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Current Research in Translational Medicine 65 (2017) 89–91

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Brief communication

Low serum selenium concentrations in French patients with measles

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ARTICLE INFO

Article history:
Received 27 September 2016
Accepted 11 October 2016
Available online 9 November 2016

Keywords:
Measles
Selenium
French patients

ABSTRACT

Objective. – Selenium deficiency adversely affects the clinical outcome of measles in the tropics. In developed countries, serum selenium level has never been investigated during acute measles. The aim of this study was to determine serum selenium concentrations in French patients with acute measles and to seek correlations with clinical and virological findings.
Patients and methods. – We studied serum selenium concentrations in 94 French patients with acute measles and in 99 healthy controls matched for age and sex.
Results. – The mean of selenium concentration was significantly lower in the patients than in the controls (46.4 ± 14.1 μg/L versus 86.5 ± 13.9 μg/L, $P < 0.0001$). In the patients, selenium concentrations were not associated with age, sex, vaccination status, clinical signs or specific antibody responses. Selenium levels did not differ significantly between patients with uncomplicated measles (45.8 ± 14.2 μg/L) and patients with complications (52.7 ± 13.2 μg/L) ($P = 0.15$).
Conclusion. – Acute measles is associated with significant reduction of selenium level that did not seem to negatively affect the course of the disease suggesting compensating mechanisms in patients from developed countries against the disease.

1. Introduction

Selenium (Se) is a trace element required for selenoprotein enzymatic function [1]. Selenoproteins such as glutathione peroxidase and thioredoxin reductase have antioxidant functions and play a key role in intracellular defenses by reducing reactive oxygen species [2]. They also play a role in immune responses [3]. Thus, dietary deficiencies in Se and other trace elements negatively affect the course of several viral infections, especially in the tropics, such as HIV, emerging influenza viruses, coronavirus (severe acute respiratory syndrome), Ebola virus and measles [4]. In industrialized countries, Se serum levels have been studied during acute gastroenteritis, upper respiratory tract infections, chickenpox, and meningitis but, to our knowledge, never during measles [5,6]. The aim of this study was to determine serum Se concentrations in French patients with acute measles and to seek correlations with clinical and virological findings.

2. Materials and methods

2.1. Patients and controls

We studied 94 patients (M:F sex ratio: 1.13) aged from 2.5 months to 57 years (mean ± SD: 17.3 ± 14.1 years) admitted to Poitiers University Hospital with measles, from 2008 to 2011. The patients were matched for age and sex with 99 healthy controls consisted of 52 males and 47 females aged from 5 to 58 years (mean 17.9 ± 13.8 years; 45 subjects < 20 y, 47 subjects 20–39 y, and 7 subjects 40–56 y). Informed consent was obtained from all the participants or from the parents of pediatric patients.

2.2. Measles serology and RT-PCR

All patients presenting with symptoms of measles underwent IgM and IgG serodiagnostic tests on hospital admission (Enzygnost®; Behring, Marburg, Germany). In addition, nasopharyngeal specimens, saliva and/or urine from 29 patients were further tested for viral RNA by real-time RT-PCR. The diagnosis of measles was based on the presence of specific IgM in serum (in the absence of vaccination within the previous two months), with or without specific IgG, and on the results of RT-PCR.

2.3. Serum Se assay

Se was measured by Zeeman electrothermal atomic absorption spectrophotometry (ZEAAS), on a longitudinal model Analyst 600 equipped with an AS 800 autosampler. The entire system was from Perkin–Elmer Corps (Norwalk, CT06856; CT, USA).

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http://dx.doi.org/10.1016/j.retram.2016.10.002
2452-3186/

Table 1
Serologic and RT-PCR results in the 94 measles patients.

Measles serology	RT-PCR positivity		
	Saliva (18 samples)	Respiratory (8 samples)	Urine (18 samples)
Positive IgM/negative IgG (79 patients)	15/16[a] (93.7%)	6/6 (100%)	12/16 (75%)
Positive IgM/positive IgG (14 patients)	1/2 (50.0%)	1/1 (100%)	2/2 (100%)
Negative IgM/negative IgG (1 patient)	0/0 (0%)	1/1 (100%)	0/0 (0%)

[a] Number of samples tested by RT-PCR.

2.4. Statistical analysis

SAS software for Windows, version 9.3 (SAS Institute, Cary, NC, USA) was used for all analyses. Statistical significance was assumed at $P < 0.05$. Quantitative variables were expressed as means ± standard deviation (SD) and categorical variables as frequencies and percentages. Associations between serum Se concentrations and categorical variables were analyzed with Student's *t* test or the Mann–Whitney test for binary variables and ANOVA or the Kruskall–Wallis test for variables with 3 or more categories.

3. Results

3.1. Clinical and virological findings of measles cases

The most frequent clinical symptoms were fever (>38 °C, 100%), exanthema (95.7%), cough (81.9%) and coryza (68.1%). Complications occurred in 22 patients (23.4%), consisting of pneumonia (10 adults and 3 children; including one case of acute respiratory distress), diarrhea (8 cases) and one preterm delivery. No deaths occurred. Serological and molecular results of the 94 measles patients are summarized in Table 1.

