0148-6071/87/1104-0368$02.00/0
JOURNAL OF PARENTERAL AND ENTERAL NUTRITION

Vol. 11, No. 4
Printed in U.S.A.

Studies on the Toxicity and Efficacy of a New Amino Acid Solution in Pediatric Parenteral Nutrition

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ABSTRACT. The optimum composition and concentration of crystalline amino acid solutions necessary for growth and brain maturation in critically ill infants requiring total parenteral nutrition (TPN) are unknown. Either an excess or a deficiency of amino acids could theoretically impair normal brain development in the neonate. The purpose of this study was to compare the toxicity and efficacy of two intravenous amino acid solutions, Neopham, modeled after the amino acid pattern found in human breast milk, and Aminosyn, a marketed product, designed for general usage.

Sixteen infants and children requiring continuous intravenous nutrition for at least 7 days received the Neopham amino acid solution, and eight infants and children received the Aminosyn amino acid solution as part of a total parenteral nutrition regimen which included glucose, the fat emulsion Intralipid, as well as routine mineral and vitamin additives.

There were no significant differences in mean gestational age, body weight, postnatal age, or mean daily nutrient intake between the patients receiving Aminosyn or Neopham. The daily nitrogen intake, excretion, and retention were similar in both groups. In addition, there were no statistically significant differences in either hematological or biochemical parameters between the two study groups.

The plasma levels of three essential amino acids, isoleucine, methionine, and valine, rose significantly higher in the Aminosyn-treated patients. The plasma levels of all the essential amino acids increased in both study groups. (*Journal of Parenteral and Enteral Nutrition* **11**:368–377, 1987)

Glycine was the only nonessential amino acid whose plasma level was significantly higher in the Aminosyn-treated children. The levels of the remaining nonessential amino acids either increased or decreased, depending upon the amino acid solution infused. In general, the plasma aminogram analyses reflected the composition of the respective parent solution.

On the basis of this study, Neopham appears to be as effective as Aminosyn in a pediatric TPN regimen in terms of weight gain, nitrogen balance, and clinical condition. No serious side effects were observed with either amino acid solution. Finally, plasma aminograms appear to reflect the amino acid composition of the infused solution.

Total parenteral nutrition (TPN) administered via a central or peripheral vein has gained wide acceptance for use in selected pediatric and adult patients.[1] A typical TPN regimen includes glucose, protein (supplied in the form of crystalline amino acids), a fat emulsion, vitamins, minerals, and trace elements. Such combinations of nutrients have proven very effective in totally supplying critically ill infants with the nutritional support necessary for growth, when enteral feedings are not feasible.[2–5] However, definitive studies delineating the optimum composition and concentration of crystalline amino acid solutions necessary for growth[6–9] and brain maturation[10–13] have not been performed. Amino acid deficiency or excess in the developing neonate could possibly impair normal development of the brain.[14–16]

The purpose of this study was to compare the toxicity and efficacy of Neopham (KabiVitrum, Inc.) with Aminosyn (Abbott Laboratories) as a nitrogen source in a TPN protocol in infants and children. The results document that Neopham is as effective as aminosyn in

TABLE I
Composition of Neopham and Aminosyn amino acid solutions

Amino acid	Neopham		Aminosyn	
	g/dl	% Total	g/dl	% Total
l-Isoleucine	0.31	4.8	0.51	7.3
l-Leucine	0.70	10.8	0.66	9.5
l-Lysine	0.56	8.6	0.51	7.3
l-Methionine	0.13	2.0	0.28	4.0
l-Phenylalanine	0.27	4.2	0.31	4.4
l-Threonine	0.36	5.5	0.37	5.3
l-Tryptophan	0.14	2.2	0.12	1.7
l-Valine	0.36	5.5	0.56	8.0
TOTAL ESSENTIAL AMINO ACIDS	2.83	43.5	3.22	46.2
l-Histidine	0.21	3.2	0.21	3.0
l-Arginine	0.41	6.3	0.69	9.9
l-Alanine	0.63	9.7	0.90	12.9[a]
l-Proline	0.56	8.6	0.61	8.8
l-Serine	0.38	5.8	0.30	4.3
l-Tyrosine	0.05	0.8	0.04	0.6
l-Glycine	0.21	3.2	0.90	12.6[a]
l-Aspartic acid	0.41	6.3[a]		
l-Glutamic acid	0.71	10.9[a]		
l-Cysteine-cystine	0.10	1.5[a]		
TOTAL NONESSENTIAL AMINO ACIDS	3.67	56.5	3.75	53.8
TOTAL AMINO ACIDS	6.50	100.0	6.97	100.0

[a] Denotes significant difference.

Received for publication, June 16, 1986.
Accepted for publication, December 1, 1986.
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promoting growth, as measured by weight gain and positive nitrogen balance, and that no adverse side effects of toxicity can be attributed to Neopham.

MATERIALS AND METHODS

Twenty-four infants and children, from one day to 10 yr old, who required continuous TPN for at least 7 days were studied. Patients receiving any enteral nutrition, those with a diagnosis of cardiac failure, renal insufficiency, diabetes mellitus, untreated infections, and those receiving concurrent corticosteroid medication were excluded from the study.

After obtaining parental informed consent, the following preinfusion tests were performed: urine-urea-nitrogen and urine osmolality, plasma amminogram analysis, complete blood count with differential white blood cell count, platelet count, blood-urea-nitrogen (BUN), serum uric acid, albumin, total protein, cholesterol, triglycerides, total bilirubin, alkaline phosphatase, lactic acid dehydrogenase (LDH), serum glutamic oxaloacetic transaminase (SGOT), ammonia, magnesium, and osmolality.

