Ameliorating Effects of Bone Marrow Transplantation and Zinc Supplementation on Physiological and Immunological Changes in γ-Irradiated Rats.

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Introduction

Acute effects of radiation include hematopoietic cell loss, immune suppression, and potential injury to other sites such as the lung, kidney and central nervous system (Augustine et al. 2005). Irradiation ruptures adult tissue homeostasis, inducing radiation syndromes, described in hematopoietic tissue (for doses higher than 2 Gy, total body irradiation). It appears that a major mechanism of these syndromes is a rapid and massive cell death in stem and/or progenitor cell populations, which can follow either apoptotic or necrotic pathways (Harfouche and Martin, 2010). Ionizing radiation works by damaging the DNA of exposed tissue leading to cellular death (Pourhomayoun et al., 2014).

It has been anticipated that a successful role played by bone marrow transplants against deleterious effect of radiation exposure would certainly be used for tissue repairs (Youn et al., 2010). After several weeks of growth in bone marrow, expansion of hematopoietic stem

The present study was carried out to determine the prophylactic impact of zinc sulphate administration to irradiated rats treated with bone marrow transplantation (BMT) as indicated by the hematological and immunologic response as well as oxidative stress. Rats were injected orally with zinc sulphate, 10 mg/Kg body wt, daily for 2 weeks before whole body 5Gy gamma irradiation and intravenous injection (i.v.) of bone marrow cells, one hour post irradiation. The results revealed a significant decrease in red blood cells (RBC), white blood cells (WBC), glutathione (GSH) and zinc superoxide dismutase (Zn/SOD), splenocyte count as well as bone marrow lymphocyte count and viability of irradiated rats. Regarding immunological data: tumor necrosis factor alpha (TNF-α) and interleukin 2 (IL-2) recorded a significant decrease while interleukin 6 (IL-6) and lipid peroxidation product (MDA) in the serum and spleen were conversely elevated. Zn supplementation before irradiation and BMT and showed significant decrease of serum and tissue MDA compared to the irradiated group. Lymphocytes, bone marrow viability percentage, splenocytes percentage, IL-2, IL-6 and GSH were significantly elevated compared to irradiated group. Conclusion: Protection with Zn, enforcing significant innate response, could trigger and augment adaptive immune response by BMT which suggests its use to protect against radiation hazards.

Keywords: BMT; gamma irradiation; zinc sulphate; immunologic response. Running title: Bone marrow transplantation, radiation protection

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cells and their progeny is sufficient to reinitiate the immune system (Gérard, 2001).

Zinc (Zn) is an essential trace element that plays structural, regulatory and catalytic roles in the body and it is necessary for a number of immune functions, including T lymphocyte activity. A deficiency of zinc affects a number of aspects of innate and adaptive immunity (Haase and Rink, 2009). Zinc is essentially required in humans and animals for many physiological functions, including immune and antioxidant function, growth and reproduction (Sun et al., 2005). It protects various membrane systems from peroxidative damages induced by heavy metals and high oxygen tension and stabilize the membrane perturbations. It has protective effects against radiation hazards (Azab et al., 2004).

This work aims to investigate the effect of boosting of immune response, by zinc administration before irradiation followed by bone marrow transplantation (BMT) on immunological recovery and oxidative stress induced by gamma irradiation.

**Materials and Methods**

Mature male albino rats of pure strain Rattus rattus (110-130 g) obtained from the animal house of the National Center for Radiation Research and Technology (NCRRT), Atomic Energy Authority, Egypt were used in the present study. Rats were kept under normal conditions, temperature 18-22°C, allowed free access to rat pellet and drinking water. Animals were acclimatized to laboratory conditions before the onset of the experiment. All animal treatments were conducted according to the Ethics Committee of the National Research Centre in accordance with international ethical considerations and conformed to the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health (HN publication No. 85-23, 1996).

**Irradiation Facility**

Whole body irradiation was performed using Gamma Cell – 40 (137 Cesium) biological irradiator manufactured by Canada Ltd, Ottawa, Ontario, Canada, located at NCRRT. Animals were irradiated at an acute single dose of 5 Gy at a dose rate of 0.49 Gy/min.

