Serum and Urine Amino Acid Analysis in Children with Biliary Atresia

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CHIBA, T. *Serum and Urine Amino Acid Analysis in Children with Biliary Atresia*. Tohoku J. exp. Med., 1983, **139** (1), 61-66 — Serum and urine amino acid levels were measured preoperatively and at varying time following successful hepatic portoenterostomy. All of the essential amino acids measured returned to normal levels during the late postoperative period over five years, whereas many of the non-essential amino acids remained in the abnormal range. — — — — — amino acid analysis; biliary atresia

Serum and urine amino acid analysis may represent a sensitive indicator of the recovery of hepatic function in patients with lipid disease. This paper reports the results of both pre- and postoperative amino acid levels in patients with biliary atresia.

MATERIALS AND METHODS

Subjects

Twenty-three children with biliary atresia were assigned to one of four clinical groups based upon the temporal relationship between their surgery and the time of evaluation: Group 1 ($n=9$) prior to surgery; Group 2 ($n=7$) 1 to 3 months following a hepatic portoenterostomy (with bile excretion); Group 3 ($n=7$) 2 to 5 years following hepatic portoenterostomy (jaundice free); and Group 4 ($n=7$) over 5 years following successful hepatic portoenterostomy (jaundice free). The children ranged in age from one month to 17 years.

Methods of measurement of amino acid level

All Group 2 patients were evaluated both before and after surgery. In order to avoid the influence of feeding and physical activity, all blood samples were obtained following a two-hour fast from the patients in a resting state. Serum and urine amino acid levels were measured with a spectrophotometer (Hitachi Company, Model 835) at Morishita Pharmacological Institute, Osaka.

Eighteen amino acids could be distinguished using this technique; phenylalanine (Phe), methionine (Met), leucine (Leu), isoleucine (Ile), lysine (Lys), tryptophane (Try), valine (Val), threonine (Thr), glutamic acid (Glu), glycine (Gly), arginine (Arg), aspartic acid (Asp), cystine (Cys), proline (Pro), histidine (His), alanine (Ala), tyrosine (Tyr), and serine (Ser). Mean values of each of the amino acids were compared to that of normal Japanese children and adults (control population).

RESULTS

Preoperatively, (Group 1) serum levels of Phe, Glu, Asp, and His were significantly higher than normal, while Trp, Val, Thr, Cys, and Ala were well below control (Table 1). During the early postoperative period, (Group 2) most of the serum amino acid levels increased slightly but were not significantly different from

TABLE 1. Serum amino acids before and 1 to 3 months after operation in biliary atresia

	Biliary atresia		Control
	Before operation	1 to 3 mo. after operation	2 to 6 mo. old
Essential amino acids (μ moles/100 ml)			
Phenylalanine	8.47*	10.65	6.44
Methionine	3.54	4.27	4.19
Leucine	12.01	13.04	13.30
Isoleucine	7.17	7.47	7.63
Lysine	17.60	23.04	18.86
Tryptophan	3.04†	3.81	7.42
Valine	18.99†	23.69	30.32
Threonine	23.05†	27.49	50.03
Non-essential amino acids (μ moles/100 ml)			
Glutamic acid	58.49*	57.02	6.26
Glycine	28.37	37.98	31.07
Arginine	9.07	9.07	10.37
Aspartic acid	3.26*	3.63	1.79
Cystine	0.23†	trace	4.35
Proline	27.71	35.65	25.0
Histidine	8.81*	10.23	7.14
Alanine	40.37†	42.97	66.60
Tyrosine	9.27	11.77	7.44
Serine	17.75	21.74	15.74

* Significantly high values ($p < 0.01$).

† Significantly low values ($p < 0.01$).

Fig. 1. Changes of essential amino acids in biliary atresia.

TABLE 2. Serum amino acids 2 to 5 years after operation in biliary atresia

	Biliary atresia	Control
	2 to 5 years after operation	4 to 6 years old
Essential amino acids (μ moles/100 ml)		
Phenylalanine	8.01*	4.47
Methionine	2.19	2.07
Leucine	11.04	8.56
Isoleucine	5.67	5.26
Lysine	14.25	13.77
Tryptophan	4.29	5.18
Valine	20.63	14.60
Threonine	9.37†	34.70
Non-essential amino acids (μ moles/100 ml)		
Glutamic acid	18.10*	4.83
Glycine	31.20*	20.35
Arginine	13.01*	8.01
Aspartic acid	2.75*	2.19
Cystine	trace†	6.03
Proline	12.19	19.30
Histidine	9.41	7.03
Alanine	30.79	28.17
Tyrosine	7.56*	3.94
Serine	15.82	11.46

* Significantly high values ($p < 0.01$).† Significantly low values ($p < 0.01$).

