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Mn-content of total parenteral and enteral nutrition[1]

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Der Mangangehalt in der kompletten parenteralen und in der enteralen Ernährung

Summary: Manganese has been proven to be an essential trace element in animals since 1931. Today, it is known that manganese deficiency results in a wide variety of structural and physiological defects in animals. For humans, the safe and adequate range of intakes for manganese by enteral nutrition is 2.0 to 5 mg per day; for parenteral nutrition a range of 0.15 to 0.8 mg per day is proposed.

The manganese content of components of enteral nutrition (EN) and total parenteral nutrition (TPN) solutions is determined using electrothermal atomic absorption spectrometry. Comparison is made between calculated and measured values. The manganese present in supplementary nutrition and flavor stuffs is also measured.

The intake of manganese by EN is calculated based on the daily administration, and is found to vary from 192 to 7373 μg per day. In prepared TPN-solutions, the manganese contribution of all components before adding the Oligo Complex is found to be less than 0.2 % of the total manganese content. After addition of the Oligo Complex mixture, a mean daily intake of 5.02 ± 0.16 mg per day is found.

Zusammenfassung: Seit 1931 ist bekannt, daß Mangan ein essentielles Spurenelement bei Tieren ist. Heute weiß man, daß Manganmangel bei Tieren zu einer Vielfalt an Stoffwechseldefekten führt. Für den Menschen ist die sichere Versorgung durch die enterale Ernährung mit 2,5–5 mg pro Tag gewährleistet, für die parenterale Ernährung wird eine Dosis von 0,15–0,8 mg pro Tag vorgeschlagen.

Die Mangangehalte von Bestandteilen der Nahrung und von Infusionslösungen wurden durch Atomabsorptions-Spektrometrie bestimmt. Die Ergebnisse wurden mit den (aus Tabellen) kalkulierten Werten verglichen. Der Mangangehalt der Kleinkomponenten und Zusatzstoffe einschließlich der Aromastoffe wurde ebenfalls berücksichtigt.

Aus dem täglichen Gesamtverzehr wurde eine Manganaufnahme von 192–7373 μg berechnet. In der parenterelen Ernährung betrug die Manganmenge der Lösung vor Zugabe einer Supplementmischung (Oligo-Komplex) 0,2 % der Gesamtdosis an

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Mangan. Nach Zugabe der Oligo-Komplex-Mischung wurde eine tägliche Aufnahme von 5,02 ± 0,16 pro Tag festgestellt.

Key words: Manganese; total parenteral nutrition; enteral nutrition; daily intake

Schlüsselwörter: Mangan; total parenterale Nahrung; enterale Nahrung; tägliche Aufnahme

Introduction

Over recent decades the importance of essential trace elements in food and total diets in order to establish various functions of metabolism has been recognized. Manganese, known to be an essential trace element in animals since 1931 (Kemmerer et al., 1931), appears in some important enzymatic systems (Expert Panel, JAMA, 1979) and is therefore often added to total parenteral nutrition formulations (TPN) and other types of artificial feedings as enteral nutrition formulations (EN).

Manganese homeostasis appears to be regulated at the excretory level via the bile (Leach, 1976). The liver, however, is the key in this regulation (Papavisiliou et al., 1966).

At the present time a lot of interest on the role of manganese is focused in brain metabolism, as it has been known for many years that the element plays a part in the normal function of the brain. Both manganese deficiency and manganese toxicity may affect brain metabolism, and human subjects with manganism show profound neurological disturbances similar to that of Parkinson's disease (Keen et al., 1984; Papavisiliou, 1978).

Little is known about the daily intake of manganese by TPN- and EN-formulations. Moreover, analytical data on the content of manganese in TPN- and EN-solutions are poor and often show serious disagreement (Hauer et al., 1978; Hoffman et al., 1976).

In this study, the manganese content of the various constituents of TPN- and EN-solutions is determined by electrothermal atomic absorption spectrometry (EAAS). The results are compared with literature values. Finally, the daily intake values are compared with the findings and recommendations of well-known institutions.

