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Formula composition and nutritional quality evaluation of three pediatric balanced compound amino acid injection

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ABSTRACT

Through the evaluation of three kinds of pediatric balanced compound amino acid injection formula composition and nutritional quality, to provide a reference for rational drug selection in clinical practice. Methods: Based on the amino acid scoring standard model and whole egg protein model that recommended by FAO/WHO in 1973, the prescription ratio, the first restricted amino acid, the essential amino acid index, the score of ratio coefficient of amino acid, and the closeness with the standard protein of 3 kinds of pediatric balanced compound amino acid injection were evaluated. Results: The percentage of essential amino acids in three kinds of pediatric compound amino acid injections exceeds 40% of the total amino acids, and the ratio of total EAA to AA nitrogen content was higher than 2.5. The formulations are all qualified. The first restriction amino 19AA-I was the highest, and the values order from high to low was 19AA-I>18AA-I>18AA-II. The essential amino acid index and the closeness to the standard protein were in the order of 19AA-I>18AA-I>18AA-II, and the ratio coefficient of amino acids was in the order of 18AA-I>19AA-I>18AA-II. Conclusion: 19AA-I and 18AA-I have higher nutritional quality, followed 18AA-II.

Keywords: balance compound amino acid injection for children; first limiting amino acid; essential amino acid; score of amino acid ratio; standard protein closeness; nutritional quality

Introduction

Pediatric amino acid injection is used for protein synthesis in premature infants, low birth weight infants, and newborns who are unable to ingest protein orally or have insufficient intake due to various etiologies which formula is designed based on the physiological characteristics of newborns. At present, there are three varieties of pediatric amino acid injection

in China, namely pediatric compound amino acid injection (18AA-I), pediatric compound amino acid injection (19AA-I), and pediatric compound amino acid injection (18AA-II). The total amino acid (AA) content, essential amino acid (EAA) content, and total EAA content vary among different varieties. Based on the first limiting amino acid, total EAA comprehensive quality, and EAA to standard protein closeness

of the three pediatric balanced compound amino acid injections, the rationality of their formula composition and nutritional quality are evaluated to provide reference for clinical drug selection.

Materials

The amino acid content data of three kinds of pediatric amino acid injection are from the latest version of the drug instructions approved by the China National Medical Products Administration.

Methods

The main function of amino acids in parenteral nutrition solution is to synthesize human protein. The more similar the EAA in amino acids is to the body pattern of children, the better it can synthesize human protein, and the higher its nutritional value. We evaluated the nutritional value of three pediatric compound amino acid injection formulas based on the whole egg protein model and the amino acid scoring standard model recommended by the Food and Agriculture Organization/World Health Organization (FAO/WHO) in 1973, including the first limiting amino acid, total EAA comprehensive quality, and EAA and standard protein closeness.

Due to the incomplete liver enzyme system in children, metabolism cannot be effectively carried out. The structure of tyrosine is similar to that of phenylalanine, which can be metabolized into tyrosine. By increasing the amount of tyrosine and reducing phenylalanine, the balance of plasma concentration is maintained. Methionine is a precursor of cysteine and taurine, and its content is reduced by adding taurine and an appropriate amount of cysteine. Therefore, in EEA calculations,

cysteine, taurine, and methionine are combined, while phenylalanine and tyrosine are combined.

Evaluation of formula for pediatric compound amino acid injection

One of the ideal protein patterns proposed by FAO/WHO is that the total amount of EAA accounts for over 40% of AA, and the E/T value is greater than 2.5, which is an important reference indicator for evaluating the rationality of the formula of compound amino acid injection(1).

The proportion of total EAA to total AA

Calculation formula: $(\text{total EAA}/\text{total AA}) \times 100\%$

The ratio of total EAA to AA nitrogen content (E/T value)

Calculation formula: $E/T = \text{EAA}/(\text{AA} \times 16\%)$
(2)

Evaluation of the first restricted amino acid in pediatric compound amino acid injection

When evaluating the nutritional value of compound amino acid injection, one or more EAAs have relatively low content, which leads to other EAAs not being fully utilized and wasted. This low content EAA is called limiting amino acid, with the lowest content being the first limiting amino acid. The lower the first limiting amino acid of amino acid injection, the less effective it is in synthesizing protein in the body, resulting in a decrease in its nutritional value.

Taking egg protein as the standard mode for chemical score (CS)(3):CS is used to evaluate the closeness of the relative content of a certain EAA in the total EAA in protein to that of relative content of corresponding EAA in total EAA in standard egg protein. The closer the CS value to 1, the higher the nutritional value of the protein.

Calculation formula: $CS=aa/AAEGG$

aa is the percentage of a specific amino acid in the test sample; AAEGG is the percentage of the same amino acid in the whole egg protein.

Taking FAO/WHO as the standard mode for amino acid score (AAS)(4): AAS is the percentage of the relative content of a certain EAA among the total EAA of the evaluated protein to the content of the corresponding amino acids in the FAO/WHO scoring model. The closer the AAS value is to 1, the higher the nutritional value of albumin is.

