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Serum and tissue levels of calcium after cis-platinum administration in wistar rats

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Abstract

The Although cis-platinum is known as one of the most commonly used antineoplastic agent in the treatment of cancer, his mechanism of action is still unclear. Cis-platinum, like most other chemotherapeutic drugs interacts with DNA to inhibit vital cell processes such as replication and transcription. Literature data show that cis-platinum administration affects the biochemical homeostasis of organism. Therefore the purpose of this study was to evaluate differences in some routine laboratory values during cis-platinum administration on tumor free Wistar rats.

For this experiment, we used adults animals from Wistar rats strain divided in two experimental groups and one control group. Wistar rats from the experimental groups were injected intraperitoneally (i.p.) with cis-platinum (the drug called Sin-Platinum) in study days 5 and 10. The animals from control group were injected with physiological solution, also in study days 5 and 10. Blood and tissues samples were collected on 15th days. The animals from experimental groups had lower calcium levels compared with control group. The results showed accumulation of cis-platinum in several different samples, (in this experiment blood samples, muscles and heart tissues) and we evaluated the modifications which appeared after repeated doses simulating chemotherapeutic treatment in tumor-free rats.

Keywords: cis-platinum, chemotherapy, calcium

1. Introduction

Many nutritional problems in cancer patients are caused by several perturbation in organism following chemotherapy. During cytostatic therapy the metabolism of carbohydrate, lipid and protein is disturbed (Alpers at al., 2002). Metal elements are implicated in maintenance of acido-basic balance, osmotic and colloid-osmotic balance. Without an adequate supply of calcium, (associated with other trace elements) the toxic effects cannot be prevented (Chabner at al., 2001; Fisher at al., 2003; Martău et al., 2004).

Literature data showes that cis-platinum administration affects the biochemical homeostasis (Velciov et al., 2007). Studies regarding the consequences of cis-platinum administration in blood serum and some tissues samples in case of experimental animals, present interest for biochemistry, nutrition, pharmacology and toxicology.

This drug has a broad spectrum of activity against many different solid tumors such as lung, ovary, testis, bladder, head and neck cancers and is also an effective agent used in treatment of some hematological malignancies such as refractory lymphomas (Lippert, 1999; Baba, 2002).

Cis-platinum (CDDP, cis-DDP, cis-diamminedichloroplatinum, cis-DDP) is a planar complex containing a central platinum atom surrounded by two ammonia molecules and two chloride atoms arranged in cis position (see fig. 1). Trans-platinum is termodinamically more stabile than the cis-compound (Farell, 2004).

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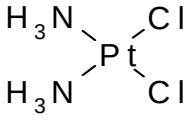

Cis-platinum mechanism of action is based on binding to DNA which determined intra-strand cross—links and formation on DNA adducts (Gârban et al., 2007, Velciov et al., 2008).

2. Materials and Method

For the experimental part, we used adults Wistar strain rats, maintained on pathogen-free conditions, at 22–25°C room temperature, at 55–65% relative air humidity, fed on normal rhythm and standard breeding food and water.

The animals were randomly divided in three groups: one control (C) and two experimental groups (E_1 and E_2). Each group contained 10 animals (males and females) with an average body weight (b.w.) of 200 ± 20 g.

Cis-platinum used for this study was the commercially available Sin-Platin (Sindan, Romania). The animals of experimental group E_1 were injected i.p. with 2.0 mg/kg b.w. Sin-Platin and with 8.0 mg/kg b.w. the animals of E_2 group. The animals from C group, were injected i.p. with saline solution.

On the 15th day of the experiment, after 12 hours of fasting (overnight), and Ketanest anesthesia, the rats were killed, and blood and tissue samples from skeletal muscles and heart were removed for analyses. The blood samples were taken after laparotomy and puncture of vena cava caudalis. Calcium concentration in blood was determined by using an analyser Hospitex Screen Master.

The contents of calcium in tissues were determined by flameless atomic absorption spectrophotometry of samples.

3. Results and Discussion

Trace elements are implicated in conversion of food into energy and also in cellular activities. Whitout an adequate supply of minerals, the incidence of toxic effects can be increased.

