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Bioavailability of Enteral Yeast-Selenium in Preterm Infants

GÁBOR BOGYE,[1] GEORG ALFTHAN,[2] AND TAMÁS MACHAY[3]

[1]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary; [2]National Public Health Institute of Finland, Helsinki, Finland; [3]1st Dept. of Perinatal Intensive Care, Semmelwies Medical University, Budapest, Hungary

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ABSTRACT

There is no data or literature on the effects of supplementing infants with yeast selenium, although its intestinal absorption and bioavailability are higher in adults compared with other selenium compounds.

The aim of the present investigation was to study the impact of selenium enriched yeast on the serum selenium concentration of preterm infants living in a low selenium area (Hungary).

Twenty-eight preterm infants with mean ± SD birth weight of 962 ± 129 g and gestational age 27 ± 1 wk were randomized into two groups at birth with respect to selenium supplementation. In the supplemented group (n = 14) infants received 4.8 mg yeast selenium containing 5 μg selenium daily via nasogastric drip during the first 14 postnatal days. The nonsupplemented infants were used as a reference group.

In the supplemented group, the serum selenium concentration increased from 32.1 ± 8.5 μg/L to 41.5 ± 6.5 μg/L and in the nonsupplemented group it decreased from 25.9 ± 6.8 μg/L to 18.2 ± 6.4 μg/L from birth in two weeks time. Compared with previous studies, our results suggest that the bioavailability of selenium in the form of yeast selenium is higher than that of other selenium compounds used for preterm infants. We did not observe any complications or side-effects owing to enteral yeast selenium supplementation.

We conclude that selenium enriched yeast is a safe and an effective form of short-term enteral selenium supplementation for infants.

*Author to whom all correspondence and reprint requests should be addressed.

Index Entries: Serum selenium; deficiency; supplementation; yeast; preterm infant; bioavailability.

INTRODUCTION

As the understanding of the role of selenium in health and diseases has grown, it has become obvious that those at risk due to selenium deprivation are to be found among premature infants. Very low birth weight (VLBW) premature infants (<1500 g birth weight) may be susceptible to selenium deficiency due to shortened gestation resulting in inadequate selenium stores compared with those of full-term infants, decreased intestinal absorption during postnatal development, high tissue demand because of rapid growth, and inadequate selenium intake *(1,2)*. The selenium status of young and especially preterm infants at birth is lower than that of children and adults living in the same community and generally, it decreases during the first 4 postnatal months. During later infancy and early childhood the selenium status begins to increase and reaches a plateau by around 20 yr *(3,4)*. There is no information on the selenium status of Hungarian infants, although we have shown that the selenium status of adult Hungarians is one of the lowest reported for Europe *(5)*.

Dietary selenium needs during infancy are not known with certainty. The US National Research Council has established a safe and adequate intake range of 10–40 μg/d for infants aged 0–6 months *(6)*. The selenium concentration of human milk depends on the level of maternal intakes of selenium and the stages of lactation *(7–9)*. Further complicating this issue is that the bioavailability of selenite, selenate and selenoaminoacids in human milk, bovine milk-based or soy-based infant formula is quite different *(10–14)*. Selenium-enriched yeast whose selenium is mostly selenomethionine is a good source of selenium that is both deposited in tissues as well as being available for glutathione peroxidase (GSH-Px, EC 1.11.1.9). synthesis *(15,16)*. There are no data in the literature on the possible impacts and side effects of yeast selenium for full-term or preterm infants, although its intestinal absorption and bioavailability are higher than for other selenium compounds in adults *(15,16)* and this form of selenium has been used in adults around more than 20 years *(17)*. The aim of the present investigation was to study the impact of selenium-enriched yeast on the serum selenium concentration of preterm infants living in a low selenium area.

SUBJECTS AND METHODS

Patients and Experimental Design

Twenty-eight single-born, VLBW preterm infants admitted to the First Dept. of Perinatal Intensive Care at Semmelweis Medical School, Budapest, Hungary, were examined during a routine clinical investiga-

tion in December 1994. These patients were randomized into two groups with respect to selenium supplementation: the supplemented group consisted of 14 infants who received 4.8 mg yeast selenium (Saccharomyces cerevisiae, BUSZESZ Co, Budapest, Hungary) containing 5 μg selenium daily with nasogastric drip; and the nonsupplemented group consisted of 14 patients who did not receive any trace element supplements.

All enteral feedings (water, breast milk) were given via nasogastric route. The parenteral regimen consisted of 130–150 mL/kg/d of 5%–10% dextrose, with crystalline amino acids (2.5–3.5 mg/kg/d) and essential fatty acids (Lipofundin, Braun Melsungen, Germany) (1.5–2 g/kg/d). Infants also received weekly blood transfusions of packed red cells and fresh-frozen plasma. There were no clinically significant differences between the enteral and parenteral regiments of the two groups, except for one patient in the nonsupplemented group. In this case we had to perform twice a whole blood exchange therapy during the first two weeks after birth. The clinical and physical characteristics of the VLBW infants are shown in Table 1.