TABLE II
Demographic data of patients administered Aminosyn (n = 8) or Neopham (n = 16) as the amino acid source in a TPN regimen

Sex	Gestational age (wk)	Age at study (D/M/Y)[a]	Initial wt (kg)	Prestudy status		Diagnosis
				Prognosis	Nutritional	
			Aminosyn-Treated Patients (Group 1)			
F	36	3D	2.48	Good	Normal	Gastroschisis
F	37	2D	2.50	Good	Normal	Gastroschisis, meconium pneumonitis
F	40	3D	2.58	Good	Normal	Duodenal atresia
M		1.5M	3.28	Good	Normal	Duodenal atresia, situs inversus
F	40	3D	2.86	Good	Normal	Intestinal malrotation-volvulus
M	40	16D	3.76	Good	Normal	Omphalocele
M		10M	7.98	Good	Normal	Intestinal volvulus, situs inversus
M	38	3D	2.30	Good	Normal	Intestinal malrotation
			Neopham-Treated Patients (Group 2)			
F		3Y	10.24	Good	Normal	Colonic aganglionosis, enterocolitis
F	33	1D	2.00	Good	Normal	Intestinal atresia
F	40	2D	2.50	Good	Normal	Gastroschisis, meconium pneumonitis
F	38	2D	2.56	Good	Normal	Gastroschisis
F		10Y	12.70	Good	Underweight	Hiatal hernia, esophagitis, mental retardation
F	38	18D	1.68	Good	Underweight	Intestinal atresia, imperforate anus
F	38	2D	2.66	Good	Normal	Intestinal atresia
M		10Y	21.40	Fair	Underweight	Esophageal stricture, mental retardation
F		1M	2.82	Good	Normal	Intestinal stricture
M	34	2D	2.18	Good	Normal	Gastroschisis
M	40	1D	2.80	Good	Normal	Gastroschisis
F		4Y	12.20	Poor	Underweight	Aspiration pneumonia, anoxic brain damage
M	35	21D	2.67	Fair	Normal	Intestinal atresia, ventricular septal defect
M	39	7D	3.44	Good	Normal	Gastroschisis, respiratory distress syndrome
M		1.5Y		Fair	Normal	Trauma, multiple enterostomies
M	36	1D	2.50	Good	Normal	Gastroschisis

[a] D = days, M = months, Y = years.

TABLE III
Gestational age, body weight, and postnatal age of the Aminosyn- and Neopham-treated patients

	Aminosyn	Neopham	*p* Value
Neonatal analysis			
Number	6	10	
Male:female	2:4	5:5	
Gestational age (wk)	38.5 ± 1.8	37.1 ± 2.5	0.26
Range	36–40	33–40	
Postnatal age (days)	5.0 ± 5.0	5.7 ± 7.5	0.84
Range	2–6	1–21	
Body wt (kg)	2.75 ± 0.66	2.50 ± 0.52	0.35
Range	2.30–3.76	1.68–3.44	
Infants and children 28 days old, or more			
Number	2	6	
Male:female	2:0	2:4	
Age (mo)	5.75 ± 6.01	57.16 ± 51.2	
Body wt (kg)	5.63 ± 3.32	11.87 ± 6.64	

Patients were randomly assigned in a 1:2 ratio to receive TPN solutions with Aminosyn (Abbott Laboratories), designated group 1, or Neopham (KabiVitrum, Inc.), designated group 2, either by periperhal or central venous routes. The amino acid composition of Aminosyn and Neopham is listed in Table 1. The solutions for centrally administered TPN consisted of 25% glucose and 3.5% crystalline amino acids, whereas the peripheral regimen consisted of 12.5% glucose and 2.5% crystalline amino acids. Intralipid was provided to a maximum of 40% of daily caloric intake. All TPN solutions contained routine vitamin and mineral additives.

Daily observations included vital signs, weight, urine tests, and a report of adverse symptoms or side effects. Estimated caloric requirements and nitrogen balance were computed daily. At weekly intervals, blood chemistries were repeated. Blood ammonia levels and plasma aminograms were analyzed twice weekly.

Nitrogen intakes were calculated for each day of TPN from the recorded infusions of amino acids. One gram of amino acids as Aminosyn provided 157.7 mg of nitrogen, 1.0 gram of amino acids as Neopham provided 143.1 mg of nitrogen. The amount of nitrogen excreted was measured to the nearest 1.0 mg on each day in which urine collections were successfully obtained. Approximate nitrogen balances were determined as the differences between nitrogen intake and nitrogen excretion. Nitrogen losses from nasogastric drainage, wounds, and fecal and enterostomy output were not quantified.

The data were subjected to two separate statistical analyses due to the heterogeneity of the population studied. The first analysis involved the 16 patients who were less than 28 days old at entrance into the study protocol (Neonatal Analysis). The second evaluation (Total Patient Analysis) pertained to all 24 patients; the age range of the eight additional patients spanned 1 month to 10 years. Data from the first 15 days of TPN formed the basis of this study.

RESULTS

Demographic Data

Demographic data (mean ± SD) of the eight patients who received Aminosyn (group 1) and the 16 patients who received Neopham (group 2) as the amino acid component of a total hyperalimentation nutritional regimen are presented in Table II.

Neonatal Analysis. There were no significant differences in mean gestational age, body weight, or postnatal age at entrance into the study ($n = 16$) between the neonates receiving either Neopham ($n = 10$) or Aminosyn ($n = 6$) (Table III). A mean gestational age of 38.5 ± 1.8 weeks, a mean initial body weight of 2.75 ± 0.66 kg, and a mean postnatal age of 5.0 ± 5.0 days were recorded for the Aminosyn (group 1) patients, while the respective values for the Neopham (group 2) patients was 37.1 ± 2.5 weeks, 2.5 ± 0.52 kg, and 5.7 ± 7.5 days.

