

Selenium Level of Umbilical Cord Blood: Is it related to Respiratory Distress Syndrome?

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Abstract

Introduction

The aim of study was to compare umbilical cord blood selenium levels in respiratory distress syndrome (RDS) and non RDS preterm babies.

Materials and Methods

Umbilical cord blood selenium levels of all preterm newborn born during a 6-month period were enrolled in the study. They were divided into two groups: RDS and non RDS. Selenium level was assessed by using electro-thermal atomic absorption spectrometry and serum concentration of selenium was compared between the two groups.

Results

During the study 150 preterm babies were studied. Mean umbilical cord blood selenium levels were 98.5 µg/L. Among 150 preterm babies 27 (18%) had RDS and 82% no RDS. Mean umbilical cord blood selenium level in RDS and non RDS groups were 96.5 and, 96.6 µg/L respectively (P=0.64). There were no significant differences between the two groups with regard to umbilical cord blood selenium levels.

Conclusion

In this study there was no significant relationship between selenium umbilical cord blood level and respiratory distress syndrome in preterm neonates.

Keyword

Respiratory distress syndrome, Preterm newborns, Selenium level, Umbilical cord blood

Introduction

Trace elements comprise less than 0.01% of total body weight. They function as constituents of metalloenzymes, cofactors for metal ion activated enzymes, or components of vitamins, hormones, and proteins. The fetus accumulates and stores trace elements primarily during the last trimester of pregnancy.¹ Therefore, the premature infant has low stores at birth and is at risk for trace mineral deficiencies if intakes are not adequate to support

requirements for growth. Immature homeostatic control of trace element metabolism also increases the risk of deficiency. Trace minerals that have physiologic importance in human health include zinc, copper, selenium, manganese, chromium, molybdenum, fluoride, and iodine.¹

Factor 3 which contain selenium is a dietary substance which prevents liver necrosis in rats. Concentrates for factor 3 also protect against multiple necrotic degeneration (heart, liver,

kidney, and muscle necrosis) in the mouse, as well as against exudative diathesis in chickens.²

The conclusion that selenium is an essential part of the active organic material is borne out by the finding that inorganic selenium salts are remarkably effective in protecting against necrotic liver degeneration.²

Indeed many of the nutritional effects of selenium can be explained by its role in glutathione peroxidase.³

Several diseases in newborns have been shown to be caused at least in part by oxygen free radicals, which suggested as oxygen radical diseases including bronchopulmonary dysplasia, retinopathy of prematurity, necrotizing enterocolitis, patent ductus arteriosus and neuronal injury of hypoxic ischemic encephalopathy.

A prospective observational longitudinal study in 39 neonates less than 1500g birth weight and less than 32 weeks gestational age showed there was a significant relationship between decreasing selenium levels of blood and increase in bronchopulmonary dysplasia (BPD); the same researchers in 2000 found that administration of selenium in very low birth weight infants could not improve the outcome and bronchopulmonary dysplasia.^{5,6}

Other study in 35 premature infants confirms that low plasma selenium and alpha-tocopherol levels in preterm infants (≤ 30 weeks' gestational age) were significantly associated with increased respiratory morbidity.⁶

The levels of breast-fed infants were significantly higher than those of both formula-fed infants until the introduction of solids. Preterm infants had significantly low plasma selenium levels up until a postnatal age of at least 6 months. The levels were lower than those of term infants fed an identical non-supplemented infant formula during the first 4 months of life.⁷ There are positive correlation between umbilical cord blood selenium levels and maternal blood.⁹ In our last study we found normal maternal serum selenium concentrations which did not differ between preterm and full term deliveries.¹⁰ In our other study maternal serum selenium concentrations were not significant predictors of preterm deliveries, but selenium level in term infants was higher than preterm infants although both were within normal range.¹¹ As studies have shown serum selenium concentrations in preterm babies are less than term ones.^{11,12,13} As concentration of

factor 3 which included selenium protected against multiple necrotic degeneration, on the other hand the antioxidant effect of selenium has glutathione peroxides and so selenium deficiency may cause necrotic effect in type II pneumocytes (producer of surfactant). The aim of study was to compare serum selenium concentrations in respiratory distress syndrome; the most common cause of death in preterm neonates.