**Bone Marrow Transplantation**

Donors and recipients were chosen of the same inbred strain, brother to brother (syngenic). Femur bones were dissected out and cleaned. The ends of the bones were chipped by a bone nibbling forceps and the marrow was blown out of the femur into isotonic solution under sterilized conditions inside a laminar flow cabinet. The marrow was collected into a sterile container surrounded by ice cubes, and mixed by drawing and expelling it several times from a syringe without needle in order to avoid mechanical damage to the cells. Femur marrow cells (1x 10^7) (Chen et al. 2007) were injected intravenously (i.v.) to each rat, 1 hour after irradiation (Sredni et al., 1992).

Zinc Supplementation: Zinc sulfate (from Sigma Alderich Chemical Co. St Louis, Mo, USA) was dissolved in sterile water to achieve a zinc stock solution of 80 mM, which was then sterile filtered. Rats were injected with 10 mg/Kg body weight (oral injection) as a single daily dose for 14 successive days before irradiation (Roosen et al., 1994).

Animals were randomly assigned into 6 groups: 1. Control rats received distilled water throughout the experiment (C). 2. Rats injected with BMT cells through the caudal vein (CBM). 3. Rats received orally 10 mg/Kg body weight of zinc sulphate as a single daily dose for 14 successive days (CZn). 4. Rats exposed to 5Gy whole body gamma rays (R). 5. Rats exposed to 5 Gy gamma rays and treated with BMT one hour after irradiation (R + BM). 6. Rats received 10 mg/Kg body weight of zinc sulphate for 14 successive days before 5 Gy irradiation (R+Zn). 7. Rats received orally 10 mg/Kg body weight of zinc sulphate as a single daily dose for 14 successive days before irradiation and treated with BMT one hour after irradiation (R+BM+Zn). All animal groups were sacrificed after 14 days from treatment, irradiation or pre-irradiation treatment and BMT.

Groups of ten rats were anaesthetized with ether obtained from SDFCL SD Fine Chemical Limited, Industrial State- 248, Mumbai, India. Blood was collected by heart puncture. Part of the blood was placed on ethylene diamine tetra acet acid (EDTA) from Sigma Alderich Chemical Co. St Louis, MO, USA, for haematological analysis. Red blood cells (RBC), white blood cells (WBC) count were performed in a hemocytometer using.
standard procedures and lymphocytes were determined according to Dacie and Lewis (1993). All chemicals and reagents were pure chemical materials from Sigma-Aldrich. Blood reduced GSH and Zn/ SOD contents were measured according to Dacie and Lewis (1993) and Yoshioka et al. (1979) respectively. Serum was separated by blood centrifugation and stored frozen until assayed. Estimation of serum MDA was performed according to (Yoshioka et al., 1979). Eliza kit from Aviscera Bioscience Inc.234 Walsh Ave, CA 95051 USA was used to determine IL-2 according to Chan and Perlstein, (1987). IL-6 was determined using the kit from Kamya Biomedical Company, Gateway, Seatle, USA according to Kaminska et al. (2000) and TNF-α concentrations were determined by ELISA kit from Viva systems Biology, San Diego,California USA according to and Aramachi, (1989). The spleen was dissected out, washed in saline and dried on filter paper. A known weight of spleen was homogenized in 0.15KCl to obtain 10% tissue homogenate using Teflon homogenizer (Glas-Col,Terre Haute,Ind., USA) . The homogenates were centrifuged at 10,000g for 15 min using refrigerated centrifuge (K3 Centurion Scientific Ltd, London, UK). Aliquots of supernatents were separated to estimate MDA (Yoshioka et al., 1979).

**Determination of viable BM cell percentage:** A uniform cell suspension of BM was prepared by dilution in saline solution (9%). A haemocytometer was used for counting BM cells using 100 x eye piece of objective lens. BM cell viability was determined using trypan blue, where only dead cells absorbed the dye, Esser et al. (2001). %viability = viable cells / total no per femur X100.

**BM lymphocytes percentage:** BM smears were prepared on microscope slides, stained with Gimsa stain. A total of 500 cells were counted from each slide and the percentage of lymphocytes was determined in relation to the total count according to the method of Sinai et al. (1978).

**Determination of splenocytes percentage:** A uniform cell suspension of spleen was prepared in saline solution. A haemocytometer was used for counting spleen cells using 100x eye piece objective microscope lens. Cell viability was determined using trypan blue to distinguish viable and non viable cells, according to and Takabatake et al. (1997).