Analysis of Older Infants and Children. There were no significant differences in mean body weight [5.6 ± 3.32 kg (Aminosyn) *vs* 11.87 ± 6.64 kg (Neopham)] and age at entrance into the study protocol [5.75 ± 6.01 months (Aminosyn) *vs* 57.16 ± 51.2 months (Neopham)] between the two patient groups (Table III).

Nutritional Data

The mean daily nutrient intakes of the group 1 (Aminosyn) and group 2 (Neopham) patients are presented in Table IV. There were no significant between- or within-

TABLE IV
Mean nutrient intake in patients who received Aminosyn (group 1) or Neopham (group 2)

	Dextrose (kcal/kg/day)	Intralipid (kcal/kg/day)	Amino acids (kcal/kg/day)	Energy intake (kcal/kg/day)	Amino acids (g/kg/day)
Neonatal analysis					
Group 1 (n = 6)	56.8 ± 8.7	24.6 ± 9.2	11.7 ± 3.4	93.1 ± 16.5	2.92 ± 0.9
Group 2 (n = 10)	57.6 ± 8.5	23.7 ± 11.3	11.3 ± 3.3	92.7 ± 15.6	2.84 ± 0.8
p Value[a]	0.98	0.80	0.75	0.77	0.76
Total patient analysis					
Group 1 (n = 8)	54.1 ± 12.5	26.6 ± 10.5	11.0 ± 3.3	91.6 ± 18.7	2.75 ± 0.8
Group 2 (n = 16)	59.0 ± 19.2	21.1 ± 12.2	10.7 ± 4.4	90.9 ± 25.6	2.67 ± 1.1
p Value[a]	0.70	0.46	0.63	0.79	0.58

[a] *p* values calculated by repeated measures analysis of variance.

TABLE V
Mean nitrogen balance data of patients who received either Aminosyn (group 1) or Neopham (group 2)

	Intake		Excretion (mg/kg/day)	Balance (mg/kg/day)	% Retention
	mg/kg/day	kcal/gN			
Neonatal analysis					
Group 1 (n = 6)	476 ± 119	207 ± 51	137 ± 63	340 ± 86	71.8 ± 8.2
Group 2 (n = 10)	405 ± 120	261 ± 102	120 ± 53	285 ± 135	70.4 ± 18.2
p Value[a]	0.27	0.25	0.58	0.39	
Total patient analysis					
Group 1 (n = 8)	458 ± 107	206 ± 44	153 ± 61	306 ± 100	66.8 ± 13.0
Group 2 (n = 16)	393 ± 103	257 ± 85	128 ± 59	264 ± 117	67.2 ± 16.8
p Value[a]	0.17	0.13	0.35	0.39	

[a] *p* values calculated by one-way analysis of variance.

TABLE VI
Mean plasma concentrations of essential amino acids (μmol/liter) in neonates who received either Aminosyn or Neopham (n = 16)

	Day 1	Week 1	Week 2	p Values	
				Between group	Within group
Isoleucine (50–100 μmol/liter)[a]					
Aminosyn	21 ± 8	88 ± 38	99 ± 24	0.01	0.0001
Neopham	27 ± 12	52 ± 23	62 ± 27		
Leucine (19–200 μmol/liter)					
Aminosyn	67 ± 23	125 ± 46	129 ± 27	0.38	0.04
Neopham	62 ± 15	138 ± 46	150 ± 49		
Lysine (80–400 μmol/liter)					
Aminosyn	116 ± 38	226 ± 91	232 ± 54	0.44	0.06
Neopham	127 ± 43	232 ± 78	285 ± 106		
Methionine (19–30 μmol/liter)					
Aminosyn	25 ± 10	54 ± 24	65 ± 17	0.02	0.0001
Neopham	31 ± 9	35 ± 11	42 ± 17		
Phenylalanine (29–110 μmol/liter)					
Aminosyn	64 ± 17	75 ± 19	89 ± 32	0.76	0.58
Neopham	74 ± 19	79 ± 19	87 ± 21		
Threonine (140 μmol/liter)					
Aminosyn	100 ± 46	311 ± 123	293 ± 87	0.51	0.12
Neopham	90 ± 33	365 ± 220	364 ± 222		
Valine (150–340 μmol/liter)					
Aminosyn	102 ± 35	283 ± 110	295 ± 58	0.006	0.0001
Neopham	98 ± 22	168 ± 55	188 ± 70		

[a] Represents normal values recalculated from Ghadimi and Pecora.[17]

TABLE VII
Mean plasma concentrations of essential amino acids (μmol/liter) in patients who received either Aminosyn or Neopham (n = 24)

	Day 1	Week 1	Week 2	p Values	
				Between group	Within group
Isoleucine (50–100 μmol/liter)[a]					
Aminosyn	21 ± 10	86 ± 33	97 ± 20	0.0005	0.0001
Neopham	26 ± 13	50 ± 20	61 ± 25		
Leucine (19–200 μmol/liter)					
Aminosyn	67 ± 27	119 ± 43	125 ± 24	0.17	0.01
Neopham	58 ± 18	133 ± 39	152 ± 53		
Lysine (80–400 μmol/liter)					
Aminosyn	115 ± 51	218 ± 84	299 ± 54	0.48	0.12
Neopham	117 ± 47	220 ± 73	263 ± 107		
Methionine (19–30 μmol/liter)					
Aminosyn	25 ± 12	53 ± 21	64 ± 17	0.001	0.0001
Neopham	25 ± 11	31 ± 11	39 ± 16		
Phenylalanine (29–110 μmol/liter)					
Aminosyn	65 ± 21	72 ± 19	84 ± 29	0.41	0.21
Neopham	62 ± 21	81 ± 19	89 ± 23		
Threonine (140 μmol/liter)					
Aminosyn	115 ± 51	301 ± 112	288 ± 78	0.84	0.66
Neopham	89 ± 46	304 ± 187	323 ± 190		
Valine (150–340 μmol/liter)					
Aminosyn	99 ± 36	275 ± 98	288 ± 53	0.0002	0.0001
Neopham	96 ± 27	163 ± 45	188 ± 66		

[a] Represents normal values recalculated from Ghadimi and Pecora.[17]

group differences in dextrose, Intralipid, amino acid, or total energy intake (expressed as kcal/kg/day) between the group 1 and group 2 patients.