Materials and Methods

From April 20, 2009 to October 20, 2009 all preterm babies born in our hospital were studied. The study was approved by the vice chancellor of Mashhad University of Medical Sciences and informed consent was obtained from each parent. Criteria for enrollment were included all newborns with gestational age ≤ 37 weeks of age determined by the last menstrual period together with physical and neurological examination of the neonate. RDS was diagnosed based on the following criteria: Tachypnea, chest retractions, expiratory grunting, cyanosis in room air, and a typical reticulogranular "ground glass" pattern on the initial chest x-ray and progressing signs and symptoms during the first 3 days of life.

We excluded neonates with congenital anomalies (e.g. congenital diaphragmatic hernia, musculoskeletal anomalies, congenital heart disease, lung anomalies, aplasia or hyperplasia of the kidney), maternal sepsis risk factors (e.g. chorioamnionitis, maternal temperature above 38.0°C, membrane rupture longer than 18 hours, positive rectovaginal culture), neonatal sepsis and prenatal asphyxia.

All preterm infants were divided in two groups RDS and non RDS. Sex, weight, gestational age, first-minute Apgar score, maternal administration of betametasone, delivery method and multiple pregnancies were recorded. Mean umbilical cord blood selenium levels were measured for each group and compared between RDS and non RDS preterm newborns.

In this study we used the t-test, Mann-Whitney test and for interventional variables the logistic regression test was used. Analysis was done by SPSS 11.5.

Laboratory analyses

In the first 24 hours after delivery, 5 ml of venous blood was drawn from mothers into selenium-free uncontaminated EDTA glass tubes. Samples were

immediately centrifuged at 3000 rpm for 15 min. and plasma was separated and kept frozen at -200C. Measurement of serum selenium concentration was determined by electro thermal atomic absorption spectrometry (ETAAS) with Zeeman correction and a graphite furnace (THGA graphite Tubes with end caps) in a Perkin- Elmer 4110 ZL apparatus. The conditions of detecting selenium were: EDL lamp for selenium with wavelength of 196.0 nm, lamp current: 290 mA, slit width: 2.0 nm and palladium matrix modifier. The detection limit of the method was via palladium modifier. Precision was <11% and inaccuracy <1%. Samples were diluted in proportion 1:3 with HNO₃ 0.2%+TRI-TON 0.2%. All samples were analyzed in duplicate. Our laboratory reference range for serum selenium was 70-160 µg/l, which is similar to published figures. All specimens were re-identified before processing, therefore, laboratory staffs were masked to clinical conditions.

Results

In this study 150 neonates were enrolled. Table 1 shows selenium umbilical cord blood levels based on demographic characteristics; all were insignificant.

Mean selenium level in newborns was 96.6 ± 18.86 µg/l. There were no significant differences between selenium umbilical cord blood levels in RDS and non RDS groups ($P=0.64\%$) Table 2.

Discussion

Respiratory distress syndrome (RDS) is one of the most common causes of death in preterm newborns. High dose oxygen therapy in RDS can decrease surfactant levels and lead to prolonged signs and symptoms. Selenium is a key component of a number of seleno-proteins, the best known of which are the antioxidant glutathione peroxidase enzymes.

It seems that selenium deficiency acts as an antioxidant to exacerbate the problem. Antioxidants such as selenium, one of the micronutrients, have an antioxidant effect which can inhibit the problem. Some studies demonstrated low selenium concentrations in preterm newborns.^{13,15} This study showed that cord blood selenium levels were not different between RDS and non-RDS preterm newborns. The selenium levels of umbilical cord blood in both groups were in the normal range of 70-160 µg/l.¹⁴ Mean selenium level in this study

was 95.84 ± 18.86 µg/l. In Sievers and colleagues' study serum selenium was 11.7 µg/l for less than 32 week infants and 31.3 µg/l for formula-fed term infants and 45.6 µg/l for breast-fed term infants.⁷ Many studies in different age, sex, newborn, children, men and women were done in Iran all of which had serum selenium concentration in normal limits.^{10,11,16,17} The normal value was near other nations in the Middle East and Europe.^{18,24} In some studies different values in umbilical cord blood of term and preterm neonates have been reported; but in our country serum selenium was in normal range.^{11,17} The selenium content of food depends to a large extent on the concentration of selenium in the soil in which the food is grown. Selenium concentrations in soil are low in various parts of the world, including Europe, China, central Africa and New Zealand. Over a similar period, measurements of selenium content of serum, plasma, or whole blood have shown similar reductions, using the same subjects at each sampling. Especially low serum and whole blood concentrations of selenium have been found recently in healthy third trimester pregnant women in Oxford.