Materials and Methods

Apparatus

The manganese levels are determined using an electrothermal atomic absorption spectrometer (EAAS) (Perkin-Elmer & Co., Überlingen, FRG; type 4000/HGA500) equipped with a mono-element manganese lamp (S & J Junniper & Co., Essex, England) and a deuterium source for background correction. Uncoated graphite tubes are used for all analyses. Samples (20 µl) are injected using a Perkin-Elmer AS40 auto-sampler with a capacity of 35 samples.

Plastic pipet tips (Eppendorf, Hamburg, FRG) and polystyrene tubes are used after washing in nitric acid for 10 h at 60 °C for preparation of all solutions and dilutions.

The constituents and the prepared TPN solutions are injected directly into the graphite furnace without prior destruction.

The solid enteral nutrition samples are destructed with nitric acid. For destruction of the water soluble powders, approximately 0.1 g of the sample is dissolved in

nitric acid in a polystyrene tube and placed in a waterbath at 60 °C for 10 h. After cooling, 1 ml of double-deionized water is added. For the other samples, approximately 1 g of the sample is weighed exactly and mixed with 10 ml of nitric acid in a teflon vessel to be put in an autoclave (Perkin-Elmer), and then digested for about 10 h at 140 °C. The resulting solution is then diluted to 25 ml.

Chemicals

Standard solutions of manganese are prepared using Titrisol ampoules (Merck, Darmstadt, FRG) based on $MnCl_2$ in water. The stock solution of 1 ppm Mn is diluted with double-deionized water (Milli-Q system, Millipore Corp., Milford, MA, USA) prior to use.

For the autoclave destructions, nitric acid of suprapur quality (Merck, Darmstadt, FRG), is used.

The graphite furnace of the EAAS is purged with argon gas (L'air Liquid, Belgium).

Parameters of analysis

The spectrometer is operated at 279.5 nm with a spectral bandwidth setting of 0.7 nm. Lamp current is 12 mA. Settings for the graphite furnace controller are listed in Table 1 and were adjusted in cases of higher viscosity or interference. In such cases, the use of a higher atomization temperature (2700 °C) in combination with a prolongation of the drying step (15 s for ramp and hold time) yields good results.

In order to permit assay of manganese in solutions containing appreciable amounts of sodium chloride, analysis is performed in a solution of 5 % L-ascorbic acid (pro analyze, Aldrich-Europe). The entire procedure has been published elsewhere (Stobbaerts et al., 1989).

The method of standard addition is used throughout the procedure and least squares analysis was applied.

The overall absolute reciprocal sensitivity of the method was found to be 4.1 pg, while for the detection limit a value of 0.04 ppb was found. Precision was 3–6 % for all samples investigated. All measurements were performed four times.

Results and discussion

Constituents of TPN

The manganese content obtained for the large volume solutions and electrolytic solutions are listed in Tables 2 and 3, respectively. The number of samples of the same lot, if more than one, is given in order to obtain a mean.

Table 2 shows that the highest values and the largest range of manganese concentrations are found in the amino acid solutions. For aminoplasmal L10 a value of 21.8 µg/l is registered, while aminoplasmal L20 contains 10.1 µg/l of manganese. Glucose solutions of different concentrations contain only 0.3 to 3.6 µg/l. Noticeable for the glucose 50 % solutions is the variability of manganese levels between two lots: 0.6 and 1.4 µg/l.

The results are in excellent agreement with those found by Kurkus et al. using solutions of other manufacturers (Kurkus et al., 1984). However, for one lot of sodiumacetate they found 80 µg/l, which is about 13 times higher than the value of 6.1 µg/l we found. Also, the high value we obtained for sodiumphosphate (109 µg/l) is in contrast with the level reported by Kurkus et al. (7.7 µg/l). Kartinos (1978) reported less than 60 µg/l of manga-

Table 1. Settings for the furnace controller.

