.6	75	185	118	3.10
5	69	156	120	1.76	73	138	100	2.89
6	75	145	110	2.28	69	136	107	2.48
Range	54–75	145–200	110–136	1.76–2.31	63–75	136–202	100–122	2.48–3.10
Mean	63.0	178	122	2.13	69.67	167.83	109.16	2.88
S.D. ±	9.5	27.96	12.24	40.32	4.84	25.90	10.36	0.29
	$\acute{P}_1$ 0.05	$\acute{P}_2$ 0.001	P_3 0.05	$\acute{P}_4$ 0.01	P_1 0.1	P_2 0.1	P_3 0.1	P_4 0.1

P_1 (1, 2, 3, 4): Significant difference between blood sugar values before and after dietetic treatment without tryptophan.
P (1, 2, 3, 4): Significant difference from group 1.

Table 3. Glucose tolerance test before and after tryptophan loading (group 3).

	Before tryptophan				After tryptophan			
	Fasting	½ h	1 h	% K	Fasting	½ h	1 h	% K
1	76	170	113	3.07	59	105	73	4.23
2	90	202	150	2.06	85	190	90	4.48
3	45	250	200	0.9	75	243	154	2.49
4	63	138	107	1.6	55	142	85	3.2
5	60	153	136	0.6	58	126	92	2.28
6	49	127	89	2.0	63	112	75	4.27
7	73	250	190	1.36	75	212	130	2.76
8	63	138	100	2.34	69	89	73	5.3
9	75	180	124	2.51	73	133	96	3.16
10	65	145	114	1.6	75	117	90	3.4
11	70	120	97	2.03	60	118	79	3.68
Range	45–90	120–250	89–150	0.6–3.07	55–85	89–234	73–154	2.28–5.3
Mean	66.27	170.27	129.09	1.75	67.9	144.27	93.45	3.57
S.D. ±	12.67	46.08	37.02	0.84	9.49	48.95	23.42	0.93
	$\acute{P}_1$ 0.05	$\acute{P}_2$ 0.001	$\acute{P}_3$ 0.05	$\acute{P}_4$ 0.01	P_1 0.1	P_2 0.1	P_3 0.05	P_4 0.001

P_1 (1, 2, 3, 4): Significant difference between blood sugar values before and after L-tryptophan.
$\acute{P}$ (1, 2, 3, 4): Significant difference from group 1.

After dietetic treatment, the values obtained for blood glucose half and one hour after glucose infusion were still markedly higher than corresponding values in normal, but slightly lower than before dietetic treatment. The difference between the levels of blood glucose before and after dietetic treatment was statistically not significant. The % K was increased after dietetic treatment, but the increase was statistically insignificant.

In table 3 the pattern obtained for malnourished children before and after dietetic treatment together with L-tryptophan loading is given. The pattern of glucose tolerance before L-tryptophan loading was more or less similar to the previous group, and shows the same characteristics relative to normals. After L-tryptophan loading and dietetic treatment, the blood glucose levels ½ and 1 hour after injection of glucose were markedly lower than corresponding values before L-tryptophan loading, particularly after 1 hour from glucose injection. The % K value was significantly increased to 3.57 ± 0.93 but was still lower than the normal value.

Discussion

The fasting blood glucose reported in our normal controls is more or less in concordance with that of Eisa et al. (6), although the value half an

hour after i.v. injection of glucose was lower and returned back to more or less the fasting level in a shorter period (1 hour). This is in concordance with Brawer et al. (10), who found that the blood glucose level returned back to the fasting level 1 hour after glucose infusion.

In kwashiorkor, our fasting, half and one hour values were lower than those of Eisa et al. (6), although in both studies there was slow disposal of infused glucose, indicating glucose intolerance in kwashiorkor patients.

In kwashiorkor patients, many abnormalities occur and affect metabolism as increased glycogenesis (13), impaired gluconeogenesis (14) and diminished glycogenolysis (7). Disorders in some organs, which have a relation to carbohydrate metabolism, have been also described in kwashiorkor patients, such as hypofunction of the suprarenal (15) and pituitary glands (16), together with enlargement of the islet cells of the pancreas (17). All these abnormalities contribute in a way or another and to different extents to the occurrence of hypoglycemia in kwashiorkor patients. It seems probable that decreased peripheral utilization of glucose plays the main role in the production of the glucose intolerance in kwashiorkor patients. Alleyne et al. (18) suggested a possible impairment in glycolysis distal to the phosphofructokinase step, which persisted after recovery.