Neonatal Analysis. The group 1 (Aminosyn) patients received 56.8 ± 8.7 kcal/kg/day of dextrose, 24.6 ± 9.2 kcal/kg/day of Intralipid and 11.7 ± 3.4 kcal/kg/day of amino acids in comparison with the group 2 (Neopham) patients who received 57.6 ± 8.5 kcal/kg/day of dextrose, 23.7 ± 11.3 kcal/kg/day of Intralipid, and 11.3 ± 3.3 kcal/kg/day of amino acids. The group 1 infants received an average of 2.92 g/kg/day of aminosyn, while the group 2 infants received 2.84 g/kg/day of Neopham. There were no significant differences in daily energy or amino acid intakes between the Aminosyn and Neopham neonatal patient groups.

Total Patient Analysis. The mean daily intake of dextrose was 54.1 ± 12.5 kcal/kg/day, of Intralipid 26.6 ± 10.5 kcal/kg/day, and of amino acids 11.0 ± 3.3 kcal/kg/day in the group 1 (Aminosyn) patients. The mean daily intake in the group 2 (Neopham) patients was 19.2 kcal/kg/day of dextrose, 21.1 ± 12.2 kcal/kg/day of Intralipid, and 10.7 ± 4.4 kcal/kg/day of amino acids. The mean daily intake of Aminosyn was 2.75 ± 0.8 g/kg/day in the group 1 patients, and 2.67 ± 1.1 g/kg/day

TABLE VIII

Mean plasma concentrations of nonessential amino acids (μmol/liter) in neonates who received either Aminosyn or Neopham (n = 16)

	Day 1	Week 1	Week 2	p Values	
				Between group	Within group
Cystine (12–50 μmol/liter)[a]					
Aminosyn	11 ± 9	12 ± 7	5 ± 5	**0.14**	**0.004**
Neopham	11 ± 9	16 ± 10	12 ± 9		
Histidine (38–130 μmol/liter)					
Aminosyn	86 ± 39	93 ± 16	100 ± 16	**0.34**	**0.22**
Neopham	70 ± 14	101 ± 27	109 ± 20		
Taurine (0–180 μmol/liter)					
Aminosyn	108 ± 73	119 ± 71	91 ± 50	0.50	**0.25**
Neopham	248 ± 189	99 ± 71	97 ± 66		
Tyrosine (17–240 μmol/liter)					
Aminosyn	54 ± 26	27 ± 10	26 ± 11	**0.38**	**0.01**
Neopham	64 ± 20	31 ± 15	40 ± 17		
Aspartic acid (0–32 μmol/liter)					
Aminosyn	37 ± 15	48 ± 13	46 ± 12	0.24	**0.03**
Neopham	32 ± 15	51 ± 24	58 ± 22		
Glutamic Acid (0–320 μmol/liter)					
Aminosyn	181 ± 110	279 ± 124	253 ± 69	0.18	0.0001
Neopham	325 ± 184	342 ± 161	376 ± 177		
Glutamine (430–1300 μmol/liter)					
Aminosyn	238 ± 191	300 ± 186	338 ± 144	0.61	**0.03**
Neopham	137 ± 121	247 ± 231	239 ± 172		
Alanine (11–770 μmol/liter)					
Aminosyn	197 ± 67	360 ± 75	386 ± 89	0.52	**0.16**
Neopham	253 ± 98	346 ± 152	406 ± 126		
Arginine (40 μmol/liter)					
Aminosyn	23 ± 29	98 ± 92	145 ± 53	0.24	**0.02**
Neopham	27 ± 24	70 ± 53	103 ± 52		
Glycine (60–350 μmol/liter)					
Aminosyn	322 ± 127	695 ± 220	747 ± 131	0.0002	0.0001
Neopham	312 ± 109	375 ± 99	452 ± 102		
Proline (110–430 μmol/liter)					
Aminosyn	109 ± 29	262 ± 102	291 ± 71	0.29	**0.05**
Neopham	156 ± 42	273 ± 119	339 ± 145		
Serine (43–230 μmol/liter)					
Aminosyn	159 ± 48	267 ± 69	283 ± 95	0.75	**0.69**
Neopham	170 ± 65	246 ± 94	267 ± 77		

[a] Represents normal values recalculated from Ghadimi and Pecora.[17]

in the group 2 patients. These differences were not statistically significant.

Nitrogen Balance

The mean daily nitrogen intake, excretion, balance and percent retention are presented in Table V.

Neonatal Analysis. The mean daily nitrogen intake in the group 1 (Aminosyn) patients was 476 ± 119 mg/kg/day, and the mean nitrogen excretion was 137 ± 63 mg/kg/day for a positive mean balance of 340 mg/kg/day. This represents a retention of 71.8 ± 8.2%. The mean daily nitrogen intake in the group 2 (Neopham) patients was 405 ± 120 mg/kg/day, and the mean excretion was 120 ± 53 mg/kg/day, for a positive mean nitrogen balance of 285 ± 135 mg/kg/day, or a mean retention of 70.4 ± 18.2%. The differences in intake, excretion, balance, and percent retention were not significantly different.

