CLINICAL AND PARACLINICAL RESEARCHES ON THE EFFICIENCY OF ANTIOXIDANTS IN ORAL PRECANCEROUS PATHOLOGIES

Domocos Daniela[*], Maghiar Marius Adrian[*], Anchidin Ovidiu[**], Bei Mariana[***], Ciavoi Gabriela[*]

*University of Oradea, Faculty of Dental Medicine, P-ta 1 Decembrie 5, Oradea, Romania, e-mail: danadd769@gmail.com
**"Niculae Stancioiu" Heart Institute Cluj-Napoca, Calea Moților 19-21 St., 400001, Cluj Napoca, România, e-mail: anchidin_ovidiu@yahoo.com
***University of Oradea, Faculty of Environmental Protection, 26 Gen. Magheru St., 410048, Oradea, Romania, e-mail: marianaf.bei@gmail.com

Abstract

Although certain alternative antioxidant supportive treatments may be effective in curing oral cancer pathologies, they do not yet have the ability to prevent recurrence and malignancy. Due to this, these pathologies must be regularly monitored, regardless of their response to topical or systemic treatment, including clinical remission.

The clinical prognosis of oral precancerous lesions confirms the favourable effects of beta-carotene and vitamin C dietary supplements on oral precancerous lesions. Favourable effects have also been observed when beta-carotene and vitamin E were administered, beta-carotene and other antioxidant nutrients act as inhibitors of oral carcinogenesis.

Certain antioxidants administered in controlled conditions are able to increase the therapeutic efficacy of chemotherapy and radiotherapy by improving tolerance and increasing tumour sensitivity to these treatments while reducing the toxic effects on healthy cellular systems. Supplemental antioxidants do not interfere with chemotherapy. On the contrary, supplemental antioxidants have a positive influence on the rate of adverse effects and on the tumour response, the positive effect in case of supplementation being even 3 times higher.

Antioxidant therapies should always be adapted to the individual therapy protocol, taking into account specific interactions between cytostatic substances and bioactive nutrients.

Keywords: antioxidants, beta-carotene, vitamin C

INTRODUCTION

Cancer is the second leading cause of death worldwide right behind cardiovascular diseases. According to WHO predictions, the overall incidence of cancer was 11 million with over 7.6 million deaths and is expected to increase to an incidence of 15.5 million with 11.5 million deaths by 2030 (AHA, 2006)

In the field of human health, large-scale epidemiological studies have demonstrated a strong connection between fruit and vegetable rich diets (including the Mediterranean diet) and the reduction of certain diseases, including certain forms of cancer and cardiovascular diseases (Ziegler, 1991). This has led to dietary intervention studies based on the use of high doses of β-carotene in smokers and in asbestos workers. Thus, two of the most influential studies were the Beta-Carotene and Retinol Efficacy Trial

(CARET) (Omenn et al., 1996) and the Alpha-Tocopherol and Beta-Carotene Cancer Prevention Study (ATBC) (Blumberg 1994). However, the results of such studies seemed to contradict the dietary studies that preceded them, highlighting the need to better understand the way carotenoids behave in biological systems, especially human, and whether carotenoids can act as antioxidants and pro-oxidants under different conditions.

These two large-scale chemoprevention trials, the Alpha-Tocopherol and Beta-Carotene Cancer Prevention Study (ATBC) and the CARET trial on the efficacy of chemoprevention with beta-carotene and retinol, showed an increased incidence of lung cancer in subjects treated with beta -carotene due to increased oxygen pressure in the lungs; a pro-oxidant effect observed in smokers (Cancer Prevention Study Group, 1994 Omenn et al., 1996). Although adverse effects were most common among smokers when beta-carotene was taken in amounts of 20 mg/day (Van der Waal and Axell, 2002), the health benefits are presented in the dietary observational studies where the dose does not exceed 10 mg per day (Van der Waal and Axell, 2002).

Taking into consideration these reported side effects, the European Union requests that doses of supplemental antioxidants in chemoprevention programs be carefully selected (SCF, 2000) due to their interacting properties; based on the demonstrated synergistic effect of carotenoids and vitamin C via an antioxidant pathway (Edge and Truscott, 1997; Pallozza, 1998).

When comparing the effect of spirulina to the effect of lycopene in the management of the oral submucous fibrosis, Patil et al., 2014 observed that after a 3-month treatment period with 2x250 mg/day of spirulina and 2x4 mg/day of lycopene patients in the experimental group with lycopene showed improvement in pain relief when opening the mouth, and patients treated with spirulina showed improvement and reduction of the ulceration. Following this study, Patil et al., 2014 concluded that lycopene can bring significant clinical improvements in relieving pain in mouth opening and both treatments showed improvement in pain associated with lesion and burning sensation.

MATERIAL AND METHOD

The study method was a prospective and retrospective, randomized double-blind study in which each patient was informed on the possible adverse effects (particularly carotenoderma and increased lung cancer risk) and on the possible favourable treatment effects. Only patients who understood and signed the informed consent were included in the study.

The inclusion and exclusion criteria from the study were established. Based on these inclusion and exclusion criteria, 60 participants were enrolled in the study. Two subjects who received supplements were advised to discontinue the administration of any micronutrient available without prescription 4 weeks before the beginning of the study. Subjects were instructed to strictly avoid tobacco consumption.

RESULTS AND DISCUSSION

Most of the lesions found in the patients included in the study were less than 4 cm. The ratio is maintained at the patients in each group (Figure 1).

