Clastogenic effects of carboplatin on SWR/J mouse bone marrow cells

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ABSTRACT

The clastogenic effect of the anticancer drug carboplatin was investigated in SWR/J mouse bone marrow cells. Males and females were used for each treatment time.The animals aging from 10- 12 weeks and weighting from 29.2 – 32.7 g were injected intraperitonealy with 10 mg/kg of carboplatin solution. A control group (3 males and 3 females) received only isotonic sterile saline (0.4 ml/animal). The animals were sacrificed 6, 12, 24, 48 and 72 h after the injection. The chromosome preparations were obtained from bone marrow cells. Chromatid and chromosome aberrations were investigated in 50 metaphases per animal.

No significant differences in the percentage of mitotic indices and in the frequency of chromosome aberrations were observed between the treated male and female mice at any time intervals used, therefore, data from the two sexes were pooled and analyzed statistically. A significant ($P<0.01$) decrease in the percentage of mitotic indices in bone marrow cells of treated mice was observed at 6, 12 and 24 h following the injection. Moreover, such treatment also significantly ($P<0.01$) increased the frequencies of chromosome aberrations in bone marrow cells of carboplatin-treated mice at all time intervals used following the injection, but it did not induce any significant changes in the diploid number of chromosomes ($2N^-/2N^+$) at any of the intervals used in this study. The chromosome aberrations induced by this drug included both chromatid and chromosome abnormalities, however, the most frequent types were chromatid gaps and breaks, the former being more frequent.

Key Words: *Carboplatin, chromosome aberrations, bone marrow cells, mice, clastogenic effects.*

INTRODUCTION

Platinum-derived drugs are playing an increasing important role in the treatment of a variety of neoplasms (Olivi *et al.*, 1993). The use of cisplatin, however, is limited by significant dose related toxicity, notably, nephrotoxicity, emesis, ototoxicity and peripheral neuropathy (VanHoff *et al.*, 1979; Olivi *et al.*, 1993). To improve the therapeutic index of platinum compounds, new analogs have been developed (Evans *et al.*, 1983), and carboplatin is one of these platinum derivatives that has been introduced into clinical practice.

Carboplatin has less non-hematologic toxicity, a similar antineoplastic activity and a better therapeutic index (Ettinger *et al.*, 1993). It