FREE AMINO ACIDS AND SOME ENZYMES OF THEIR METABOLISM IN THE EARLY DEVELOPMENT OF THE PLACENTA

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Changes in the activity of glutamate dehydrogenases and of aspartate and alanine aminotransferases and in the concentration of free amino acids in the guinea pig placenta were discovered in the course of its development. These parameters attained their highest values on the 25th-30th day of pregnancy, i.e., at the time of definitive formation of the placenta. By the 40th day of pregnancy the activity of these enzymes and concentration of free amino acids showed a reduction and after the 45th day they remained at a certain stable level until parturiton.

KEY WORDS: amino acids and their metabolic enzymes; guinea pig placenta; embryogenesis.

There is no information in the literature on the content of free amino acids in the placenta and there are only isolated communications, contradictory in character, on the activity of enzymes of amino acid metabolism in the placenta during its development [8, 9].

The object of this investigation was to study the concentration of amino acids and the activity of aspartate and alanine aminotransferases and of glutamate dehydrogenase in placentas of hemochorial type throughout the period of intrauterine development.

EXPERIMENTAL METHOD

Altogether 70 chorions and placentas from guinea pigs at different stages of pregnancy and also after its termination were investigated. Free amino acids were determined in protein-free tissue extracts by ion-exchange chromatography on a type ND1200E automatic amino acid analyzer (Czechoslovakia). Aminotransferase activity was investigated by Umbreit's method in Paskhina's modification [5]. Glutamate dehydrogenase activity was determined from the increase in $NAD \cdot H_2$ [1]. Protein was determined by Lowry's method [7].

EXPERIMENTAL RESULTS

At all stages of development of the placenta the concentration of glutamic and aspartic acids in it was high (about 40-50% of the total placental amino acid content). Large quantities of glycine, alanine, glutamine, and serines were found, with smaller amounts of methionine, tryptophan, and phenylalanine (Table 1).

The content of most amino acids changed during development of the placenta. The smallest quantity of amino acids in the chorions of the guinea pigs was found on the 10th-15th day of pregnancy, except in the case of lysine, the concentration of which was higher at the beginning of pregnancy than at its end ($P < 0.01$).

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TABLE 1. Content of Free Amino Acids (in mg %) in Placentas of Guinea Pigs at Different Periods of Pregnancy (M±m)

Amino acid	Period of pregnancy (in days)						Parturition
	10—15	15—25	25—30	30—40	45—50	55—60	
Lysine	6,20±0,20	6,97±0,19	7,12±0,21	6,81±0,18	5,62±0,17	5,41±0,19	5,37±0,16
Histidine	3,88±0,15	5,64±0,20	6,98±0,21	6,12±0,19	4,17±0,16	4,02±0,15	4,21±0,16
Arginine	3,11±0,14	5,51±0,21	5,84±0,19	4,81±0,17	4,62±0,18	4,29±0,16	4,18±0,19
Aspartic acid	13,22±0,38	27,92±0,47	30,27±0,49	20,11±0,39	15,52±0,41	16,22±0,36	16,83±0,38
Threonine	2,54±0,08	3,92±0,12	4,21±0,13	3,42±0,11	3,25±0,10	3,07±0,12	3,14±0,09
Serine	4,22±0,15	8,41±0,20	10,33±0,23	7,12±0,19	5,57±0,15	5,71±0,21	5,94±0,23
Glutamine	4,91±0,27	8,23±0,36	8,56±0,31	7,25±0,20	6,32±0,19	6,20±0,21	6,14±0,16
Glutamic acid	22,52±0,43	44,22±0,61	47,38±0,58	35,52±0,51	25,61±0,45	27,44±0,48	29,52±0,43
Glycine	5,10±0,22	8,43±0,27	11,41±0,31	9,51±0,21	7,12±0,22	6,93±0,19	7,01±0,17
Alanine	4,88±0,24	8,45±0,31	9,23±0,29	7,72±0,20	6,54±0,18	6,36±0,21	6,29±0,19
Cystine	3,92±0,14	6,51±0,17	10,13±0,25	8,05±0,19	5,14±0,21	4,22±0,15	4,51±0,17
Valine	3,98±0,12	4,61±0,15	6,34±0,18	5,42±0,15	4,53±0,17	4,71±0,16	4,66±0,15
Methionine	1,87±0,11	2,98±0,14	3,79±0,16	3,02±0,15	2,23±0,13	2,01±0,11	2,10±0,14
Leucine	4,13±0,11	4,86±0,16	5,58±0,15	5,01±0,19	4,54±0,18	4,61±0,14	4,57±0,13
Tyrosine	4,21±0,21	8,12±0,34	8,48±0,24	7,74±0,22	7,53±0,30	7,28±0,24	6,91±0,18
Phenylalanine	1,45±0,08	2,72±0,12	2,81±0,14	2,63±0,14	2,23±0,15	2,06±0,12	2,11±0,14
Tryptophan	2,21±0,09	3,82±0,14	4,25±0,16	3,22±0,12	2,81±0,14	2,72±0,12	2,63±0,13

TABLE 2. Activity of Some Enzymes of Amino Acid Metabolism (in μmoles reaction product formed — $NAD \cdot H_2$ or pyruvic acid —/mg protein/min) in Placentas of Guinea Pigs (M±m)

Enzyme	Period of pregnancy (in days)						Parturition
	10—15	15—25	25—30	30—40	45—50	55—60	
Glutamate dehydrogenase	6,21±0,24	7,13±0,25	9,52±0,31	7,88±0,29	6,12±0,22	6,17±0,24	6,06±0,23
Aspartate aminotransferase	15,42±0,45	17,81±0,47	21,63±0,52	18,14±0,50	16,98±0,48	16,22±0,46	16,04±0,43
Alanine aminotransferase	2,21±0,14	2,88±0,16	3,74±0,19	2,79±0,16	2,02±0,13	1,93±0,11	1,96±0,14

During development of the placenta the amino acid level rose to reach a maximum on the 30th day, i.e., at the time of definitive formation of the guinea pig placenta [2]. The greatest increase was found for cystine, glutamic and aspartic acids, serine, and alanine, the content of which was more than doubled by this time ($P < 0.001$). By the 40th day of pregnancy the content of most amino acids was significantly reduced ($P < 0.01$) compared with 25-30 days, except for lysine and phenylalanine, the concentration of which was almost unchanged at these times. A further decrease in the levels of aspartic and glutamic acids ($P < 0.001$), alanine, tryptophan, and lysine ($P < 0.05$) also was found on the 45th-50th day of pregnancy. At the time of parturition (the 60th day), and also in placentas obtained after parturition, the content of the various amino acids was virtually unchanged compared with the 45th-50th day of pregnancy, except in the case of glutamic acid, for which a significant increase ($P < 0.05$), on the average by 15%, was found. The activity of transamination and oxidative deamination reactions of glutamic acid was low on the 10th-15th day of pregnancy. It then increased gradually and reached its maximum on the 25th-30th day of pregnancy ($P < 0.001$). On the following days (until the 40th) the activity of these enzymes fell statistically significantly ($P < 0.01$) compared with the previous time, but from the 45th day of pregnancy until parturition it remained stable (Table 2).

The decrease in the level of free amino acids in the placentas at the late stages of pregnancy compared with the period of formation of this organ correlates with views according to which the rate of protein synthesis in the organs and tissues decreases as they approach complete maturity and during subsequent "aging" [3, 4, 6].

The character of the changes in concentration of free amino acids and in enzyme activity in the placentas at the periods of its development studied in these experiments is evidently determined by evolutionary factors ensuring that these parameters can meet the changing demands of the maturing fetus.

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