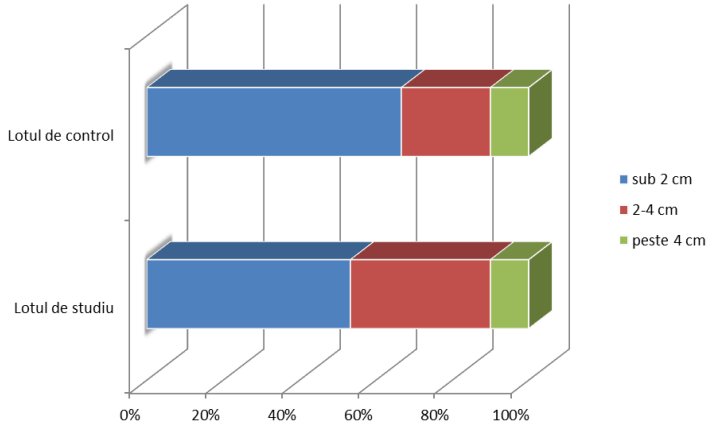

Fig. 1. The size of the oral precancerous lesion for the two patient groups (%)

The distribution of patients by groups based on the degree of dysplasia detected during the histopathological examination shall be unitary considering the stratification criteria used in randomisation (Figure 2).

No patient was excluded from the study due to carcinoma transformation within the first 6 months. No case of carotenoderma or confirmed pulmonary tumour was observed, indicating no side effects.

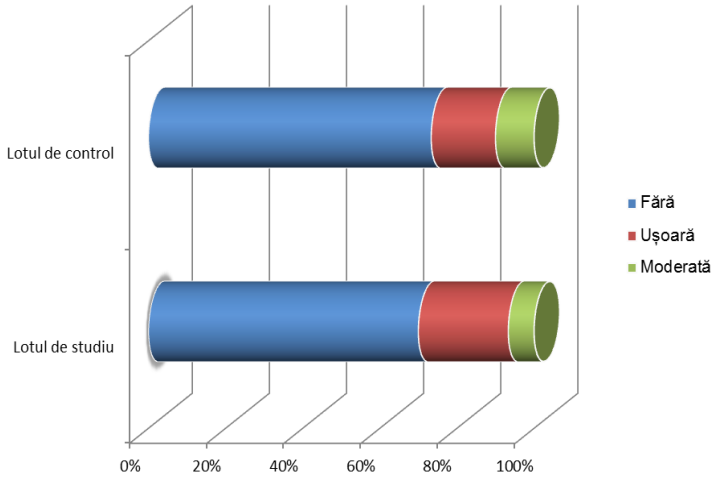

Fig. 2. The degree of dysplasia of the oral precancerous lesions for the patients in the groups of patients (percentage%)

Four new cases of oral cancer (microinvasive well-differentiated squamous cell carcinoma) were detected in the control group 13, 15, 15, respectively 17 months after inclusion. Three cases of oral carcinoma (microinvasive well-differentiated squamous cell carcinoma) were detected in the study group 20, 21 and 23 months since the beginning of the treatment. This result led to a relative risk of 0.77 (IC 95%: 0.28-1.89) for malignant transformation in patients receiving vitamin C and beta-carotene supplements (using the Cox proportional regression model). The statistical study demonstrates a slightly improved evolution of the oral precancerous lesions in patients receiving vitamin supplements without this difference reaching statistical significance.

The percentages for different evolutionary stages of the oral precancerous lesions show a more benign evolution in the patients from the experimental group. Thus, the two cases of complete remission (Figure 3) and three cases of partial remission in the study group compared to the two cases of partial remission and no case of complete remission in the control group confirm the favourable effects of antioxidant food supplements on oral precancerous lesions (Figure 3).

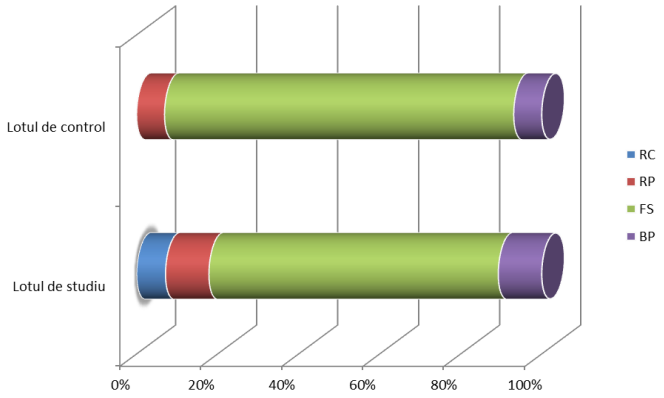

Fig. 3. The comparative clinical prognosis of oral precancerous lesions for the two groups of patients (CR= complete remission, PR = partial remission, NC = no change, PD = progressive disease)

CONCLUSIONS

The clinical prognosis of the precancerous lesions in the oral cavity following antioxidant therapy was a more benign one for patients in the experimental group.

The favourable effects of dietary supplements that included beta-carotene and vitamin C on oral precancerous lesions were confirmed by the two cases of complete remission and by the three cases of partial remission in the study group as compared to the two cases of partial remission and no case of complete remission in the control group.

The cumulative positive effect of dietary supplements regarding the complete remission (CR) and partial remission (PR) in the experimental group was 17.9%, indicating a difference of 11% compared to the control group where the complete remission (CR) and partial remission (PR) represented 6.9%.

Vitaminotherapy in the supportive treatment of oral neoplasm requires the focus of research on several antioxidants with malignant specificity in each case, target-oriented and with high bioavailability in order to obtain the expected results.

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