The increase in %K value, denoting the improvement in glucose tolerance to the given glucose load after dietetic and L-tryptophan treatment of kwashiorkor cases, proves the beneficial value of L-tryptophan in this respect. The necessity of extra-L-tryptophan supplementation to the high protein diet offered to the patients is confirmed through the limited increase in %K value (35.5 %) for kwashiorkor cases given dietetic treatment without tryptophan relative to an increase of (104 %) in kwashiorkor children given L-tryptophan together with the dietetic treatment. These results are in concordance with previous work by Wattman (19), which implicates an effect of L-tryptophan loading on glucose tolerance in rats fed diet deficient in tryptophan.

The mode of action of L-tryptophan on glucose tolerance is not clearly known. It has been reported that glucose intolerance is not reversed by niacin or vitamin B_6, not dependent on dietary protein source, not a necessary consequence of decreased food consumption and growth and not duplicated by a lack of dietary lysine (19). Although L-tryptophan has been reported to stimulate insulin secretion (4), yet this effect is suggested to be non-operative in kwashiorkor cases which showed evidence of hyperinsulinism (20).

The effect of L-tryptophan on glucose tolerance can still be through some sort of action in the glycolytic process, the activity of the Krebs' cycle or the increase of peripheral utilization of glucose.

The answer to these open questions will be the subject of other publications. However, it is shown from our results that supplementation of kwashiorkor patients with extra L-tryptophan during treatment is valuable in improving glucose tolerance in these patients.

Key words: kwashiorkor, glucose tolerance, tryptophan loading

References

1. Baliga, B. S., A. W. Pronizuk, H. N. Munro: J. Mol. Biol. **34,** 199 (1968).
2. Fernstrom, J. D., R. J. Wurtman: Nutrition and the brain. Scientific Amer. **230,** 84 (1974).
3. Krehl, W. A., L. Tepley, P. S. Sarma, C. A. Elvehjen: Science **101,** 489 (1945).
4. Floyd, J. C. Jr., S. S. Fajans, J. W. Conn, R. F. Knoff, J. Rull: J. Clin. Invest. **45,** 487 (1966).
5. Gaut, Z. N., R. Pacelinko, H. M. Soloman, G. B. Thomas: Metabolism **20,** 1031 (1971).
6. Eisa, E. K., A. Shukry, I. M. Fayed, O. M. Metwally, S. M. Ismail: Gazette of the Egyptian Pediatric-Association, Vol. **15,** 9 (1967).
7. Eisa, E. A., A. S. Shukry, I. M. Fayed, O. M. Metwally, and S. M. Ismail: Gazette of the Egyptian Pediatric Association, Vol. **15,** 132 (1967).
8. Schendel, H. E., J. D. L. Hansen: J. Pediatrics **60,** 280 (1962).
9. Metwalli, C. M., A. S. Shukry, I. Ghali, I. Shukry, S. Ismail, A. El-Bishlawy: Gazette of the Egyptian Pediatric Association **26,** 52 (1977).
10. Brawer, J. D., C. A. Toro, P. G. Chewpher: Bray's clinical laboratory methods. p. 254. 6th ed. The C. V. Mosby Company (St. Louis 1962).
11. Mertz, W. & K. Schwarz: Amer. J. Physiol. **203,** 53 (1962).
12. Feteris, W. A.: Amer. J. Med. Tech. (1965).
13. Metcoff, J., S. Frenk: G. lab. clin. Med. **62,** 995 (1963).
14. Slone, D., L. S. Teitz, G. S. Gilchrist: South Afr. Med. J. **33,** 1024 (1959).
15. Docke, J. N. G., V. H. T. James, J. Jandon, V. Wynn: Brit. Med. **1962/I,** 662.
16. Gillman, J., T. Gillmann: Respective in human malnutrition, Grune & Stratton, New York.
17. Shehata, A. H., K. Khalifa, A. Abdel Hay, G. Kamel, I. Fayed: J. end. and Met. (Egypt). Vol. II, No. I (1965).
18. Alleyne, G. A. O., P. M. Trust, H. Flores, H. Robinson: Brit. J. Nutrit. **27,** 585 (1972).
19. Wattman, J. S.: J. Nutr. **106,** 631 (1976).
20. Gamain, R., M. Pierchon: Malnutrition in African mothers, infants and young children, p. 146, H. M. S. O. (London 1954).

Authors' address:

Dr. El-M. M. El-Bassousy, Faculty of Medicine, Pediatric Dept., El-Mansoura University, El-Mansoura (Egypt)