The results were analyzed using one way analysis of variance (ANOVA) followed by Duncan's test according to Steel and Torrie (1980).

### Results

**TABLE 1. Effect of BMT and Zn supplementation on some blood parameters in irradiated and non-irradiated rats.**

<table>
<thead>
<tr>
<th>Groups</th>
<th>RBCs (10^6/mm³)</th>
<th>WBCs (10⁹/mm³)</th>
<th>Lymphocytes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>44.8±0.37</td>
<td>6.04±0.57</td>
<td>44.8±0.37</td>
</tr>
<tr>
<td>CBM</td>
<td>6.92±0.31</td>
<td>5.14±0.42</td>
<td>37.4±0.73</td>
</tr>
<tr>
<td>CZn</td>
<td>6.74±0.43</td>
<td>6.14±0.44</td>
<td>38.6±0.6</td>
</tr>
<tr>
<td>R</td>
<td>5.0±0.3</td>
<td>2.3±0.46</td>
<td>22.2±0.86</td>
</tr>
<tr>
<td>R + BM</td>
<td>6.18±0.27</td>
<td>3.52±0.45</td>
<td>31.4±0.25</td>
</tr>
<tr>
<td>R + Zn</td>
<td>6.3±0.46</td>
<td>5.1±0.31</td>
<td>37.2±0.35</td>
</tr>
<tr>
<td>R + BM + Zn</td>
<td>6.54±0.44</td>
<td>4.66±0.73</td>
<td>39.4±0.5</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SE. c: Significant difference compared to control. r: Significant difference compared to R group.

**TABLE 2. Effect of BMT and Zn supplementation on BM percentage and viability also splenocyte percentage in irradiated and non-irradiated rats.**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Bone marrow lymphocyte count (%)</th>
<th>Viable bone marrow count (%)</th>
<th>Splenocyte (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>20.4±0.5</td>
<td>66.4±0.5</td>
<td>77±0.7</td>
</tr>
<tr>
<td>CBM</td>
<td>21±0.7</td>
<td>65±0.7</td>
<td>74.6±1.2</td>
</tr>
<tr>
<td>CZn</td>
<td>20±0.54</td>
<td>64.4±0.81</td>
<td>77.2±1.86</td>
</tr>
<tr>
<td>R</td>
<td>13.4±0.5</td>
<td>41.2±0.38</td>
<td>44.4±1.91</td>
</tr>
<tr>
<td>R + BM</td>
<td>16.1±0.60</td>
<td>50.4±0.51</td>
<td>52.4±0.81</td>
</tr>
<tr>
<td>R + Zn</td>
<td>13.3±0.80</td>
<td>52.6±0.94</td>
<td>52.8±0.86</td>
</tr>
<tr>
<td>R + BM + Zn</td>
<td>18±0.31</td>
<td>67.8±0.37</td>
<td>57±0.54</td>
</tr>
</tbody>
</table>

Exposure of animals to 5Gy gamma radiation induced a significant (P<0.05) drop of RBC, WBC and lymphocytes (Table 1) as well as BM percentage, BM viability also splenocyte percentage (Table 2). BMT together with irradiation showed a significant elevation of RBC, lymphocytes, as well as BM and splenocytes percentage compared to irradiated group. The same trend was observed by Zn supplementation.

before irradiation compared to irradiated group. Protection with Zn to irradiated animals receiving BMT elevated RBCs, lymphocytes, BM percentage and viability and also splenocyte percentage (P<0.05) compared to irradiation group. CBM alone induced significant elevations of IL-1 and IL-6, while TNF-α was decreased. Gamma irradiation (5Gy) induced a significant decrease of serum IL-2 and TNF-α values (P<0.05) while IL-6 level showed a significant increase. Each of treatments ameliorated irradiation effect, whereas their combination induced a significant increase in IL-2 and TNF-α whereas IL-6 level recorded a significant decrease compared to the irradiated group (Table 3).

Results presented in Table 4 demonstrated a significant decrease of blood GSH and Zn/SOD (P<0.05) and a significant increase (P<0.05) of serum and spleen MDA two weeks post exposure to 5Gy gamma radiation. Protection with zinc before irradiation and BMT of rats resulted in a significant elevation of GSH and Zn/SOD (P<0.05) whereas a significant decrease in serum and spleen MDA (P<0.05) compared to irradiated group.