Step	Temp. (°C)	hold (s)	ramp (s)	rec.	gasfl.	baseln.	read
1	100	10	1				
2	120	10	10				
3	1000	20	10				
4	1000	10	1				
5	2500[1])	6	0	−10	50	−15	−1
	2600	6	1	−10	50	−15	−1
	2700[2])	6	1	−10	50	−15	−1
6	100	3	1	+			
7	2700	4	1				

[1]) Oligo complex solution
[2]) Sodium chloride solution

Table 2. Manganese content in µg/l of large volume solutions.

Solution	Number of lots	Mean per lot in µg/l
Sterile water	2	N.D.*
Glucose Viaflex 5 %	1	0.33 ± 0.02
Glucose 20 %	2	0.63 ± 0.05
		0.68 ± 0.05
Glucose 30 %	1	1.00 ± 0.05
Glucose 50 %	2	1.4 ± 0.1
		0.62 ± 0.06
Glucose Viamin	2	2.4 ± 0.2
		3.6 ± 0.3
Konakion	2	0.85 ± 0.05
		1.00 ± 0.05
Combusteril	1	0.89 ± 0.05
Protein Hepa	1	1.9 ± 0.08
Protein Nephro	2	5.2 ± 0.3
		5.9 ± 0.3
Travasol 10 %	2	8.0 ± 0.2
		10.6 ± 0.2
Aminoplasmal	2	5.5 ± 0.5
		1.0 ± 0.1
Aminoplasmal L10	2	21.8 ± 0.3
		18.2 ± 0.7
Aminoplasmal L20	1	10.1 ± 0.2
Intralipid 10 %	1	1.4 ± 0.1
Intralipid 20 %	1	1.6 ± 0.1
Pancebrin Multivitamin	2	5.3 ± 0.3
		5.3 ± 0.3

* N.D.: non-detectable

Table 3. Manganese content (in µg/l) of electrolytic solutions.

Solution	Number of lots	Mean per lot in µg/l
Sodium chloride	1	19.5 ± 0.5
Sodium acetate	1	6.1 ± 1.0
Disodiumphosphate	1	109 ± 5
Potassium dihydrogenphosphate	1	128 ± 5
Potassiumphosphate (potassium 30 meq)	2	66 ± 4 56 ± 4
Zinc sulphate	1	22 ± 2
Calcium gluconate 10 %	2	49.4 ± 2.3 49.0 ± 2.3
Magnesium sulphate	3	36.9 ± 1.5 44.3 ± 1.2 44.9 ± 2.0
Oligo complex	1	950 ± 50 mg/l

nese in Travasol 10 %, while Kurkus et al. found a mean of 1.21 µg/l. In the present work, a value of 9.3 µg/l is calculated, indicating that the manganese content of this amino acid solution can vary considerably, which is probably due to the preparation procedure.

When disregarding the Oligo Complex, it should be noted that all electrolytes are used in such small quantities that the mean contribution is only about 8 µg of manganese per day. The highest concentration of manganese is found in the phosphate solutions: 128.0 and 108.8 µg/l for potassium dihydrogen-phosphate and disodiumphosphate, respectively.

Prepared TPN-solutions

In order to gain an adequate view of the actual content of prepared TPN-solutions, 17 samples derived from different patients on several days are analyzed.

Table 4. Calculated versus analyzed values of the manganese intake via 10 prepared TPN-solutions chosen at random.

Solution number	Calculated value mg/day	Analyzed value mg/day
1	5.05	5.04 ± 0.27
2	5.05	5.08 ± 0.33
3	5.05	4.85 ± 0.28
4	5.05	4.88 ± 0.30
5	5.05	5.19 ± 0.18
6	5.05	5.03 ± 0.18
7	5.05	5.09 ± 0.30
8	5.05	5.35 ± 0.30
9	5.04	4.87 ± 0.30
10	5.04	4.85 ± 0.20

The manganese content of 10 randomly chosen TPN-solutions is calculated using the values obtained by analysis of the components (Tables 2 and 3). These values are compared with the values obtained by direct analysis of the TPN-solutions (see Table 4).