Total Patient Analysis. The mean daily nitrogen intake in the group 1 (Aminosyn) patients was 458 ± 107 mg/kg/day, and the mean nitrogen excretion was 153 ± 61 mg/kg/day, resulting in a net balance of 306 ± 100 mg/kg/day. The mean retention was 66.8 ± 13.0%. Similarly, the values for the group 2 (Neopham) patients were 393 ± 103 mg/kg/day nitrogen intake and 128 ± 59 mg/kg/day nitrogen excretion, representing a net balance of 246 ± 117 mg/kg/day, or a retention of 67.2 ± 16.8%. These differences were not statistically significant.

Body Weight

Two of eight patients in the Aminosyn group lost weight over the course of the TPN therapy, while three of 14 patients in the Neopham study group lost weight during TPN.

Neonatal Analysis. The Aminosyn patients had an initial mean body weight of 2.75 ± 0.53 kg and a final mean weight of 2.94 ± 0.41 kg, resulting in a mean percent weight increase of 0.87 ± 2.33/day. In contrast, the Neopham patients had an initial mean body weight of 2.5 ± 0.48 kg, and a post-study mean weight of 2.56 ± 0.45 kg, which represents a mean percent weight increase of 0.32 ± 3.79/day. These differences between the study groups were not statistically significant.

Total Patient Analysis. The group 1 Aminosyn patients

had an initial mean body weight of 3.47 ± 1.89 kg, which increased to a final mean body weight of 3.6 ± 1.67 kg, with a mean percent increase of 0.65 ± 2.36/day. The Neopham study group had an initial mean body weight of 4.5 ± 3.96 kg, and a final mean body weight of 4.88 ± 4.68 kg, resulting in a mean percent increase of 0.47 ± 3.47/day. These changes were not statistically significant.

TABLE IX

Mean plasma concentrations of nonessential amino acids (μmol/liter) in patients who received either Aminosyn or Neopham (n = 24)

	Day 1	Week 1	Week 2	p Values	
				Between group	Within group
Cystine (12–50 μmol/liter)[a]					
Aminosyn	12 ± 8	10 ± 7	4 ± 5	**0.14**	**0.005**
Neopham	8 ± 8	13 ± 10	12 ± 8		
Histidine (38–130 μmol/liter)					
Aminosyn	85 ± 36	92 ± 14	98 ± 16	**0.85**	**0.77**
Neopham	66 ± 14	92 ± 25	103 ± 21		
Taurine (0–180 μmol/liter)					
Aminosyn	135 ± 120	119 ± 78	97 ± 57	**0.81**	0.63
Neopham	174 ± 174	82 ± 64	79 ± 60		
Tyrosine (17–240 μmol/liter)					
Aminosyn	50 ± 26	25 ± 9	27 ± 9	**0.48**	0.08
Neopham	52 ± 24	29 ± 14	35 ± 15		
Aspartic acid (0–32 μmol/liter)					
Aminosyn	39 ± 20	45 ± 13	43 ± 11	**0.10**	0.01
Neopham	31 ± 15	50 ± 21	58 ± 20		
Glutamic acid (0–320 μmol/liter)					
Aminosyn	190 ± 128	255 ± 125	282 ± 98	**0.40**	0.0008
Neopham	249 ± 171	285 ± 154	324 ± 169		
Glutamine (430–1300 μmol/liter)					
Aminosyn	255 ± 169	300 ± 168	304 ± 138	**0.96**	**0.84**
Neopham	228 ± 217	287 ± 201	312 ± 202		
Alanine (11–770 μmol/liter)					
Aminosyn	214 ± 83	360 ± 77	376 ± 81	0.16	0.03
Neopham	243 ± 91	358 ± 137	455 ± 180		
Arginine (40 μmol/liter)					
Aminosyn	26 ± 25	96 ± 84	140 ± 50	0.24	0.02
Neopham	39 ± 38	809 ± 48	104 ± 45		
Glycine (60–350 μmol/liter)					
Aminosyn	325 ± 117	675 ± 196	699 ± 142	0.0001	0.0001
Neopham	299 ± 145	350 ± 107	416 ± 109		
Proline (110–430 μmol/liter)					
Aminosyn	110 ± 33	272 ± 93	284 ± 66	0.34	0.13
Neopham	132 ± 55	264 ± 107	328 ± 144		
Serine (43–230 μmol/liter)					
Aminosyn	160 ± 67	248 ± 72	271 ± 84	0.62	0.45
Neopham	151 ± 72	223 ± 86	354 ± 74		

[a] Represents normal values recalculated from Ghadimi and Pecora.[17]

TABLE X

Mean serum alkaline phosphatase, total and direct bilirubin, LDH, and SGOT in neonates treated with Aminosyn and Neopham (n = 16)

	Day 1	Week 1	Week 2	p Values	
				Between group	Within group
Alkaline phosphatase (30–115 U/liter)[a]					
Aminosyn	134 ± 36	163 ± 49	252 ± 36	0.10	**0.0001**
Neopham	135 ± 46	241 ± 93	349 ± 119		
LDH (100–225 U/liter)					
Aminosyn	1531 ± 1687	380 ± 315	560 ± 507	**0.25**	**0.007**
Neopham	992 ± 462	545 ± 200	364 ± 98		
SGOT (8–40 U/liter)					
Aminosyn	510 ± 1036	35 ± 18	31 ± 6	0.27	**0.15**
Neopham	147 ± 113	66 ± 83	39 ± 11		
Total bilirubin (0.3–1.2 mg/dl)					
Aminosyn	**6.4 ± 4.6**	5.5 ± 4.2	1.9 ± 1.1	**0.48**	**0.0001**
Neopham	**5.5 ± 4.0**	10.0 ± 6.1	2.8 ± 2.5		
Direct bilirubin (0.0–0.3 mg/dl)					
Aminosyn	**0.5 ± 0.4**	**0.4 ± 0.3**	0.5 ± 0.5	**0.50**	**0.81**
Neopham	**0.3 ± 0.3**	**0.9 ± 0.8**	0.8 ± 0.8		

[a] Values in parentheses represent normal values.

