Influence of metallic compound cis-platinum on some haematological parameters in blood samples

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Abstract

Cisplatinum is known as one of the most commonly used antineoplastic agent in the treatment of cancer. Literature data show that cisplatinum administration affects the biochemical homeostasis of organism. Therefore the purpose of this study was to evaluate differences in some routine laboratory values during cisplatinum administration on tumor free Wistar rats. For this experiment, we used adults animals from Wistar rats strain divided in four experimental groups and one control group. Wistar rats from the experimental groups were injected intraperitoneally (i.p.) with cisplatinum (the drug called Sin-Platinum) in study days 3 and 8. The animals from control group were injected with physiological solution, also in study days 3 and 8. Blood samples were collected on 13th days for haematological tests. The animals from experimental groups had a lower red blood cells, white blood cells and platelets counts compared with control group. The results showed that the haematological parameters status is modified proportionally with administrated doses.

Keywords: cisplatin, chemotherapy, haematological effects

1. Introduction

The knowledge of the changes induced by chemotherapy on blood parameters are very important for the specific diet applied in case of cisplatinum treatment. Several nutritional problems in chemotherapy are caused not only by effects derived from the treatment, but also by metabolic alterations following cytostatic administration (Avacovici et al., 2003).

Cisplatinum, as a compound, was the first time described by Peyrone in 1845, and the structure was elucidated in 1895 by Alfred Werner. In 1960s, Rosenberg and his team research discovered that electrolysis products from a platinum electrode inhibited mitosis in Escherichia coli bacteria. Regarding the structure cisplatin (CDDP, cis-diamminedichloroplatinum) is a planar platinum complex consisting of two chloride leaving groups in the cis-position around platinum (Jamieson and Lippard, 1999).

In antitumoral chemotherapy a various number of drugs are used (Wright, 2001). Cisplatinum is a chemotherapeutic agent with a broad spectrum of activity, being used in the treatment of different solid tumors, such as lung, bladder, head and neck cancers, but also in haematological malignancies, e.g.: refractory lymphomas (Lippert, 1999; Hoffbrand and Pettit, 2001; Price and Sikora, 2002). Antitumor action of cisplatinum is attributed to its action on DNA macromolecule, but it is limited because of its toxicity to normal tissues (Rosenberg, 1985; Kelland, 2000). In addition to its high antitumour activity, cisplatin is a drug with potential side effects including nephro-, neuro-, myelo- and ototoxicity, as well as liver damage and severe emesis (Hartmann and Lipp, 2003). These toxicities are dose-dependent and dose- and therapy-limiting.

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2. Materials and methods

In case of experimental part, we used adults Wistar rats, maintained on pathogen-free conditions, at 22–25°C room temperature, at 55–65% relative air humidity, and fed on normal rhythm and standard breeding food and water. The animals were randomly divided in five groups: one control (C) and four experimental groups (E₁, E₂, E₃ and E₄).

Each group contained 8 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 were injected intraperitoneally (i.p.) with 2.0 mg/kg body weight (b.w.) - in case of E₁ group, 4.0 mg/kg b.w., 6.0 mg/kg b.w. - in case of E₃ group and 8.0 mg/kg b.w. - in case of E₄ group. The animals from (C) control group, were injected i.p. with physiological saline solution. Animals doses have been received the doses on days 3th and 8th of the experiment, and on day 13th they were killed.

On the last day of the experiment, after 12 hours of fasting (overnight), and Ketanest anesthesia, the rats were killed, and blood samples were taken for analysis. The samples were taken after laparotomy and puncture of vena cava caudalis. Blood from each animal was collected in a clean centrifuge tubes. The tube was not heparinized before use, and blood was allowed to coagulate and the tube was centrifuged for serum separation. The haematological parameters, including red blood cells (RBC), white blood cells (WBC) and platelets counts were assayed using a Nikon Kohden analyzer. Results are expressed as means ± SD and to calculate the statistical significance the t test was used as appropriate and p values of less than 0.05 and 0.01 were considered as significant.

3. Results and discussion

The studies regarding chemotherapy are developed especially using experimental studies on laboratory animals. The type and dose of the chemotherapy could influence the blood cells counts (Schneider, 1994; Perry, 1996; Marshall and Bangert, 2004).

