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Original article

Serum levels of selenium in patients with brain metastases from non-small cell lung cancer before and after radiotherapy

Concentration plasmatique de sélénium avant et après radiothérapie chez des patients atteints de métastases cérébrales d'un carcinome bronchique non à petites cellules

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ABSTRACT

Purpose. – This study was to evaluate the influence of radiotherapy on the selenium serum levels of non-small cell cancer patients with brain metastases.
Patients and methods. – This prospective study included 95 non-small cell cancer patients with brain metastases treated by radiotherapy from December 2007 until November 2010. Plasma selenium levels were determined before and at the end of the radiotherapy. Age, body mass index (BMI), prior chemotherapy, pathological type and personal habits (smoking and alcoholism) were recorded for each patient.
Results. – The mean age was 63 years; the mean BMI was 27.6. Seventy-six patients (80%) were non-smokers. Sixty-two patients (65.3%) showed no drinking habits and 8 (8.4%) have no prior chemotherapy. Thirty-nine patients (41.1%) were adenocarcinoma, 51 (53.7%) were squamous cell carcinoma and five (5.3%) were large cell carcinoma. At the beginning of radiotherapy, the mean selenium level for all patients was 90.4 μg/l and after radiation this value dropped to56.3 μg/l. Multivariate analysis showed statistically significant difference in the plasma selenium concentration before and after radiotherapy for age ($P < 0.001$), BMI ($P < 0.001$), smoking ($P < 0.001$), alcoholism ($P < 0.001$), prior chemotherapy ($P < 0.001$) and pathological type ($P < 0.001$).
Conclusion. – Significant reduction in plasma levels of selenium was recorded in patients undergoing radiotherapy, suggesting attention to the nutritional status of this micronutrient and other antioxidant agents.

Mots clés :
Carcinome bronchique non à petites cellules
Carence
Radiothérapie
Sélénium

RÉSUMÉ

Objectif de l'étude. – Cette étude avait pour objectif d'évaluer l'influence de la radiothérapie sur la concentration plasmatique de sélénium chez des patients atteints de métastases cérébrales d'un carcinome bronchique non à petites cellules.
Patients et méthodes. – Cette étude prospective a inclus 95 patients atteints de métastases cérébrales de carcinome bronchique non à petites cellules irradiées entre décembre 2007 et novembre 2010. La concentration plasmatique de sélénium a été mesurée avant et à la fin de la radiothérapie. L'âge, l'indice de

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masse corporelle avant la chimiothérapie, le type histologiques et les habitudes personnelles (tabagisme et alcoolisme) ont été notées pour chaque patient.
Résultats. – L'âge moyen des patients était de 63 ans, l'indice de masse corporelle moyen de 27,6. Soixante-seize patients (80 %) ne fumaient pas, 62 (65,3 %) ne buvaient pas et huit (8,4 %) n'avaient pas reçu préalablement de chimiothérapie. Ils étaient atteints d'adénocarcinome (39 patients, soit 41,1 %), de carcinome épidermoïde (51 patients, soit 53,7 %) ou de carcinome à grandes cellules (cinq patients, soit 5,3 %). La concentration plasmatique moyenne de sélénium était au début de la radiothérapie de 90,4 μg/L et de 56,3 μg/L à la fin. L'analyse multifactorielle a mis en évidence une différence entre les concentrations plasmatiques de sélénium avant et après la radiothérapie pour l'âge ($p < 0{,}001$), l'indice de masse corporelle ($p < 0{,}001$), le tabagisme ($p < 0{,}001$), l'alcoolisme ($p < 0{,}001$), une chimiothérapie préalable ($p < 0{,}001$) et le type histologique ($p < 0{,}001$).
Conclusion. – Une diminution significative de la concentration plasmatique de sélénium chez patients irradiés a été notée, ce qui suggère de porter attention à la nutrition, notamment aux micronutriments et agents oxydants de l'alimentation.