Serum samples were obtained from blood collected for normal clinical management of the infants at the first and 14th days after birth. The clinical laboratory requires about 1 mL of blood but generally uses somewhat less. Blood in excess of laboratory requirements was used for this study and no blood samples were taken expressly for the present study. Our investigation was approved by the Ethical Committee of the participant institutes. Blood samples were drawn by heel or finger prick into plastic tubes. It was centrifuged and the serum was stored in polyethylene vials at –20°C. The samples were transported to the National Public Health Institute of Finland in dry ice and analyzed in the middle of January 1995. All storage and analytical containers were acid-washed and only purified water was used throughout the study.

Determination of the Serum Selenium Concentration

Selenium was determined by an electrothermal atomic absorption spectrophotometric method using nickel nitrate and nitric acid as matrix modifiers *(18)*. The precision of the method between series (n = 10) for two serum pools at the levels of 65.3 μg/L and 78.3 μg/L were 3.5 CV% and 3.1 CV%, respectively. The accuracy was verified by analysing an external reference serum, SN 112 (Nycomed, Oslo, Norway, recommended value 90 μg/L) which gave the result 90.8 ± 2.0 μg/L (n = 5). The detection limit of the method for serum is 4.5 μg/L.

Statistical Analyses

Effect of treatment with selenium within groups was compared by paired t-test. Pearson correlations were calculated for selenium and characteristics of the patients (SAS statistical program for VAX computers).

Table 1
Clinical and Physical Characteristics of the Infants at Birth

	Supplemented group (n=14)	Nonsupplemented group (n=13)
Sex: male	7	6
female	7	7
Birth weight ± SD *(g)*	980 ± 129	952 ± 130
Gestation age ± SD *(week)*	27.2 ± 1.1	27.4 ± 1.1
Blood transfusion ± SD *(ml/kg/week)*	14.4 ± 7.2	13.9 ± 4.4
Respiratory therapy ± SD *(day)*	13.5 ± 2.3	12.6 ± 3.4
Clinical diagnosis:		
IRDS*	7	6
Apnoe	2	4
Pneumonia	4	3
Wet lung	1	0

*IRDS: idiopathic respiratory distress syndrome.

RESULTS

The clinical and physical characteristics of the two groups of infants were similar (Table 1). The mean ± SD serum selenium concentration of all (n = 28) VLBW preterm infants was 28.6 μg/L at birth. The patients were randomized into two groups using a random list. The mean serum selenium concentration of the supplemented group was higher than the nonsupplemented group ($p < 0.05$) so comparisons between the two groups were not carried out. No statistically significant correlations were found between the serum selenium concentration and gestation time, body weight at birth, or blood transfusion needs and duration of oxygen therapy in the observed period.

The changes in serum selenium concentration of the 28 infants during the first 14 postnatal days are shown in Table 2. From the nonsupplemented group we excluded data for one patient (code C.5.) who received whole blood exchange therapy, since the selenium concentrations of fresh-frozen plasma collected from blood donors are significantly higher than the serum selenium concentration of neonates living in the same area. The serum selenium concentration of this patient increased from 16 μg/L to 32 μg/L in the observed period, although she did not receive any enteral selenium supplementation. The 13 nonsupplemented patients' mean ± SD serum selenium concentration decreased significantly in 2 wk ($p < 0.004$) from 25.9 ± 6.8 μg/L to 18.2 ± 6.4 μg/L. There was a significant increase in the serum selenium concentration of the infants given enteral selenium supplementation, 5 μg/d in the form of yeast-selenium ($p < 0.004$). The mean ± SD value increased from birth in

Table 2
The Changes of Serum Selenium Concentration in the Supplemented and Nonsupplemented Groups during the First 14 Postnatal Days

Supplemented group			Nonsupplemented group		
Code of participants	Serum selenium concentration (μg/l) **Day 0**	Serum selenium concentration (μg/l) **Day 14**	Code of participants	Serum selenium concentration (μg/l) **Day 0**	Serum selenium concentration (μg/l) **Day 14**
Se.1.	39	50	C.1.	23	21
Se.2.	50	38	C.2.	34	26
Se.3.	29	38	C.3.	21	20
Se.4.	40	42	C.4.	25	13
Se.5.	26	45	C.5.*	16	32
Se.6.	24	27	C.6.	23	28
Se.7.	30	52	C.7.	39	25
Se.8.	17	41	C.8.	30	23
Se.9.	37	35	C.9.	35	20
Se.10.	31	40	C.10.	25	11
Se.11.	34	42	C.11.	16	10
Se.12.	21	40	C.12.	22	12
Se.13.	37	50	C.13.	18	10
Se.14.	35	41	C.14.	26	18

*In this case we had to perform whole blood exchange therapy twice during the first two weeks after birth, so we excluded data for this patient.

