DETERMINATION OF PLATINUM DISTRIBUTION IN ADENOCARCINOMA BLACK-MICE BY NEUTRON ACTIVATION ANALYSIS

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30 female C57 bl. mice were treated with Adenocarcinoma im. in the right hind leg. Three days later cis-dichlorodiammine platinum was applied orally /15 mg/kg/ to all animals and additional 0.05 mg Prednisolone i.p. to 20 animals. Tissue samples from bloods, livers, kidneys, spleens, hearts, lungs, tumors and gastrointestinal tract were analyzed for their Pt concentration after therapy with cis-dichlorodiammine platinum complexes and Prednisolone by instrumental neutron activation analysis. Even 5 animals were sacrificed. The amount of Pt in most of the organs examined remained under 0.05% of the quantity applied. Maximum values were detected at the end of the experiment, except for the gastrointestinal tract, the liver and the kidneys. Treatment of the animals with Prednisolone did not produce a significant different distribution of Pt. Only in tumor tissues a significantly higher amount of Pt was observed after Prednisolone treatment at 48 h but not at 72 h. Blood levels increased with time after Prednisolone treatment, without Prednisolone blood levels decreased.
INTRODUCTION

Cis-diamminedichloro-platinum (DDP) is one of the first inorganic antitumor agents which is active in different tumors including sarcomas. Rosenberg et al. could show the successful regression of tumors caused by this new class of platinum compounds. This drug makes complexes with DNA and forms also crosslinks. The side effects seen during therapy result mainly from the non-tumor specificity. DNA repair can remove this compound from DNA. A lower dose during therapy and possibly also an enhancement of tumor specificity due to a possible increase of error prone to DNA repair in tumors could be obtained using DNA repair inhibitors. In earlier experiments we could show that Prednisolone inhibits the replicative DNA synthesis and also DNA repair incorporation of H3-TdR after γ and UV radiation. Also the reconstitution of supercoiled DNA after damage was delayed. In the present investigation Pt was determined in different organs, tumors and blood after administration of a Pt-compound alone or in combination with Prednisolone.

MATERIALS AND METHODS

In 30 females C57 bl. mice (~25 g), adenocarcinoma cell suspension was injected intramuscularly in the right hind leg. 3 days later cis-dichlorodiammine platinum (Ventron LT 031400311) was applied per os /15 mg/kg/ to all animals and 0.05 mg/kg Prednisolone to half of the Pt-treated animals intravenously. From both groups 5 animals were sacrificed 24, 48 and 72 h after treatment. Liver, kidney, spleen, heart, lung, gastrointestinal tract /git/ blood and the tumor were isolated, lyophilized