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Effects of orally administered antioxidants on micronuclei and sister chromatid exchange frequency in workers professionally exposed to antineoplastic agents

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ABSTRACT

The widespread use of antineoplastic drugs in cancer treatment increased concern about possible hazard to workers involved in the preparation and administration of these drugs. In the present study, the effects of commercial antioxidative drug Oligogal Se® on genome protection were analyzed in 15 nurses handling the antineoplastic drugs at the Oncology Department in comparison to twenty healthy volunteers. The nurses took antioxidant mixture Oligogal Se®, consisting of vitamins C, E, A and selenium, one capsule per day, over a period of 6 months. Genome damage was measured in peripheral blood lymphocytes by usage of sister chromatid exchange test and the cytokinesis-block micronuclei test. The frequency of sister chromatid exchange (SCE) and micronuclei (MN) in the exposed group was significantly higher when compared to the control group (SCE, $p < 0.05$; MN, $p < 0.01$ respectively). After antioxidant supplementation, the frequency of sister chromatid exchange and micronuclei decreased ($p < 0.05$) when compared with the values from the beginning of the study, but were still above the values of the control group. The effects of confounding factors such as cigarette smoking and cytostatics exposure time were also evaluated. The data indicated that Oligogal Se® contributed to the decreasing of genome damages in workers handling the cytostatics.

1. Introduction

Workers at the Oncology Department are occupationally exposed to antineoplastic drugs during preparation and administration of those agents. Antineoplastic drugs constitute a heterogeneous group of chemicals and their common characteristic is the ability to inhibit cancer growth. These agents include cytostatic drugs, hormones and antibiotics. Cytostatic drugs may act as alkylating agents, antimetabolites and mitotic inhibitors, free radical generators with strong oxidative properties and topoisomerase II inhibitors. According to the International Agency for Research on Cancer (IARC), 11 antineoplastic drugs belong to the Group 1 (human carcinogens), 9 to the Group 2A (probable human carcinogens) and 10 to the Group 2B (possible human carcinogens) (IARC, 2006). A particularly aggravating circumstance is the fact that the majority of antineoplastic drugs show nonselectivity in their action: they exhibit effects in both cancerous and non-cancerous cells. These characteristics of antineoplastic drugs lead to possible danger of genome damaging in persons, professionally exposed to these therapeutics. Majority of studies on occupational exposure to antineoplastic agents confirm that handling the antineoplastic drugs might lead to contamination (Yoshida et al., 2009; Cavallo et al., 2005; Laffon et al., 2005; Mrđanović et al., 2005; Testa et al., 2007; Cornetta et al., 2008). A previous study indicated that oncology workers have serial changes on chromosomes that are associated with the increase of adverse reproductive effects and increased risk of cancer (Au, 2003; Dranitsaris et al., 2005; Yoshida et al., 2009). The most commonly used indicators of exposure to genotoxic agents are micronuclei, sister chromatid exchange, chromosomal aberrations and urine mutagenicity.

Cytokinesis-block micronucleus test (CBMN), as a widely used biomarker of exposure to genotoxic agents, allows simultaneous evaluation of damage both to mitotic spindle apparatus and to chromosomes (Norppa and Falck, 2003). This is possible because micronuclei originate from acentric chromosome fragments or whole chromosomes that left behind the anaphase and left outside of the daughter nuclei (Fenech, 2000).

SCE represents the interchange of the DNA replication products at apparently homologous chromosomal loci and these exchanges presumably involve the DNA breakage and reunion (Knudsen and

Abbreviations: AO, antioxidant; CBMN, cytokinesis-block micronucleus test; MN, micronuclei; NDI, nuclear division index; PBL, peripheral blood lymphocytes; SCE, sister chromatid exchanges.

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