3.2. Serum Se concentrations

Se levels were significantly lower in the patients than in the controls (46.4 ± 14.1 μg/L versus 86.5 ± 13.9 μg/L, $P < 0.0001$) (Fig. 1). In the patient group, Se levels did not differ significantly with age. In the control group, Se levels were significantly higher in subjects aged 15–29, 30–39 and ≥40 years than in subjects aged < 15 years ($P < 0.0001$, $P < 0.0001$ and $P = 0.0263$; respectively). No significant association was found between Se levels and specific clinical symptoms, but patients with exanthema tended to have higher Se concentrations ($P = 0.05$). In the patient group, Se levels did not differ between vaccinated and unvaccinated subjects (42.3 ± 21.0 μg/L versus 44.9 ± 15.5 μg/L, respectively; $P = 0.69$) or between subjects with and without specific IgG antibodies (45.3 ± 15.4 μg/L versus 46.9 ± 13.5 μg/L, respectively; $P = 0.60$). Likewise, Se levels did not differ between patients with and without pneumonia or diarrhea ($P = 0.96$ and $P = 0.47$, respectively). Finally, Se levels did not differ significantly between patients with uncomplicated measles (45.8 ± 14.2 μg/L) and patients with complications (52.7 ± 13.2 μg/L) ($P = 0.15$).

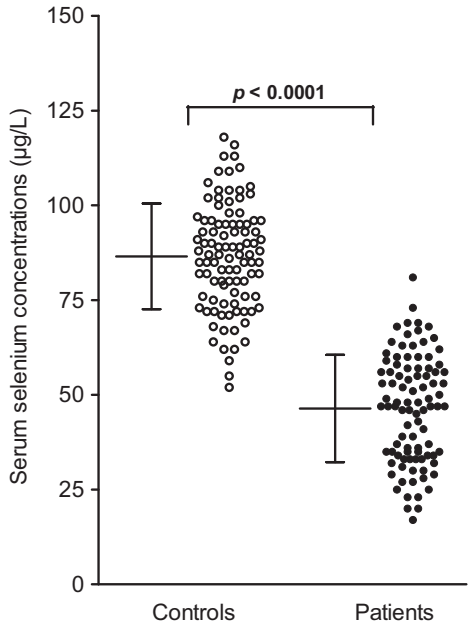

Fig. 1. Serum selenium concentrations in the 99 controls (○) and 94 measles patients (●). The horizontal bars and vertical bars indicate the mean serum selenium concentration ± one standard deviation.

4. Discussion

To our knowledge, serum Se concentrations have not previously been studied in Europe during the acute phase of measles. The role of Se in human health was highlighted in a 9-year prospective study of French individuals aged from 59 to 71 years, in which baseline plasma Se concentrations were significantly lower among subjects who died during follow-up than among survivors (77.6 ± 15.3 μg/L versus 84.6 ± 15.3 μg/L) [7]. It is interesting to note that Se concentrations in survivors in this study were similar to those observed in our healthy controls (86.5 ± 13.9 μg/L; range: 52–118 μg/L) but nonetheless lower than the values (96–122 μg/L) recommended to ensure optimal functioning of selenoproteins such as glutathione peroxidase suggesting that dietary Se intake is inadequate in the French general population [1,3,7]. It is thus likely that Se concentrations in our measles patients (46.4 ± 14.1 μg/L) significantly lower than in controls were probably already low at disease onset, although none of them had signs of poor nutrition. As Se is involved in CD4+ T-cell differentiation into Th-1 cells essential for viral clearance [2], the very low Se levels observed in measles patients due to a strong mobilization of this trace element could be responsible for a potential deficit of the antiviral immune response. It should be noted that inadequate Se intake adversely affects the T-cell cytokine profile and in some situations, viruses like coxsackievirus B3 may become more virulent under low Se status in the infected host leading to Keshan disease, a myocarditis mainly occurring in regions of China with low soil Se [8]; in this case, Se supplementation has been particularly effective as a preventive measure for Keshan disease [2]. However, no association between Se concentrations and demographic or clinical features was found in our work. In particular, patients with complications (diarrhea or pneumonia) did not have lower Se levels than patients with rapidly favorable evolution of the disease. Paradoxically, in the 30–39-year age group of our study, Se concentrations were even higher among patients with pneumonia than among those who did not develop complications. Overall, these intriguing data that did not show association between low Se levels and pejorative outcome of the disease, suggest still unknown compensating mechanisms in patients from developed countries as other micronutrients involvement such as zinc or copper in immune mechanisms against the disease.

In conclusion, this study performed in French patients hospitalized with acute measles showed serum Se levels

significantly lower than those of healthy controls. However, no association was found between Se levels and clinical outcome which is a noteworthy difference with the patients from developing countries where deficiency of dietary antioxidants such as Se has a significant impact on infection related morbidity. These data suggest the intervention of compensating mechanisms to control measles virulence in patients from developed countries. Finally, Se in patients with measles both in industrialized countries and developing countries would deserve further studies for clarifying its role during measles and other viral infections.

Disclosure of interest

The authors declare that they have no competing interest.

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