The Effect of Deuterium Depleted Water Administration on Serum Glycoproteins of Cytostatics Treated Rats

ANETA POP[1], EMILIA BALINT[1], N. MANOLESCU[1], I. STEFANESCU[2], MANUELLA MILITARU[1]
[1]University of Agronomical Sciences and Veterinary Medicine Bucharest, Faculty of Veterinary Medicine aneta_pop_ro@yahoo.com
[2]National Institute of Cryogenics and Isotope Separation

Abstract

The aim of the current research was to investigate the deuterium depleted water (DDW) effect on animals treated with anticancer drugs Vinblastine, Cyclophosphamide, 5-Fluorouracil and Farmarubicine. There were used two groups of 10 rats for each cytostatic, one group received 60 ppm DDW as daily diet before, during and after chemotherapy and the second group received tap water in the same conditions. Other two groups housed in the same conditions received DDW and tap water without any medication. There were recorded differences in the amount of serum glycoproteins and also the glycosylation degree and pattern. DDW administration induced a significant decrease of serum total glycoproteins and of glycosylation degree in all animals, both cytostatics treated or not. Fucose Raphanus sativus lectin interaction revealed that DDW induced also changes in the glycosylated domain, because it interacted only with the sera from 5-Fluorouracil treated rats that had not received DDW.

Keywords: deuterium depleted water, vinblastine, cyclophosphamide, 5-fluorouracil, farmarubucine, serum glycoproteins.

Introduction

Malignancy is usually accompanied by changes in the oligosaccharidic domain of glycolipids and glycoproteins. Carbohydrate alterations are not limited to surface antigens but also are exposed by serum glycoproteins. Identification serum glycoproteins isoforms is becoming a useful tool for diagnosis and management of malignant illnesses (1).

Besides their beneficial role in cancer treating, cytostatics have numerous side effects. Cancer prevention and therapy through diet manipulation is subject of increasing interest, mainly because it has been estimated that 35% of cancer death may be related to dietary factors (2). Cancer chemoprevention effect of different natural compounds was largely investigated. Encouraging results have recently been reported for green tea and seabuckthorn extracts that significantly diminished tumor growth (3). Phenolic compounds obtained from different dietary sources were proved to have anticancer action due to the influence on gene expression regulation and consequently on protein biosynthesis. These compounds can modulate cellular pathways like proliferation, differentiation, apoptosis, inflammation, angiogenesis and metastasis (4). Deuterium depleted water is among the natural compounds investigated with positive results for antitumoral properties (5, 6). A novel approach to cancer cure, especially with natural compounds that have a non aggressive impact of the whole organism should be an alternative to chemotherapy. It should be of great interest to combine chemotherapy, which disintegrates not only the tumor cells but affects the whole organism, with some natural compounds, in order to diminish their side effects. The natural non-toxic

compound chosen for this study was deuterium depleted water, and because of the crucial role played by glycan structures in many biological processes, including metastasis, we investigated the serum glycoproteins of cytostatics treated rats.

Materials and Methods

Mono-chemotherapy was applied to healthy Wistar outbread rats divided in two groups for each cytostatic. One group received tap water (TW) 5 days before treatment, during the treatment and 5 days after the last administration, and the other group received 60 ppm DDW. Other two groups, considered as controls, received one only TW and the other DDW and no medication. Each group consisted of 10 rats of 172 g body weight. Cytostatics Vinblastine (0.1 mg/kg body weight), Cyclophosphamide (5 mg/kg body weight), 5-Fluorouracil (10 mg/kg body weight) and Farmarubicine (1 mg/kg body weight) were intraperitoneally injected for 5 days. Sera were collected after 5 days from the last dose. Glycosidic content was assayed after ethanol protein precipitation by colorimetric orcinol based reaction in the presence of sulphuric acid and reported to total protein determined by biuret method to calculate the glycosylation degree. Total serum glycoproteins were evaluated by Glycoprotein estimation kit provided by Pierce. Lectins were purified by affinity chromatography. Serum – lectin interaction was performed by agarose double diffusion assay.

Results and Discussion

There were recorded significant differences among the glycoprotein content of the sera of all the animals that received 60 ppm DDW and those that received TW. Both glycoprotein amount and the glycosylation degree were diminished in the sera from animals with DDW diet (fig.1 and fig. 2).