Although selenium deficiency has a necrotic effect but in our study as selenium serum level was within normal limit therefore we did not find any relation between RDS and serum selenium levels. It was the first study to compare serum selenium level in RDS and non RDS preterm neonates. In spite of low selenium status has been documented in preterm infants and has been suggested to be a risk factor for chronic lung disease. But in this study in acute lung disease such as RDS did not relate to selenium deficiency.

Further studies with larger size and comparison of selenium deficient RDS with normal selenium RDS is required.

Conclusion

In this study umbilical cord blood selenium in preterm neonates was in normal limits and there were no significant differences between RDS and non RDS neonates.

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References

1. Poindexter B, Denne S. Enteral nutrition. In: Martin R, Fanaroff A, Walsh M. Fanaroff and Martin's neonatal perinatal medicine. 8th ed. Elsevier Mosby: 2011; 651-668.
2. Klaus Schwarz, Calvin M. Foltz Schwartz K, Foltz C. Selenium as an integral part of factor 3 against dietary necrotic liver degeneration. Journal of the American chemical society. Journal of the American Chemical Society, J Am Chem Soc 1957; 79(12): 3292-3293
3. Rotruck JT, Pope AL, Ganther HE. Selenium; biochemical role as a component of glutathione peroxidases. Science 1977; 179: 588-590
4. Darlow BA, Inder TE, Graham PJ, Sluis KB, Malpas TJ, Taylor BJ, et al. The relationship of selenium status to respiratory outcome in the very low birth weight infant. Pediatrics 1995; 96: 314-319.
5. Darlow BA, Winterbourn CC, Inder TE, Graham PJ, Harding JE, Weston PJ, et al. The effect of selenium supplementation on outcome in very low birth weight infants a randomized controlled trial. The New Zealand neonatal study group. J pediatr 2000; 136(4): 473-480.
6. Falciglia HS, Johnson JR, Sullivan J, Hall CF, Miller JD, Riechmann GC, Falciglia GA. Role of antioxidant nutrients and lipid per oxidation in premature infants with respiratory distress syndrome and bronchopulmonary dysplasia. Am J perinatol 2003; 20(2): 97-107.
7. Sievers E, Arpe T, Scleyerbach V, Garbe-Schonberg D, Schoub J. Plasma selenium in preterm and term infant, during the first 12 month of life. Journal of trace element in medicine and biology. J Trace Elem Med Biol 2001; 14(4): 218-222.
8. Gathwala G, Yadav OP. Selenium in the neonate. Indian journal of pediatrics Indian J Pediatr 2002; 69(5): 443-446
9. Alonso L, Barrera B, De Juan C JA, Bermudez F, Barrera P. Selenium levels in related biological samples: human placenta, maternal and umbilical cord blood, hair and nails. J Trace Elem Med Biol 2005; 19(1): 49-54
10. Mohammadzadeh A, Farhat AS, Valaee L, Khadem N, Khajedaluae M, Parizadeh S.M.R. Maternal serum selenium and low birth weight neonates. Journal of Neonatal – Perinatal Medicine 2009; 2(2): 103-107.
11. Iranpour R, Zandian A, Mohammadzadeh M, Mohammadzadeh A, Balali – Mood M, Hajiheydari M. Comparison of maternal and umbilical cord blood selenium levels in term and preterm infants. Zhongguo Dang Dai Er Ke Za Zhi 2009; 11(7): 513-516
12. Gimenez G, Beriain PRM, Moises V R, De Jalon CAG, et al. Serum selenium levels in neonates. An Pediatr (Barc) 2003; 59(2): 149-154.
13. Dobrzynski W, Trafikowska U, Trafikowska A, Pilecki A, Szmaniowski W, Zachara BA. Decreased selenium concentration in maternal and cord blood in preterm compared with term delivery. Analyst 1998; 123(1): 93-97.
14. Litov RE, Combs GF. Selenium in pediatric nutrition. Pediatrics 1991; 87(3): 339-351
15. Bogden JD, Kemp FW, Chen X, Stangnaro-Green A, Stien TP, Scholl TO. Low normal serum selenium early in human pregnancy predicts lower birth weight. Journal nutrition research, J Nutr Res 2006; 26(10): 497-502.
16. Safaralizadeh R, Sirjani M, Pourpak Z, Kardar G, Teimourian S, Shams SH, et al. Serum selenium concentration in healthy children living in Tehran. Biofactors 2007; 31(2): 127-231.
17. Safaralizadeh R, Kardar GA, Pourpak Z, Moin M, Zare A, Teimourian S. Serum concentration of selenium in healthy individuals living in Tehran. Nutr J 2005; 14(4): 32
18. Ozdemir HS, Karadas F, Pappas AC, Cassey P, Oto G, Tuncer O. The selenium levels of mothers and their neonates using hair, breast milk, meconium and maternal and umbilical cord blood in Van Basin. Biol trace Elem Res 2008; 122(3): 206-215
19. Makhoul IR, Sammour RN, Diamond E, Shohat I, Tamir A, Shamir R. Selenium concentrations in maternal and umbilical cord blood at 24-42 weeks of gestation: basis for optimization of selenium supplementation to premature infants. Clin Nutr 2004; 23(3): 373-381
20. Micetic TD, Rossipal E, Krachler M, Li F. Maternal selenium status in Slovenia and its impact on the selenium concentration of umbilical cord serum and colostrums. Eur J clin Nutr 2000; 54(6): 522-524
21. Al- Saleh E, Nadakumaran M, Al- Shammari M, Al- Falah F, Al- harouny A. Assessment of maternal-fetal status of some essential trace elements in pregnant women in late gestation: relationship with birth weight and placental weight. J Matern Fetal neonatal Med 2004; 16(1): 9-14
22. Mihajlovic M, Cvetkovic M, Ljubic A, Kosanovic M, Nedeljkovic S
Selenium and malondialdehyde content and glutathione peroxidase activity in maternal and umbilical cord blood and amniotic fluid. Biological trace element research 2000; 73(1): 47-53
23. Iijima K, Otake T, Yoshinaga J, Ikegami M, Suzuki E, Naruse H, et al. Cadmium, lead, and selenium in cord blood and thyroid hormone status of newborns. Biol Trace Elem Res 2007; 119(1): 8-10
24. Schulpis KH, Karakonstakis T, Gavrili S,