The studies regarding chemotherapy are developed especially by using experimental studies on laboratory animals

Analytical data that are resulting from our experiment that is using laboratory animals, and may have a predictive character. These values can be used as preliminary data in case of cancer chemotherapy, some studies regarding metabolic processes, nutrition and markers utilization.

Our results concerning the concentration of calcium in blood, skeletal muscle and heart samples after cis-platinum administration in Wistar rats are presented in Table 1.

Results are expressed as means (X) and standard deviations (SD) and to calculate the statistical significance, the *t* test was used as appropiate and *p* values.

Depressions of trace elements (in our case calcium) can be correlated with some changes of acid - base balance, osmotic and osmotic – colloidal balance (e.g. calcium can realise stabile combinations with aminoacids).

Table 1. Mean concentration of Ca in blood, muscles and heart samples of Wistar rats after cis-platinum administration.

Specifications	n	Ca in blood mg/dL	Ca in muscle (µg/g tissue)	Ca in heart (µg/g tissue)
		$\overline{X} \pm SD$	$\overline{X} \pm SD$	$\overline{X} \pm SD$
Group C	10	9.77 ± 0.70	42.19 ± 6.83	21.36 ± 3.26
Group E_1	10	9.54 ± 0.56	40.87 ± 6.71	20.28 ± 3.08
$\Delta\overline{X}$		-0.23	-1.32	-1.08
Grup E_2	10	9.15 ± 1.32	37.13 ± 6.18*	18.82 ± 2.13*
$\Delta\overline{X}$		-0.57	-5.06	-2.54

n – number of animals in case of each group;*p< 0,01;** p<0,05

From the obtained data we can observe that Ca concentration in experimental groups is lower as compared with the values obtained in the control group(see fig. 2).

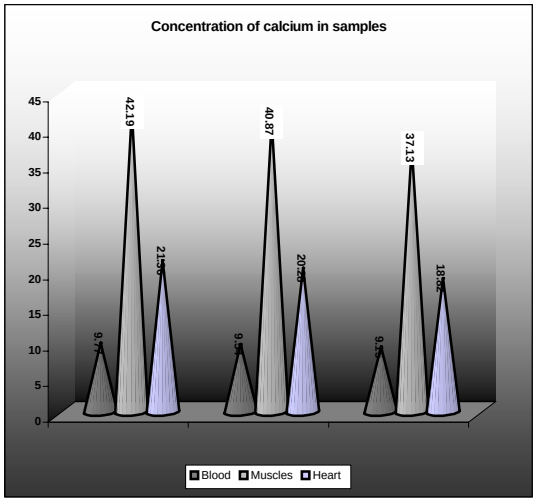

Fig. 2 Concentration of calcium in blood and tissue samples of Wistar rats

Calcium is an important component of a healthy diet and a mineral necessary for life. Approximately ninety-nine percent of the body's calcium is stored in the bones and teeth.

The rest of the calcium present in the body has other important uses, such as some exocytosis especially neurotransmitter release, and muscle contraction (Klukowska et al., 2001; Itoh et al., 2004; Chinopoulos et al., 2006).

Long-term calcium deficiency can lead to rickets and poor blood clotting and in case of a menopausal woman, it can lead to osteoporosis, in which the bone are deteriorated and there is an increased risk of fractures. While a lifelong deficit can affect bone and tooth formation, over-retention can cause hypercalcemia (elevated levels of calcium in the blood), impaired kidney function and decreased absorption of other minerals. Vitamin D is needed to absorb calcium.

Calcium plays a structural and regulatory role in living organisms. It has an essential role in metabolism of several minerals, through he's function as an activator of all enzymatic systems.

4. Conclusions

In case of blood samples, we can observe a depression of calcium levels, in experimental groups compared to control groups. Hypocalcemia can be determined by the nephrotoxic effects induced by cis-platinum, and by the modifications in case of vitamin D metabolism.

Administration of cis-platinum in Wistar rats is characterized by calcium depression in skeletal muscles indirectly proportional with administrated doses.

The concentration of calcium in heart tissue are decreased after cis-platinum administration maybe because toxic effects of the metallic compound.

Metal elements are implicated in biochemical homeostasis, which is very important for the normal development of physiological processes, such as: acido-basic balance, osmotic and colloid-osmotic balance. Without an adequate supply of metal elements the toxic effects cannot be prevented.

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