2 weeks from 32.1 ± 8.5 μg/L to 41.5 ± 6.5 μg/L. We did not observe any complications that could be related to selenium deficiency either at the beginning of the study or later, nor were there any signs of adverse effects in the supplemented group.

DISCUSSION

Serum selenium concentration is considered one of the most practical and widely used indicators of an individual's selenium status. Our results show that the serum selenium concentration of randomly selected VLBW preterm infants at birth in Hungary is among the lowest reported (Table 3). Similar low selenium concentrations of infants have been reported only from New Zealand (26.1 μg/L) *(4)* and still lower levels in children in Dechang county of China (13.0 μg/L) *(20)*. The incidence of Keshan disease in this county is among the highest in China *(20)*.

Serum selenium levels equilibrate within a few days, responding rapidly to major changes in intake *(19)*. Therefore, serum selenium measurements should reflect changes in selenium status during rapid growth and development better than other parameters *(22)*. In our investigation the serum selenium concentrations of the nonsupplemented preterm infants decreased 30% in two weeks after birth. Other studies of infants

Table 3
Serum and Plasma Selenium Concentration of Preterm Infants at Birth in Various Countries*

Area/Country	Selenium concentration (μg/L*) mean ± SD and/or minimum - maximum	References
Oslo Norway	50.7 *(s)* (30.1 - 73.1)	Hågå et al. (35)
East Meadow USA	88 ± 32 *(s)*	Amin et al. (37)
Ontario Canada	90 ± 30 *(s)*	Friel et al. (38)
New York USA	100 ± 30 *(p)*	Rudolph et al. (36)
Vancouver Canada	59.2 ± 13.0 *(p)* (36.1 - 100.0)	Lockitch et al. (21)
Utah USA	53.7 ± 2.5 *(p)*	Smith et al. (12)
Christchurch New Zealand	26.1 ± 10.0 *(p)*	Sluis et al. (4)
South Island New Zealand	38 ± 11 *(p)*	Darlow et al. (39)

(p) = plasma; *(s)* = serum; * The comparison data are given in μg/L.

whose selenium intake was considered to be adequate showed increases in serum or plasma selenium levels after birth *(4,10)*, and infants with plasma selenium concentration at birth of approx 100 μg/L showed no significant changes in the first 6–8 weeks of life even though fed formulas containing less than 5 μg selenium/L *(23)*. Thus a decrease of the selenium status does not appear to be physiologic.

There are limited data available on the requirements of selenium for preterm infants *(24,25)* and on the absorption of different selenium compounds by VLBW preterm infants. Yeast-selenium has not been studied yet for this group of patients although organic selenium compounds have been shown to have a much higher intestinal absorption in adults *(16,26,27,28)* and infants *(10,11)* compared to inorganic selenium compounds. It was questionable to what extent selenium incorporated into yeast can be absorbed from the intestinal tract of preterm infants because they usually have problems with absorption during early postnatal development *(1)*. In our study the intestinal absorption of selenium in the form of yeast selenium seems to be higher compared to other selenium compounds used for preterm infants in other studies *(11,12,22,33,34)*. Although the initial serum selenium concentrations were lower in our investigation than in previous studies our results are in line with data on intestinal absorption in adults *(16,26,27,28)* or infants *(10,11)*.

In the observed period the serum selenium value of five of the 13 nonsupplemented infants decreased below the mean value of 13.4 μg/L reported for the population at risk for Keshan disease *(29)*. We did not find any evidence of adverse clinical outcomes of selenium deficiency such as cardiomyopathy or muscle weakness. However, such conditions are very difficult to assess in VLBW infants. Neither other more rarely observed complications of selenium deficiency such as pseudoalbinism or macrocytosis were observed *(30,31)*.

The serum selenium concentration of the infant in the nonsupplemented group who received whole blood exchange therapy was doubled, but it still did not reach the level of infants living, for example, in Finland where selenium status is considered to be adequate *(33)*. This finding suggests that even neonates receiving whole blood exchange therapy living in a low selenium area may also be at risk for selenium deficiency and its complications.

In conclusion we report that short-term selenium supplementation of 5 μg/d in the form of yeast selenium significantly increased the serum selenium concentration of premature infants without any obvious side-effects. We propose that yeast-selenium is a safe and an effective means for short-term enteral selenium supplementation of very low birth weight infants.

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