Plasma Aminograms (Essential Amino Acids)

The plasma aminogram data for essential amino acids are presented in Tables VI and VII for the neonatal and total patient analyses, respectively. *P*-Values are listed for both between-group (Neopham *vs* Aminosyn) and within-group (changes during the course of the study period) analyses.

Neonatal Analysis. Significant between-group differences were found for three amino acids, namely, isoleucine, methionine, and valine. Significant within group increases occurred with isoleucine, leucine, methionine, and valine in both the Aminosyn and Neopham patient groups. The levels of all the amino acids increased in both study groups (Table VI).

Total Patient Analysis. The levels of all the amino

TABLE XI

Mean serum alkaline phosphatase, total and direct bilirubin, LDH and SGOT in patients treated with Aminosyn or Neopham (n = 24)

	Day 1	Week 1	Week 2	*p* Values	
				Between group	Within group
Alkaline phosphatase (30–115 U/liter)[a]					
Aminosyn	126 ± 34	168 ± 48	259 ± 31	0.21	0.0001
Neopham	786 ± 557	199 ± 93	283 ± 126		
LDH (100–225 U/liter)					
Aminosyn	1244 ± 1523	468 ± 397	500 ± 405	0.16	0.006
Neopham	786 ± 557	488 ± 236	360 ± 133		
SGOT (8–40 U/liter)					
Aminosyn	393 ± 902	39 ± 17	31 ± 5	0.34	0.07
Neopham	178 ± 291	94 ± 152	37 ± 12		
Total bilirubin (0.3–1.2 mg/dl)					
Aminosyn	5.8 ± 4.5	5.6 ± 3.8	4.1 ± 2.2	0.99	0.0001
Neopham	3.6 ± 4.0	7.9 ± 6.6	2.0 ± 2.3		
Direct bilirubin (0.0–0.3 mg/dl)					
Aminosyn	0.4 ± 0.4	0.5 ± 0.4	1.2 ± 0.8	0.92	0.36
Neopham	0.2 ± 0.3	0.7 ± 0.8	0.6 ± 0.7		

[a] Values in parentheses represent normal values.

TABLE XII

BUN, plasma ammonia, serum total protein, and albumin levels in neonates treated with Aminosyn or Neopham (n = 16)

	Day 1	Week 1	Week 2	*p* Values	
				Between group	Within group
BUN (8–20 mg/dl)[a]					
Aminosyn	8.5 ± 3.7	10.8 ± 4.4	11.3 ± 2.1	0.25	0.21
Neopham	14.0 ± 5.0	12.2 ± 4.9	17.1 ± 11.4		
Ammonia (17–80 μg/dl)					
Aminosyn	154 ± 186	165 ± 78	91 ± 44	0.73	0.10
Neopham	97 ± 79	180 ± 151	137 ± 88		
Total protein (6.0–8.0 g/dl)					
Aminosyn	4.6 ± 0.5	5.0 ± 0.7	5.1 ± 0.9	0.71	0.001
Neopham	4.2 ± 0.9	4.9 ± 0.8	5.0 ± 0.6		
Albumin (3.4–4.8 g/dl)					
Aminosyn	3.9 ± 0.4	3.2 ± 0.6	3.2 ± 0.7	0.86	0.001
Neopham	2.7 ± 0.5	3.2 ± 0.5	3.2 ± 0.6		

[a] Values in parentheses represent normal values.

TABLE XIII

BUN, plasma ammonia, serum total protein, and albumin levels in patients treated with Aminosyn or Neopham (n = 24)

	Day 1	Week 1	Week 2	*p* Values	
				Between group	Within group
BUN (8–20 mg/dl)[a]					
Aminosyn	7.6 ± 3.5	12.4 ± 5.5	13.3 ± 2.3	0.94	0.23
Neopham	11.4 ± 5.4	9.3 ± 4.7	12.6 ± 9.9		
Ammonia (17–80 μg/dl)					
Aminosyn	119 ± 163	215 ± 171	123 ± 66	0.09	0.01
Neopham	71 ± 72	152 ± 136	120 ± 87		
Total protein (6.0–8.0 g/dl)					
Aminosyn	4.7 ± 0.5	5.2 ± 0.7	5.1 ± 0.7	0.81	0.002
Neopham		5.1 ± 0.8	5.3 ± 0.8		
Albumin (3.4–4.8 g/dl)					
Aminosyn	3.0 ± 0.5	3.3 ± 0.5	3.2 ± 0.5	0.93	0.02
Neopham	2.9 ± 0.7	3.1 ± 0.5	3.2 ± 0.6		

[a] Values in parentheses represent normal values.

TABLE XIV
Mean serum sodium, chloride, potassium, calcium, and magnesium in neonates treated with Aminosyn or Neopham (n = 16)

	Day 1	Week 1	Week 2	*p* Values	
				Between group	Within group
Sodium (137–149 mEq/liter)[a]					
Aminosyn	139 ± 4	143 ± 3 (22)	138 ± 2	0.08	0.03
Neopham	136 ± 7	139 ± 6 (37)	136 ± 6		
Chloride (99–111, mEq/liter)					
Aminosyn	107 ± 6	110 ± 2	112 ± 5	0.11	0.10
Neopham	105 ± 5	[illegible]	105 ± 5		
Potassium (3.5–5.0 mEq/liter)					
Aminosyn	4.5 ± 0.9	5.1 ± 0.8	5.6 ± 0.1	0.96	0.74
Neopham	5.3 ± 1.3	4.9 ± 1.1	5.0 ± 1.0		
Calcium (8.5–10.5 mg/dl)					
Aminosyn	8.8 ± 0.8	9.9 ± 1.2	9.8 ± 0.4	0.40	0.0001
Neopham	7.9 ± 0.9	9.2 ± 1.0	9.9 ± 1.0		
Magnesium (1.5–2.3 mEq/liter)					
Aminosyn	1.53 ± 0.25	2.07 ± 0.22	1.80 ± 0.0	0.59	0.0001
Neopham	1.46 ± 0.25	1.91 ± 0.35	2.12 ± 0.39		

[a] Values in parentheses represent normal values.