Fig. 2. Changes of non-essential amino acids in biliary atresia.

preoperative measurements (Table 2). In Group 3 patients the values for Phe, Glu, Gly, Arg, Asp, and Tyr were substantially higher than normal while the values of Thr and Cys were low. In Group 4 all of the essential amino acids remained in the abnormal range. Evaluating the changes in the levels of each amino acid in each group demonstrated a stable pattern for one-half of the amino acids measured (Figs. 1, 2). Thr, Glu, and Pro varied markedly, however.

TABLE 3. *Serum amino acids more than 5 years after operation in biliary atresia*

	Biliary atresia	Control
	More than 5 years after operation	Adult
Essential amino acids (μ moles/100 ml)		
Phenylalanine	8.00	6.48
Methionine	2.98	3.03
Leucine	11.52	13.30
Isoleucine	5.56	7.63
Lysine	15.67	18.77
Tryptophan	4.50	5.07
Valine	21.77	25.58
Threonine	11.70	12.80
Non-essential amino acids (μ moles/100 ml)		
Glutamic acid	13.98*	7.21
Glycine	36.54*	21.40
Arginine	13.39*	9.68
Aspartic acid	2.87*	0.54
Cystine	trace†	4.35
Proline	14.76†	20.25
Histidine	9.25	7.16
Alanine	38.29	40.56
Tyrosine	6.39	7.44
Serine	18.05	15.12

* Significantly high values ($p < 0.01$).† Significantly low values ($p < 0.01$).TABLE 4. *Urinary amino acids in biliary atresia*

	Before operation	After operation		
		1 to 3 months	2 to 5 years	5 years
Essential amino acids (μ moles/100 ml)				
Phenylalanine	6.2	6.5	9.7	12.6
Methionine	2.9	2.9	4.9	3.3
Leucine	6.7	3.6	4.5	4.9
Isoleucine	4.6	2.5	4.7	4.4
Lysine	28.3	35.4	31.1	38.0
Tryptophane	8.68	4.5	6.8	18.1
Valine	4.0	2.0	5.3	5.0
Threonine	57.5	64.3	16.2	22.4
Non-essential amino acids (μ moles/100 ml)				
Glutamic acid	2.3	1.8	trace	trace
Glycine	109.4	83.6	108.6	190.4
Arginine	2.9	2.0	2.9	2.7
Aspartic acid	9.54	3.9	6.76	5.1
Cystine	14.2	7.8	5.2	5.7
Proline	4.63	trace	trace	trace
Histidine	72.3	71.3	124.1	182.8
Alanine	40.6	25.7	34.5	45.8
Tyrosine	13.9	13.0	20.5	28.3
Serine	59.3	62.75	63.54	63.7

Table 4 shows the mean values of urinary amino acids in each group. Excretion rates of most of the amino acids remained remarkably stable, whereas Thr, Gly, and His levels were quite variable. The relationship between serum levels and urinary excretion of the amino acids was not predictable.

DISCUSSION

The liver has a pivotal role in many body functions including hematopoiesis, protein, fat, and carbohydrate metabolism, vitamin storage, and bilirubin excretion. A better understanding of the physiologic consequences of biliary atresia on each of these functions is important. In children with biliary atresia, the patterns of recovery of the various liver functions are far from uniform. Serum bilirubin, plasma protein fractions, and serum turbidity tests usually return to normal levels within three months if surgery is successful. The alkaline phosphatase and serum transaminase levels, however, frequently take over two years to return to normal (Kasai et al. 1975). Hepatic excretion of sulfobenzyl penicillin (an indicator of bile concentrating ability) demonstrates a very slow normalization (Perry et al. 1965).

As far as amino acids are concerned, Sherlock (1968) has described no change in the patterns of serum or urinary amino acid excretion in patients with cholestatic jaundice. High serum levels of Glu and decreased values for L-Pro, Met, Ile, and Trp have been reported in biliary atresia, however (Takada 1970; Chiba and Kasai 1981). In patients with cirrhosis, increased levels of Met, Ala, Arg, Gly, His, Pro, and Tyr have been reported (Vacanti and Folkman 1979). In this study, one-half of the amino acids demonstrated little variability with age. In spite of the fact that all of the measured essential amino acids returned to normal, many of the non-essential amino acids remained in the abnormal range. Comparing the branched chain amino acids (Ile, Leu, Val) to the aromatic compounds (Phe, Tyr) a ratio of 2.16 was noted in Group 1, 1.97 in Group 2, 2.40 in Group 3, and 2.70 in Group 4 (normal=2.9). These findings suggest a gradual normalization of the serum amino acid levels in children with biliary atresia following a successful hepatic portoenterostomy.

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