### Discussion

Most of cellular alteration induced by ionizing radiation is indirect and is mediated by the generation of free radicals and related reactive species, mainly derived from oxygen. Overproduction of reactive oxygen species (ROS) in cells and tissues increases oxidative stress (Nunia et al., 2007). Gamma irradiation is an immunosuppressive agent (Kajioka et al., 2000). Adaptive immune system is affected by deficient lymphopoiesis and apoptosis of lymphocytes (Wikins et al., 2002).

In the present results whole body gamma irradiation (5Gy) causes considerable decrease in the hematological values like RBC WBC and lymphocytes percentage as well as bone marrow lymphocyte, splenocytes and viable BM cells. This decrease is probably an indication of impairment of cell division and obliteration of blood-forming organs (Nunia et al., 2007) besides defective haemopoiesis (Gridley et al., 2001) in addition to their high radiosensitivity (Smart and Kumar, 2003). This is followed by thrombocytopenia and concomitant hemorrhages beside the effects in adaptive immune system resulting from apoptosis of lymphocytes and deficient lymphopoiesis (Wikins et al., 2002). Nevertheless, the decrease of RBC count might be attributed to alimentary tract injury, hemorrhage or leakage through capillary walls and/or the direct destruction of mature circulating cells (Ashry et al., 2013).

The detected decrease of splenocyte and viable BM cells which might be attributed to that irradiation kills or damages the major classes of parenchymal cells of the lymphohematopoietic system.

### Tables

#### Table 3. Effect of BMT and Zn supplementation on IL-2, IL-6 and TNF-α in irradiated and non-irradiated rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>IL-2 (pg/ml)</th>
<th>IL-6 (pg/ml)</th>
<th>TNF-α (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>165.8±1.24</td>
<td>164.4±1.8</td>
<td>353.2±2.15</td>
</tr>
<tr>
<td>CBM</td>
<td>178±1.41</td>
<td>172.8±2.81</td>
<td>344±1.76</td>
</tr>
<tr>
<td>CZn</td>
<td>162.4±1.02</td>
<td>167.2±2.59</td>
<td>348.2±1.06</td>
</tr>
<tr>
<td>R</td>
<td>118.6±1.36</td>
<td>301.8±2.51</td>
<td>185±1.7</td>
</tr>
<tr>
<td>R + BM</td>
<td>108.2±1.39</td>
<td>256±2.38</td>
<td>254±1</td>
</tr>
<tr>
<td>R + Zn</td>
<td>134±1.41</td>
<td>256±2.03</td>
<td>219.6±1.32</td>
</tr>
<tr>
<td>R + BM + Zn</td>
<td>137.6±1.36</td>
<td>238±1.51</td>
<td>235.2±1.77</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SE.

c: Significant difference compared to control.
r: Significant difference compared to R group.

#### Table 4. Effect of BMT and Zn supplementation on blood GSH and Zn/SOD, serum MDA and spleen MDA in irradiated and non-irradiated rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>GSH (mg/ml)</th>
<th>MDA (µ mol/ml)</th>
<th>MDA (nmol/g tissue)</th>
<th>Zn/SOD (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>31.2±0.58</td>
<td>37±0.7</td>
<td>40.8±0.73</td>
<td>4.62±0.39</td>
</tr>
<tr>
<td>CBM</td>
<td>29.8±0.58</td>
<td>40±1</td>
<td>50±1</td>
<td>4.24±0.2</td>
</tr>
<tr>
<td>CZn</td>
<td>30.8±0.37</td>
<td>36.6±1.12</td>
<td>46.6±1.12</td>
<td>4.26±0.34</td>
</tr>
<tr>
<td>R</td>
<td>10.8±0.58</td>
<td>62.2±0.86</td>
<td>70±1</td>
<td>2.56±0.18</td>
</tr>
<tr>
<td>R + BM</td>
<td>16.2±0.86</td>
<td>46.2±1.15</td>
<td>53.2±1.46</td>
<td>3.26±0.23</td>
</tr>
<tr>
<td>R + Zn</td>
<td>18.4±0.51</td>
<td>47.4±0.2</td>
<td>57.6±0.02</td>
<td>3.3±0.4</td>
</tr>
<tr>
<td>R + BM + Zn</td>
<td>23.2±0.66</td>
<td>43.8±1.59</td>
<td>53.8±1.59</td>
<td>3.6±0.41</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SE.