TABLE XV
Mean serum sodium, chloride, potassium, calcium, and magnesium levels in patients treated with Aminosyn or Neopham (n = 24)

	Day 1	Week 1	Week 2	*p* Values	
				Between group	Within group
Sodium (137–149 mEq/liter)[a]					
Aminosyn	140 ± 7	140 ± 6	138 ± 4	0.08	0.25
Neopham	136 ± 6	138 ± 5	136 ± 5		
Chloride (99–111 mEq/liter)					
Aminosyn	106 ± 7	105 ± 10	103 ± 10	0.72	0.99
Neopham	105 ± 4	106 ± 6	103 ± 6		
Potassium (3.5–5.0 mEq/liter)					
Aminosyn	4.6 ± 0.9	5.2 ± 1.0	5.4 ± 0.5	0.36	0.92
Neopham	5.0 ± 1.2	4.7 ± 1.0	4.6 ± 1.0		
Calcium (8.5–10.5 mg/dl)					
Aminosyn	8.8 ± 0.9	9.9 ± 1.1	9.8 ± 0.4	0.13	0.0001
Neopham	8.2 ± 0.8	9.0 ± 0.9	9.5 ± 1.0		
Magnesium (1.5–2.3 mEq/liter)					
Aminosyn	1.51 ± 0.23	2.07 ± 0.20	1.80 ± 0.0	0.75	0.0001
Neopham	1.56 ± 0.30	1.96 ± 0.33	1.94 ± 0.36		

[a] Values in parentheses represent normal values.

acids increased in both study groups. Between- and within-group analyses were identical to those of the neonatal analysis for the essential amino acids (Table VII).

Plasma Aminograms (Nonessential Amino Acids)

The plasma aminogram analysis for the non-essential amino acids is presented to Table VIII (neonatal analysis) and Table IX (total patient analysis).

Neonatal Analysis. The only amino acid which was significantly different between the two study groups was glycine. Significant within-group changes occurred with a number of amino acids. Significantly decreased levels of cystine occurred in the Aminosyn-treated patients, while tyrosine decreased significantly in both the Aminosyn and Neopham groups. Significant increases occurred in aspartic acid, glutamic acid, glutamine, arginine, glycine, and proline in both patient groups. Histidine, alanine, and serine increased during the course of therapy in both groups, but not significantly. Taurine levels decreased in both the Aminosyn and Neopham groups, but not significantly (Table VIII).

Total Patient Analysis. The only significant between-group difference was in glycine concentration, which was significantly elevated in the Aminosyn-treated patients. Within-group significant increases occurred in cystine in the Neopham patients, while aspartic acid, glutamic acid, alanine, arginine, and glycine were significantly increased in both the Neopham and Aminosyn groups. In the Aminosyn group, cystine was significantly decreased. Taurine and tyrosine decreased in both groups, but not significantly; in contrast, histidine, glutamine, proline, and serine were increased insignificantly in both the Aminosyn and neopham groups (Table IX).

Hematological Data

Neonatal Analysis. There were no significant differences between treatment groups for any of the hematological parameters.

Total Patient Analysis. There were no significant differences between treatment groups in the hematological parameters studied.

Biochemical Data

Mean, standard deviation, and significance levels for between- and within-group analysis of biochemical data are presented in Tables X through XVII.

Neonatal Analysis. There were no significant between-group differences in alkaline phosphatase, LDH, SGOT, total and direct bilirubin. Within-group significant decreases were seen in alkaline phosphatase, LDH, and total bilirubin for both the Aminosyn and Neopham groups (Table X).

There were no significant between-group differences in BUN, plasma ammonia, serum total protein, or albumin levels. Within-group analyses showed a significant increase in total protein and albumin in the Neopham treatment group (Table XII).

There were no significant between-group differences in serum sodium, chloride, potassium, calcium, or magnesium levels in either study group. Serum sodium, calcium, and magnesium increased significantly in both groups during the course of the study (Table XIV).

There were no significant between-group differences in serum glucose, triglyceride, cholesterol, or phosphorus levels; however, initial uric acid values were significantly elevated in the Neopham group. Within-group significant increases occurred in cholesterol levels, while uric acid levels significantly decreased in both treatment groups (Table XVI).

Total Patient Analysis. There were no significant between-group differences in alkaline phosphatase, LDH, SGOT, and total and direct bilirubin. There were significant within-group decreases in LDH and total bilirubin in both treatment groups, and in alkaline phosphatase in the Neopham treatment group (Table XI).

There were no significant between-group differences in BUN, plasma ammonia, serum total protein, or albumin levels. Within-group analyses indicated a significant increase in ammonia, total protein, and albumin levels in the Neopham and Aminosyn treatment groups (Table XIII).

There were no significant between-group differences in serum sodium, chloride, potassium, calcium, or magnesium levels in either group. Calcium and magnesium increased significantly in both groups (Table XV).