For the 10 samples, the mean calculated value of manganese daily intake is 5.05 ± 0.01 mg per day, while the mean value found by analysis is 5.02 ± 0.16 mg per day.

In order to evaluate the influence of storing TPN-solutions for 3 months at 4 °C on the manganese content, 0.5 ml of a 1 ppm stock solution of manganese was added to 2 ml of the sample. A recovery of 104 ± 6 % is found.

Enteral nutrition

Most of the commercially available products for enteral nutrition mention the amount of the essential trace elements present; some others do not offer this information.

In Table 5 the manganese content of 18 different samples of enteral nutrition is summarized. Values given on the label are presented. The manufacturer is indicated by a code, as given in the footnotes of Table 6.

Table 5. Manganese content of enteral nutrition formulations.

Product	Manufacturer	Packing (content)	Mn level (ppm)		Daily intake (in µg)
			found	given	
Powdered form:					
Biosorbin MCT	1	bag (89 g)	0.34 ± 0.02	–	192
Nutricia bananas	2	bag (2.5 g)	0.16 ± 0.01	–	
mocha	2	bag (2.5 g)	0.97 ± 0.06	–	
Pepti 2000	2	can (101 g)	14.6 ± 1.0	16	7373
Pulmocare vanilla	3	can (8 fl. oz)	3.33 ± 0.15	–	
Steramine	4	can (175 g)	1.64 ± 0.15	–	
Survimed renal	5	bag (80 g)	5.1 ± 0.5	6.2	2448
bananas	5	bag (90 g)	3.9 ± 0.3	5.5	2106
Vivonex standard	6	bag (80 g)	5.78 ± 0.24	–	2774
Vivonex T.E.N.	6	bag (80.4 g)	4.93 ± 0.19	–	1741
Liquid form:					
Enrich vanilla	2	can (250 ml)	2.40 ± 0.17	3.3	4960
Fresubin chocolate	5	bottle (0.5 l)	1.73 ± 0.16	1.5	1730
nuts	5	bottle (0.5 l)	1.60 ± 0.15	1.5	1600
toffee	5	bottle (0.5 l)	1.97 ± 0.17	1.9	1970
vanilla	5	bottle (0.5 l)	1.47 ± 0.15	1.5	1470
Pre-nutrison	2	bottle (0.5 l)	3.52 ± 0.30	4	3520
Nutrison	2	bottle (0.5 l)	3.92 ± 0.35	4	3920
Nutrison Na-min	2	bottle (0.5 l)	3.90 ± 0.35	4	3900

It appears that, in most cases, the amounts of manganese determined do not differ significantly from the value mentioned by the manufacturer. An exception must be made, however, for Enrich vanilla (Nutricia, Zoetermeer, Holland) and Survimed bananas (Fresenius, FRG: for both a difference of 30 % is noted.

In general, the amount of enteral nutrition to be administered daily is calculated to represent about 2000 kcalories (8368 kJ). The daily intake of manganese through administration of enteral nutrition is calculated and indicated in Table 5. The values calculated seem to vary quiet widely, with a minimum of 192 µg per day for Biosorbin MCT and a maximum of 7373 µg per day for Pepti 2000. Therefore, when using long-term enteral nutrition, care should be taken in order to avoid manganese deficiency.

Supplemental nutrition and flavor stuffs

In some cases of EN-formulations, supplemental nutrition is added to increase the caloric content. In other cases, flavor constituents are added in order to improve taste. In Table 6, the manganese content of these components is displayed. There is no content of manganese given on any of the labels. Since the amounts of these components supplemented differ for each diet, it is difficult to estimate the contributed intake of manga-

Table 6. Manganese content of supplemental nutrition and flavor stuffs.