c: Significant difference compared to control. r: Significant difference compared to R group.
Cytokines have been used to refer to the immunomodulating agents and play a key role in modulation of immune responses. Cytokine networks regulate lymphocyte turnover, differentiation, and activation. IL-2 is a cytokine released by T helper lymphocytes, while (TNF-α) is a proinflammatory cytokine that is synthesized by monocytes/macrophages, natural killer cells, large granular lymphocytes, and T lymphocytes subsets (Simon, 2011). Because of irradiation influence on all these types of cells, the present study demonstrated decreased IL-2 level in irradiated animals which might be due to that spleen cells of total lymphoid irradiated (TLI) mice secrete 5-9% of the mean normal level of IL-2 (Field et al. 1997). Gamma irradiation is known to significantly inhibit the proliferation of effective T cells by reducing the levels of Th1 type cytokines (such as IL-2) (Han et al., 2005). Irradiation induced a significant decrease in TNF-α which could be explained through supregulation of mitogen-activated protein kinase phosphatase-1 (MKP-1) in mouse macrophage (Tsukimoto et al., 2009) and its attributed to irradiation effect leading to differential regulation of T-helper cell gene expression (Seon-Kyu et al., 2002). IL-6 levels showed a significant increase post irradiation which was attributed by Chang et al. (1997) to that ionizing radiation induced DNA damage has been shown to initiate the expression of various circulatory cytokines such as IL-6 and some of these responses may be related to apoptosis. IL-6 itself is a pluripotent cytokine which is involved in acute pro-inflammatory process associated with overexposure to ionizing radiation (Petit-Frère et al., 2000).

The present results demonstrated a significant reduction in blood GSH, SOD activity and parallel elevation in serum and spleen MDA post irradiation which could be attributed to enhanced utilization of the antioxidant system in an attempt to detoxify radiation generated free radicals (Krishna and Kumar, 2005). The decrease in the activity of antioxidant enzymes might result from radiation-induced cell membrane damage and alterations in dynamic permeability of membranes due to peroxidation. Damage of plasma membranes, which contain high percentage of polyunsaturated fatty acids, is followed by the release of intracellular enzymes to the blood stream (Saada et al., 2003).

The present results discerned that BMT alone lead to a significant elevation in RBCs, WBCs as compared to the control group after 14 days which comes in accordance with Nunia et al. (2007). BMT post irradiation showed significant elevation of RBC, lymphocytes and BM viable cells which might be attributed to the accelerated restoration of remaining functional hematopoietic cells that is believed to be the major factor in the survival of irradiated mice (Berdan et al., 2011 and Meng et al., 2013). Survival after irradiation actually results from the recovery of several target systems, such as the bone marrow, gastrointestinal tract, skin and hemostatic systems (Widel et al., 2003). Splenocyte elevation after irradiation is attributed to that recovery was dependent on extramedullary cell division in the thymus and spleen (Abu-Sinna et al., 2005).

In the present study, BMT to irradiated animals induced a slight reduction in IL-2 concentration compared to irradiated animals. Wang (2002) explained that IL-2 concentrations in recipient mouse serum were relatively low, because of cytokine autocrine and paracrine physiological characteristics, their expression in a microenvironment may be sufficient to reconstitute the immunological and hematopoietic depression after BMT. Also, BMT could cause the lack of IL-2-producing cells and/or the increased activity of suppressor cells of the helper function. The depression in IL-2 level in the present results support the successful engraftment of bone marrow cells (Nakamura et al., 2004). The decrease of IL-6 after BMT to irradiated rats compared to the increased level in irradiated group could be due to that IL-6 might mitigate acute GVHD without losing the significant antitumor benefits of allogeneic BMT (Tawara et al., 2010) thus might support the successful engraftment of bone marrow cells. Amelioration of serum TNF-α levels of irradiated rats after BMT may be related to absence of the immunological reaction against non-HLA allogeneic antigens as a result of the immunosuppressive effect of irradiation. Furthermore, neutralization of TNF-α have been reported by Brown and Thiele (2000) to reduce complications after BMT. It is well documented that total body irradiation followed by BMT, has been shown to raise the erythropoietic activity
in both bone marrow and spleen (De Rooij et al. 2002). The elevation in red blood cells, the important source of GSH, can ameliorate the GSH depletion in blood and organs and hence decrease oxidative stress (Ashry et al., 2009).