There were no significant between group differences in serum glucose, triglyceride, cholesterol, phosphorus, or uric acid levels. Significant within-group increases

TABLE XVI

Mean serum glucose, triglycerides, cholesterol, phosphorus, and uric acid levels in neonates treated with Aminosyn or Neopham (n = 16)

	Day 1	Week 1	Week 2	*p* Values	
				Between group	Within group
Glucose (73–115 mg/dl)[a]					
Aminosyn	100 ± 57	94 ± 22	93 ± 23	0.98	0.53
Neopham	84 ± 44	89 ± 26	102 ± 29		
Triglycerides (40–150 mg/dl)					
Aminosyn	98 ± 18	101 ± 43	82 ± 62	0.75	0.34
Neopham	90 ± 41	112 ± 50	118 ± 32		
Cholesterol (0–250 mg/dl)					
Aminosyn	97 ± 41	185 ± 24	249 ± 28	0.93	0.0001
Neopham	67 ± 24	208 ± 67	238 ± 88		
Phosphorus (2.4–4.5 mg/dl)					
Aminosyn	5.7 ± 0.8	6.3 ± 2.0	6.2 ± 1.1	0.43	0.86
Neopham	5.8 ± 1.0	6.1 ± 2.0	5.7 ± 1.5		
Uric acid (3.9–9.0 mg/dl)					
Aminosyn	4.2 ± 0.6	3.5 ± 0	3.5 ± 0.0	0.04	0.0005
Neopham	6.7 ± 2.4	3.1 ± 0.6	3.2 ± 0.6		

[a] Values in parentheses represent normal values.

TABLE XVII

Mean serum glucose, triglycerides, cholesterol, phosphorus, and uric acid levels in patients treated with Aminosyn or Neopham (n = 24)

	Day 1	Week 1	Week 2	*p* Values	
				Between group	Within group
Glucose (73–115 mg/dl)[a]					
Aminosyn	106 ± 49	89 ± 22	78 ± 19	0.42	0.88
Neopham	95 ± 41	102 ± 42	107 ± 29		
Triglycerides (40–150 mg/dl)					
Aminosyn	95 ± 34	124 ± 71	119 ± 78	0.98	0.04
Neopham	96 ± 48	132 ± 72	129 ± 61		
Cholesterol (0–250 mg/dl)					
Aminosyn	98 ± 40	221 ± 66	284 ± 74	0.24	0.0001
Neopham	79 ± 33	187 ± 67	217 ± 83		
Phosphorus (2.4–4.5 mg/dl)					
Aminosyn	5.3 ± 1.1	6.3 ± 1.7	6.1 ± 1.0	0.14	0.57
Neopham	5.1 ± 1.3	5.2 ± 2.1	4.8 ± 1.7		
Uric acid (3.9–9.0 mg/dl)					
Aminosyn	3.8 ± 0.9	3.2 ± 0.6	3.5 ± 0.0	0.11	0.0003
Neopham	5.7 ± 2.5	3.2 ± 0.7	3.0 ± 0.4		

[a] Values in parentheses represent normal values.

occurred in cholesterol levels, whereas uric acid decreased significantly in both treatment groups (Table XVII).

CONCLUSIONS

Although nitrogen balances have to be viewed with caution in this study due to the difficulty with quantitative urine collections and the unaccounted losses of nitrogen through non-urinary routes, the similarity in nutrient intake, weight gain, and nitrogen retention in both groups indicates that Neopham and Aminosyn are equally effective in promoting growth in a TPN program. The weight increase per day in the Neopham neonatal group was lower (0.32 ± 3.79% compared to 0.87 ± 2.33% in the Aminosyn group), but this change was not statistically significant. The nitrogen balance data was also slightly lower in the Neopham group (285 ± 135 mg/kg/day, 70.4% retention, compared with the Aminosyn group, 340 ± 71.8 mg/kg/day, 7.18% retention).

The plasma aminogram analyses reflected, in general, the composition of the respective parent solutions. All of the essential amino acids (isoleucine, leucine, lysine, methionine, phenylalanine, threonine, and valine) increased over the time course of the study in both treatment groups. Significant increases in isoleucine, methionine, and valine in the Aminosyn *vs* the Neopham treatment group probably reflect the higher concentration of these amino acids in the Aminosyn preparation. Four of the essential amino acids (isoleucine, leucine, methionine, and valine) increased significantly in both treatment groups over the course of the study.

Analysis of the nonessential amino acids revealed a significantly greater increase in glycine in the Aminosyn group, probably because of the higher concentration of this amino acid in Aminosyn. Significant changes occurred in cystine, tyrosine, aspartic acid, glutamic acid, glutamine, arginine, glycine, and proline. Decreased plasma levels of cystine in the Aminosyn patients probably reflect the lack of cysteine in the Aminosyn solution. Levels of taurine decreased over the course of the study; neither amino acid solution contains taurine. Neopham contains 410 mg/dl of aspartic acid and 710 mg/dl of glutamic acid, whereas Aminosyn contains neither. However, the two patient groups had similar plasma levels of these amino acids.

Therefore, it appears that the serum amino acid profile of these patients closely reflects the amino acid composition of the parent solution.

Hemoglobin, hematocrit, and the erythrocyte count all significantly decreased during the course of the study. Also, white blood cell count, especially neutrophils and immature bands, decreased. In contrast, the lymphocyte and platelet counts increased significantly. There is no obvious explanation for these changes; however, frequent blood sampling may explain the decreases in hemoglobin, hematocrit, and erythrocyte count.

The increase in alkaline phosphatase, total protein, and albumin were significant but not readily explainable, although all of these changes could result from the TPN therapy.

On the basis of this limited study, it appears that Neopham is as effective as Aminosyn in a TPN regimen in terms of weight gain, nitrogen balance, and overall clinical well-being. No serious side effects were seen with either amino acid solution. In addition, plasma aminograms appear to be a direct reflection of the amino acid composition of infused solution.

ACKNOWLEDGMENT

This study was supported by KabiVitrum, Inc., Alameda, California.

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