Calculation formula: $AAS=aa/AAFAO/WHO$

aa is the percentage of amino acid in the test sample, AAFAO/WHO is the percentage of the amino acid in the FAO/WHO scoring standard mode.

Evaluation of the comprehensive quality of EAA in pediatric compound amino acid injection

For evaluating the quality of a specific protein, in addition to a certain EAA content, the comprehensive quality of the total EAA should be considered.

Taking egg protein as the standard mode for essential amino acid index (EAAI)(5,6): EAAI is used for evaluating the comprehensive quality of a protein by considering the ratio of all EAA in the target protein to all EAA in egg protein. The closer the EAAI value is to 100, the higher the nutritional value of the evaluated protein is.

Calculation formula: $EAAI=(100A/AE \times 100B/BE \times 100C/CE \dots)1/n$

n is the number of essential amino acids; A, B, and C are the percentages of the essential amino acid content of the detected amino acids; AE, BE, and CE are the percentage of the essential amino acid content of the whole egg

protein.

Taking FAO/WHO as the standard mode for the score of the ratio coefficient of amino acid (SRCAA)(5,6): Using amino acid balance theory and FAO/WHO EAA model, the ratio of amino acid (RAA) and ratio coefficient of amino acid (RCAA) of EAA in the evaluated protein were calculated. Then, SRCAA was calculated. The closer the SRCAA is to 100, the better synthesizes human protein, indicating a higher nutritional value.

Calculation formula: $RAA=EAA \text{ content of the target protein (mg/g protein)}/\text{corresponding EAA content in the WHO/FAO formula (mg/g protein)}$

$RCAA= RAA/\text{Average of RAA}$

$SRCAA = 100 - CV \times 100$

CV is the coefficient of variation of RCAA; $CV = \text{standard deviation}/\text{mean}$.

Evaluation of the closeness of pediatric compound amino acid injection total EAA to standard protein (whole egg protein or FAO/WHO model): Evaluate the closeness $\mu(a, u_i)$ of the subject's u_i and standard protein a (whole egg protein or FAO/WHO model) according to Lan and Apos's distance method(7).

Calculation formula:

$$\mu(a, u_i) = 1 - 0.09 \sum_{k=1}^{\infty} \frac{|a_k - u_{ik}|}{a_k + u_{ik}}$$

$a_k(k = 1, 2 \dots 8)$ is the kth EAA content(mg·g⁻¹) of standard protein a(whole egg protein or FAO/WHO model), $u_{ik}(k = 1, 2 \dots 8)$ is the ith content of EAA of the kth (K-type EAA corresponding to the standard protein) of each evaluated protein(mg·g⁻¹).

The closeness value reflects the closeness of the protein quality of the evaluated protein to the standard protein (whole egg protein or FAO/WHO model). The closer the value is to

1, the better the synthesis of human protein and the higher the nutritional value of the evaluated protein is.

Results

The rationality evaluation results of three pediatric balanced compound amino acid injection formulas: the percentage content of

EAA in AA and the E/T ratio are shown in Table 1. The evaluation results showed that the EAA/AA of the three pediatric compound amino acid injections exceeded 40%, and the E/T ratio was higher than 2.5. The formula proportions are all qualified.

Table 1 Composition of three pediatric balanced compound amino acid injections, EAA/AA and E/T values

	18AA-I (g · 1000mL ⁻¹)	18AA-II (g · 1000mL ⁻¹)	19AA-I (g · 1000mL ⁻¹)
Isoleucine	3.1	4.9	4.9
Leucine	7	8.4	8.4
Lysine	7.9	6.9	4.9
Methionine+Cysteine	2.3	2.2	2.2
Phenylalanine+Tyrosine+Taurine	3.3	3.45	3.45
Threonine	3.6	2.5	2.5
Tryptophan	1.4	1.2	1.2
Valine	3.6	4.7	4.7
Σ EAA	32.2	34.25	32.25
Histidine	2.1	2.9	2.9
Alanine	6.3	3.2	3.2
Arginine	4.1	7.3	7.3
Proline	5.6	4.1	4.1
Glycine	2.1	2.2	2.2
Glutamate	7.1	3	3
Serine	3.8	2.3	2.3
Aspartate	4.1	1.9	1.9
Σ AA	67.4	61.15	59.15
Σ EAA/ Σ AA	48%	56%	55%
E/T	3.0	3.5	3.44

For the convenience of unified evaluation, the dosage of each EAA prescription g·1000mL⁻¹ was converted to the content of each amino acid in the total amino acid, mg·g protein⁻¹. The results are shown in Table 2.