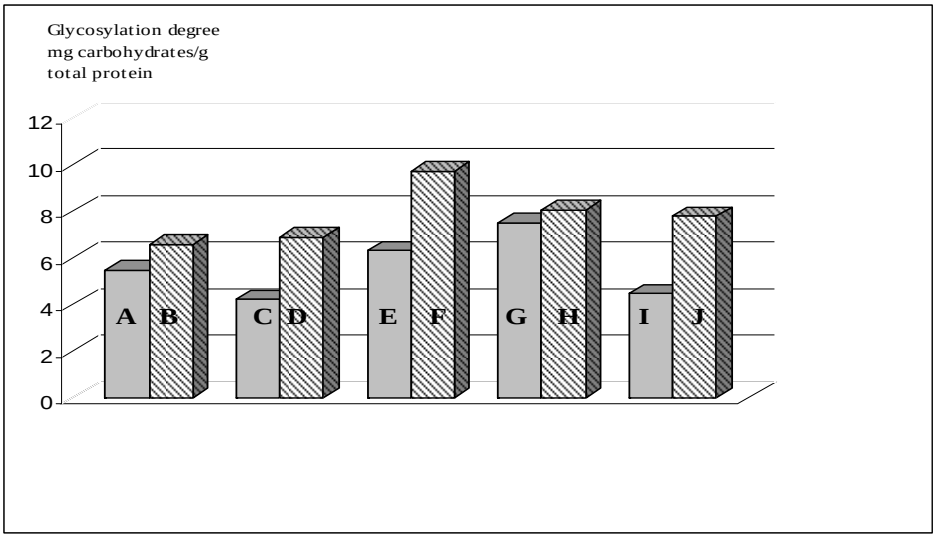

Figure 1. Glycosylation degree expressed as mg carbohydrates/g protein

A- Cyclophosphamide + DDW, B –Cyclophosphamide+ TW, C - 5-Fluorouracil + DDW , D - 5-Fluorouracil + TW, E – Farmarubicine + DDW, F – Farmarubicine + TW, G- Vinblastine + DDW, F-Vinblastine + TW, G – Untreated rats + DDW, H -Untreated rats + TW

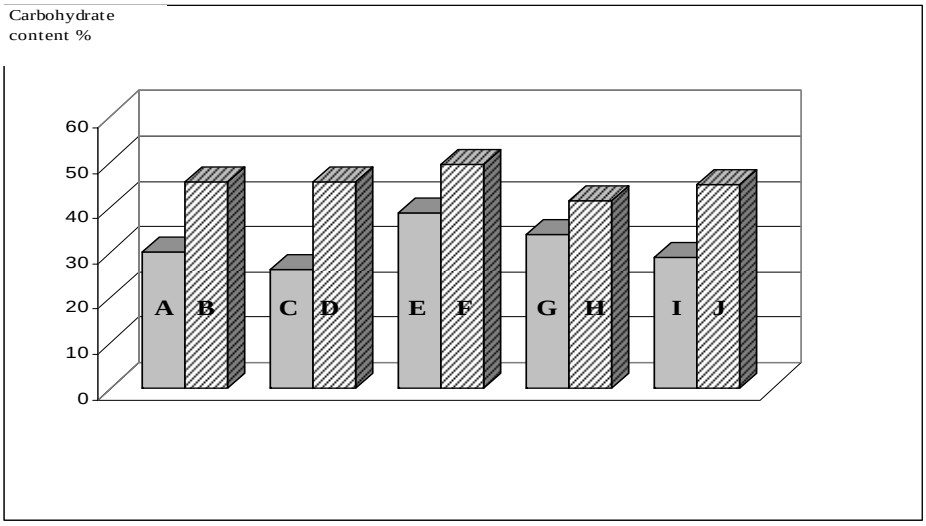

Figure 2. Glycoprotein content of serum
A- Cyclophosphamide + DDW, B –Cyclophosphamide+ TW, C - 5-Fluorouracil + DDW , D - 5-Fluorouracil + TW, E – Farmarubicine + DDW, F – Farmarubicine + TW, G- Vinblastine + DDW, F-Vinblastine + TW, G – Untreated rats + DDW, H -Untreated rats + TW

Lectin interaction was used to investigate the possible changes in the glycosidic pattern of the glycoproteins. The only interaction was shown by the *Raphanus sativus* seed fucose isolectin. It had interacted only with the sera from 5-Fluorouracil treated rats that had not received DDW.

Histological examination revealed the hepatoprotective effect of DDW administration to cytostatics treated animals sustained by the presence of hepatocytes morphologically unmodified and limited areas of degeneration as compared to the samples from animals treated with cytostatics that had TW in their daily diet that presented larger degeneration territories accompanied by hepatosteatosis which is considered an aggravating factor for these lesions.

Glycoproteins from the sera of cytostatic treated animals are represented by the ordinary glycoproteins of this tissue, but also by those resulted from the disintegrating cells resulted as a consequence of chemotherapy. The decrease of the glycoprotein level could be associated with the protective effect induced by DDW daily diet. Other published results stated that tumor cells are deuterium consuming and the deuterium content of the healthy human blood serum is higher than the mean deuterium content of the tap water (7). Administration of DDW should induce a stress to the tumor cells development, depriving them of the deuterium.

It is worth mentioning that these results also emphasize that deuterium content of the drinking water is an important modulating factor for glycoprotein biosynthesis since it determined a significant influence on these molecules concentration in all the experimental animals. Glycoprotein content decrease could be interpreted as beneficial for animal organism because of the important role of these molecules in tumor proliferation. It should also be highlighted that if the deuterium content of the water can induce such qualitative and quantitative changes at the molecular level in vivo, the use of this isotope to study different molecules conformational changes in vitro could lead to results quite different from what they perform in vivo.

The conclusion of the presented results was that 60 ppm DDW may be used as a novel approach to cancer therapy.

References

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