Administration of cisplatin causes changes in some blood parameters in Wistar rats (Chabner et al., 2001). Our obtained data in case of control group are appropriate with the values found in literature data (Aschkenasy, 1971; Falcă, 2004). Mean concentration of RBC, WBC and platelets in blood of Wistar rats (U/µL) are presented in Table 1.

Our results concerning the counts of RBCs in blood after cisplatinum administration are presented in Figure 1. From the data we have obtained, it can be observed that after cisplatinum administration, red blood cells values are decreased in experimental groups compared with control group.

Also, it can be observed a decreased white blood cells count, in experimental groups in comparison with control group (see Fig. 2). The blood values of WBCs are significantly decreased in experimental group E₄ who received the highest dose of cisplatinum.

Because of the implication of the WBCs level in immune response, the appearance of leukopenia (as a consequence of a decrease in WBCs counts) can perturb the immune response of the organism (Chabner et al., 2001; Veal et al., 2001; Velciov et al., 2006).

In order to prevent the appearance of leukopenia in chemotherapy, it should be administrated growth factors that are implicated in the WBC synthesis and in increasing immunity.

In case of platelets, it can be observed a decreased platelets count, in experimental groups in comparison with control group (see Fig. 3).
<table>
<thead>
<tr>
<th>Specification</th>
<th>n</th>
<th>RBC $10^6/\mu$L</th>
<th>WBC $(10^3/\mu$L)</th>
<th>Trombocytes $10^3/\mu$L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$\bar{X} \pm SD$</td>
<td>$\bar{X} \pm SD$</td>
<td>$\bar{X} \pm SD$</td>
</tr>
<tr>
<td>Group C</td>
<td>8</td>
<td>8.29±0.37</td>
<td>10.70± 0.15</td>
<td>873.60±27.96</td>
</tr>
<tr>
<td>Group E₂</td>
<td>8</td>
<td>8.18±0.19</td>
<td>10.46±1.54</td>
<td>869.40±20.06</td>
</tr>
<tr>
<td>$\Delta \bar{X}$</td>
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<td>-0.24</td>
<td>4.2</td>
<td></td>
</tr>
<tr>
<td>Group E₃</td>
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<td>7.04±0.49</td>
<td>9.54±1.69</td>
<td>855.00±141.14</td>
</tr>
<tr>
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<td>-1.16</td>
<td>-18.6</td>
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<tr>
<td>Group E₄</td>
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<td>7.01±0.21</td>
<td>9.12±0.60</td>
<td>794.20±119.86</td>
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<td>-1.58</td>
<td>-79.40</td>
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<tr>
<td>Group E₅</td>
<td>8</td>
<td>6.32±0.07*</td>
<td>8.74±1.69*</td>
<td>793.70±97.00</td>
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<td>-1.96</td>
<td>-79.90</td>
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</tbody>
</table>

n – number of animals per each working group;
*p< 0.05 compared with control group; p<0.01 compared with control group

Figure 1 Evolution, compared to control, of RBC counts $10^6/\mu$L in blood of Wistar rats after cisplatinum administration; *p< 0.05

Figure 2 Evolution, compared to control, of WBC counts $10^3/\mu$L in blood of Wistar rats after cisplatinum administration
From the obtained data we can observe a decreasing in platelets count, that can be responsible for trombocytopenia. The blood platelets are cells that play a key role in blood clotting. Low platelets count can induce bleeding. Platelets are also responsible for increasing immunity, because it is suggested that they are rapidly deployed to any sites of infection or injury and potentially modulate inflammatory processes.

General informations regarding dose-effect relation and haematological effects in case of our experimental model can be useful for some predictive data important for nutritional aspects in case of cytostatic therapy.

4. Conclusions
1. Studies regarding concentration some haematological parameters values are very important for defining the influence of chemotherapy on normal health status
2. In case of RBC we can observe a decreasing level, some even significant, in experimental groups compared to control group.
3. In case of WBC we can observe the appearance of leukopenia that can be due to the the implication of the WBCs level in immune response.
4. The platelets are responsible for trombocytopenia, and also for blood clotting.
5. Cisplatinum administration exerted a significant negative effect on haematological parameters, and this effect was cumulative with repeated doses.
6. The RBCs, WBCs and platelets counts in samples are decreased after cisplatinum administration maybe because toxic effects exerted by this drug on bone marrow, which is the origin of all three kinds of cells.

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References