Table 2 The content of various EAAs in the total amino acids of three varieties of pediatric compound amino acid injections

	whole egg protein (mg •g protein ⁻¹)	FAO/WHO (mg •g protein ⁻¹)	18AA-I (mg •g protein ⁻¹)	18AA-II (mg •g protein ⁻¹) I	19AA-I (mg •g protein ⁻¹)
Lysine	70.00	55.00	117.21	112.84	82.84
Valine	66.00	50.00	53.41	76.86	79.46
Threonine	47.00	40.00	53.41	40.88	42.27
Isoleucine	54.00	40.00	45.99	80.13	82.84
Tryptophan	17.00	10.00	20.77	19.62	20.29
Methionine+Cysteine	57.00	35.00	34.12	35.98	37.19
Leucine	86.00	70.00	103.86	137.37	142.01
Phenylalanine+Tyrosine	93.00	60.00	48.96	56.42	58.33
Σ EAA	496.00	360.00	477.75	560.10	545.22

Evaluation results of the first restriction amino acid of three pediatric compound amino acid injections

The evaluation results of CS and AAS are shown in Table 3. The evaluation results indicate that compared with whole egg protein, the 18AA-II CS is 0.54, which is the lowest; The CS value of 19AA-I is 0.59, which is the highest. The order from high to low is: 19AA-I>18AA-I>18AA-II.

Compared with the FAO/WHO standard protein, the AAS value of 18AA-II is the lowest at 0.60, while the AAS value of 19AA-I is the highest at 0.70. The order from high to low is: 19AA-I>18AA-I>18AA-II.

Table 3 The CS and AAS of three types of pediatric compound amino acid injections

	18AA-1		18AA-2		19AA-1	
	CS	AAS	CS	AAS	CS	AAS
Lysine	1.74	1.61	1.43	1.32	1.08	0.99
Valine	0.84	0.80	1.03	0.99	1.09	1.05
Threonine	1.18	1.01	0.77	0.66	0.82	0.70
Isoleucine	0.88	0.87	1.31	1.28	1.40	1.37
Tryptophan	1.27	1.56	1.02	1.26	1.08	1.34
Methionine+Cysteine	0.62	0.73	0.59	0.66	0.59	0.70
Leucine	1.25	1.12	1.41	1.26	1.50	1.34
Phenylalanine+Tyrosine	0.55	0.61	0.54	0.60	1.08	0.99

Results of comprehensive quality evaluation of total EAA content in three pediatric compound amino acid injections

The results of EAAI, SRCAA, and their closeness to standard proteins are shown in Table 4.

The table 4 shows that compared with egg protein, the lowest EAAI value was obtained for 18AA-II at 98.09, the highest value obtained from 18AA-I at 99.62. The order of the EAAI values for the formulations was 18AA-I>19AA-I>18AA-II.

The table 4 shows that compared with the FAO/WHO standard protein mode, the lowest SRCAA value was obtained for 18AA-II at 39.9, the highest value obtained from 19AA-I at 41.57. The order of the SRCAA values for the formulations was 19AA-I>18AA-I>18AA-II.

The table 4 shows that compared with egg protein, the best closeness to egg protein was 18AA-I, with a value of 1, the values of 19AA-I and 18AA-II were same at 1.18. The order of the closeness values for the formulations was 18AA-I>19AA-I=18AA-II.

The table 4 shows that compared with FAO/WHO protein standard mode, the closest value to 1 was 18AA-I, with a value of 1.36, 19AA-I was the same as 18AA-II, with a value of 1.54. The order of the closeness values for the formulations was 18AA-I>19AA-I=18AA-II.

Table 4 The EAAI, SRCAA and closeness of three kinds of pediatric compound amino acid injections

	18AA-II	18AA-I	19AA-I
EAAI	98.09	99.62	101.49
SRCAA	39.9	41	41.57
Egg closeness	1.18	1	1.18
FAO / who closeness	1.54	1.36	1.54

Discuss

Premature infants and newborns are unable to receive gastrointestinal feeding due to incomplete physical development or certain causes, and parenteral nutrition is necessary for their survival and growth and development. The various amino acid ratios and formulas in the three pediatric compound amino acid injections evaluated in this study were designed based on the physiological characteristics of premature infants and newborns, and their formula ratios were all qualified. However, there are differences in the nutritional quality of different varieties. The higher the score of the first limiting amino acid, EAAI, SRCAA, the closer the closeness value is to 1, the higher the closeness is to the standard protein, the higher the nutritional value, and the higher the amino acid availability. Through the evaluation

of three types of pediatric compound amino acid injections, the results showed that: the first limiting amino acid and SRCAA, the value of 19AA-I was the highest, the order of values for the formulations was 19AA-I>18AA-I>18AA-II. The closeness of standard protein 18AA-I is closest to 1, the order of closeness values for the formulations was 18AA-I>19AA-I=18AA-II. The EAAI of 18AA-I is the highest, the order of EAAI values for the formulations was 18AA-I>19AA-I>18AA-II. Therefore, 18AA-I and 19AA-I have higher amino acid nutritional quality and can synthesize human protein well, followed by 18AA-II.

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