Product	Manufacturer	Packing	Content	Manganese in µg/g found	Class
Powdered form:					
Alburone	7	plastic bottle	200 g	1.53 ± 0.1	supplem.
Dextropur	8	box	400 g	0.07 ± 0.01	supplem.
Fortimel vanilla	2	box	200 ml	0.12 ± 0.01	supplem.
mocha	2			0.20 ± 0.02	supplem.
Glucose polymers					
CAL 400	7	plastic bottle	400 g	0.30 ± 0.02	supplem.
Vivonex citron*	6	bag	2 g	0.14 ± 0.01	flavor
mocha*	6	bag	2 g	0.97 ± 0.08	flavor
orange*	6	bag	2 g	0.15 ± 0.01	flavor
strawberry*	6	bag	2 g	2.00 ± 0.15	flavor
Liquid form:					
Nutrical neutral	2	bottle	200 ml	8.19 ± 0.45	supplem.
orange	2	bottle	200 ml	10.8 ± 0.1	supplem.

List of manufacturers:
1) Pfrimmer & Co, Pharmazeutische Werke Erlangen GmbH, FRG; 2) N.V. Nutricia, Zoetermeer, Holland; 3) Ross Laboratories, Columbus, Ohio, USA; 4) N.V. Pharmacobel, Brussels, Belgium; 5) Fresenius, Bad Homburg, FRG; 6) Norwich Eaton Pharmaceuticals, Inc., Norwich, New York, USA; 7) N.V. Roussel, Brussels, Belgium; 8) N.V. Mais-Mondi, Antwerp, Belgium;
* destruction in waterbath

nese. It should be noted that the amount of manganese from these sources is negligible.

Conclusion

For prepared TPN-solutions investigated in this work a mean intake value of 5.051 ± 0.004 mg of manganese per day is found. It should be noted that only less than 0.2 % of the manganese in prepared solutions originates from the electrolytes used (before adding the Oligo Complex), which clearly demonstrates the effect of adding the Oligo Complex. In October 1977, a panel of experts in pediatrics, surgery, biochemistry, and pharmacy, as well as representatives of the Food and Drug Administration (FDA), the U.S. Pharmacopeia and pharmaceutical industries, organized a meeting on the subject of the presence of essential trace elements in TPN-formulations. Their findings were published in 1979 (Expert Panel, JAMA, 1979). Based on several publications, a daily intraveneous intake of 0.15 to 0.8 mg per day for adult humans was suggested. They stated, however, that this value should not be referred to as a recommendation, but merely as a guideline, and should be adapted according to the specific needs of the patient under consideration. Nevertheless, the mean intake value in this work indicates that, for all solutions investigated, the manganese content exceeds the most recent recommendation. Even when manganese is among the least toxic elements, parenterally fed patients may be at increased risk of manganese toxicity because administration of supplemented manganese by the intravenous route bypasses hepatic control. According to our present knowledge there are no clinical studies or functional parameters available to measure the response to intakes of manganese.

For EN-formulations, the manganese intake values in this study vary from 0.19 to 7.37 mg per day. For infants, 2 to 10 μg per kg of body weight may be taken as a guideline, as resulted from balance studies (James and McMahon, 1976; Ricour et al., 1980). The safe and adequate intake for adults proposed by the WHO Expert Committee for manganese is 2.5 mg per day, with an absolute requirement of 1 mg per day, while 2.0 to 5 mg per day is taken as a safe dietary allowance (WHO Expert Committee Report, 1973, National Academy of Sciences, 1989). The values found in this study indicate that care should be taken in using EN-formulations to avoid manganese deficiency or toxicity.

It is, however, important to stress that there are at present only limited data concerning the effects of individual dietary components on manganese absorption, transport, and utilization (i.e., bioavailability). An interaction between iron and manganese was demonstrated in several species (Keen et al., 1984). Therefore, further studies are necessary on dietary levels of iron and other elements such as calcium in the different TPN and EN solutions, and even on the type of manganese compound, contained in the EN formulations.

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