Chronopoulou G, Karikas GA, Vlachos G, et al. Maternal-neonatal serum selenium and copper levels in Greeks and Albanians. Eur J Clin Nutr 2004; 58(9): 1314-1318.

25. Milne D.B. Laboratory assessment of trace element and mineral status. In: J.D. Bogden and L.M. Klevay, Editors, clinical nutrition of the essential trace elements and minerals. Humana Press, Totowa (NJ) 2000; 69-90

26. Daher S, Trindade C.E, Rezende C, Miranda A, Crossi R. Blood selenium level of very low birth weight infants during the first month of life. Pediatric Res 2001; 49: 297

Table 1: blood selenium level based on demographic characteristic

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Variables		Numbers (%)	Blood selenium level($\mu\text{g/l}$) mean \pm 2SD	P- value
Sex	boy	83(55.4%)	92.5 \pm 18.6	t=1.9
	girl	67(44.6%)	99.1 \pm 19.1	p=0.91
GA(wk)	<32	44(29.3%)	96.3 \pm 17.8	f=0.17
	32-34	54(36%)	96.7 \pm 18.9	p=0.83
	\geq 35	52(34.7%)	98.5 \pm 19.9	
BW(gm)	<1000	17(11.3%)	99.5 \pm 22.4	f=2.54
	1000-1500	27(18%)	91.2 \pm 13.7	p=0.05
	1501-2500	77(51.3%)	94.5 \pm 18.6	
	>2500	29(19.3%)	104.4 \pm 19.7	
Apgar score	0-3	15	93.2 \pm 24.4	f=0.07
	4-7	33	95.9 \pm 17.6	p=0.92
	\geq 8	102	95.9 \pm 20.2	
Beta	taken	128(85.4%)	96.5 \pm 18.8	t=0.18
	Not taken	22(14.6%)	95.5 \pm 22.1	p=0.85

GA=gestational age, BW=birth weight, Beta= Betametasone

Table 2. Comparison of umbilical cord blood selenium levels in RDS and non-RDS groups

Groups	Numbers (%)	Blood selenium level($\mu\text{g/l}$) mean \pm 2SD	P-value
RDS	27	96.5 \pm 20.1	p=0.64
Non RDS	123	96.6 \pm 18.7	