1. Introduction

Non-small cell lung cancer is the most common source of brain metastases, accounting for nearly 50% of brain metastases. Metastases to the brain develop in approximately 30% to up to 55% in autopsy series of all patients with non-small cell lung cancer [1,2]. Radiotherapy is an excellent palliative modality for patients with symptoms from brain metastases [3,4]. It has long been known that both chemotherapy and radiotherapy cause malnutrition and vitamin deficiency [5].

Patients with cancer have reduced concentrations of serum antioxidants. The intake of enriched antioxidant food will restore this biochemical deficiency. Antioxidants, in the form of oral or intravenous supplementation, may be required to remedy patient's depleted nutritional status [6]. Reduced selenium blood level has been described for most malignancies and a further decrease is expected caused by antitumoral treatment. It is assumed that radiotherapy increases selenium deficiency, possibly enhancing radiation side-effects. The primary focus in radiotherapy is to increase DNA damage in tumor cells, as double-strand breaks are important in cell death. Another course of action is to alter cellular homeostasis, modifying signal transduction pathways, redox state and disposition to apoptosis. Exposure to ionizing radiation produces oxygen-derived free radicals in the tissue environment. Antioxidants, including selenium, protect cells from DNA oxidative damage by scavenging free radicals in epithelial cells [7].

Selenium is an essential mineral found in trace amounts in the body. It works as an antioxidant, especially when combined with vitamin E, by scavenging damaging particles in the body known as free radicals. Free radicals can damage cell membranes and DNA, and may contribute to aging and a number of conditions, including heart disease and cancer. Antioxidants, such as selenium, can neutralize free radicals and may reduce or even help prevent some of the damage they cause [8,9].

The objective of this study was to evaluate the influence of radiotherapy on serum levels of selenium, in patients with brain metastases from non-small cell lung cancer.

2. Patients and methods

This prospective study included 95 non-small cell lung cancer patients with brain metastases treated by external beam radiotherapy from December 2007 until November 2010, who were not taking any selenium preparation, according to their medical history. These patients did not receive any radiation before this study. Plasma selenium concentrations were determined before and at the end of radiotherapy. Selenium levels were determined by atomic absorption spectrometry of whole blood. Based on healthy individual measurements, the optimal serum selenium levels range from 75 until 120 μg/l. Age, body mass index (BMI), prior chemotherapy (cisplatin based regimens, no less than three months), pathological type and personal habits (smoking and alcoholism) were recorded for each patient.

Radiotherapy was given to the whole brain using opposed 6MV lateral beams with a dose of 30 Gy in 15 fractions in 3 weeks. We compared categorical variables between groups (selenium levels before and after external beam radiotherapy) using the Chi^2 tests. The *t*-test was applied to compare the continuous variables between groups. A significance level of 5% probability ($p < 0.05$) and a 95% confidence interval were adopted. Statistical analysis was made using the SPSS 13.0 (SPSS Inc., Chicago, IL). This study was approved by the Ethics Research Committee of Shengjing Hospital of China Medical University.

3. Results

Patient characteristics are listed in Table 1.

At the beginning of radiotherapy, the mean selenium value for all patients was 90.4 μg/l. Sixty patients (63.2%) showed selenium concentrations within the normal range (75–120 μg/l). Twenty-seven patients (28.5%) had decreased values (< 75 μg/l) and eight patients (8.4%) had increased indices, above 120 μg/l. No patient showed critical values below 45 μg/l. After radiation treatment, the mean selenium value for all patients was 56.3 μg/l. Eleven patients (11.6%) showed concentrations within the normal range (75–120 μg/l) and 84 (88.4%) had decreased values (< 75 μg/l). No

Table 1
Patient characteristics.
Caractéristiques des patients.

	Mean (95% CI)
Age (years)	63 (61–65)
Body mass index	27.6 (27.0–28.2)
	Patients (%)
Smoking	
Yes	19 (20)
No	76 (80)
Alcoholism	
Yes	33 (34.7)
No	62 (65.3)
Prior chemotherapy	
Yes	87 (91.6)
No	8 (8.4)
Pathological type	
Adenocarcinoma	39 (41.1)
Squamous cell carcinoma	51 (53.7)
Large cell carcinoma	5 (5.3)