In the present study zinc sulphate (10mg / Kg body weight) supplementation before irradiation significantly improved bone marrow lymphocytes and viability which was attributed by ( Rink and Gabriel, 2000) to that the zinc deficient organism shows impaired functions in all kinds of immune cells in vivo. Zinc supplementation causes a significant elevation in splenocyte cells after gamma irradiation, is probably the consequence of enforcing the immune response via reduced apoptosis of splenocytes. These changes were probably caused by increased synthesis of HSP-70 by splenocytes, which might enhance survival of mice with LPS-induced endotoxemia (Unoshima et al., 2001).

Baltaci et al. (2003) recorded that zinc supplementation has a positive influence on hematological parameters which comes in accordance with the detected elevation of RBC, WBC and lymphocytes. Zinc substrates are recommended as radioprotectors as well as for treatment of radiation hazards (Hanan et al., 2007).

In the current study, there was a significant elevation of IL-2 and TNF-α in irradiated rats treated with zinc sulphat. This is explained by that zinc plays a role in cytokine production. Prasad (2008) and Rahfiludin et al. (2013) indicated that TNF-α and IL-2 production is improved when zinc level is maintained by giving zinc supplement. In a study by Yalçın et al. (2011), zinc supplementation had a beneficial effect on immune response and increased serum TNF-α level after irradiation. In this study zinc supplementation before irradiation showed a reduction in serum levels of IL-6. Wellinghamhausen et al. (1997) observed that zinc affects a functional activation or inhibition of isolated immune cells and also appears to influence cell growth and cytokine production and is used for treatment of radiotherapy caused dermatitis (Alterio et al., 2007).

Zinc supplementation has documented a significant increase in GSH level in irradiated rats, which might be due to that zinc protects sulphhydryl groups from oxidation induced by gamma irradiation( Bray and Bettger 1990). The data showed that there was a decrease of serum and spleen tissue MDA level in Zn supplemented groups treated with gamma irradiation. The generation of oxidative burst were impaired by decreased zinc levels (Keen and Gershwin, 1990). Zinc supplementation to irradiated treated rats, significantly attenuated the adverse effects caused by gamma irradiation on the levels of MDA, GSH and SOD. There are significant oxidant/antioxidant changes in RBC following irradiation in rats, while zinc was shown to act as a radioprotective agent (Dani and Dhawan, 2006). The previous study showed that zinc supplementation increased the activity of Zn SOD in blood. Zinc sulphate could modulate apoptosis of thymocytes induced by glucocorticoid; the mechanism might involve the exchange of intracellular calcium, the redox of cells, and the forms of zinc might go different ways in the regulations (Ze-peng et al., 2005). Dietary zinc exerts its beneficial effects on growth performance in irradiated rats through increasing serum Zn-SOD levels (Wang et al., 2012). Zinc sulphate was found to protect BMT that was reflected upon accelerated haematopoietic reconstitution, decreased oxidative stress and enhanced immune response.

Conclusion

The present findings support the protective role of zinc sulphate administration against the severity of radiation induced disturbance via enforcing allogenic bone marrow transplantation and the immune response.

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AMELIORATING EFFECTS OF BONE MARROW TRANSPLANTATION


AMELIORATING EFFECTS OF BONE MARROW TRANSPLANTATION


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دراسة التأثيرات التشخيصية الناتجة عن زراعة نخاع العظم والتغذية النيتروجينية معالجتان الزنك على التغيرات الفسيولوجية والمناعية في الجرذان المشعومين بالإشعاع

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يهدف البحث إلى دراسة تأثير المحفزات البيولوجية على رفع الإستجابة المناعية الفسيولوجية للجرذان المصعومين بالإشعاع عن طريق التنازير بين زرع نخاع العظم وإعطاء معدن الزنك وكذلك تحسين مستوى الطاقة للتنكيس والحماية من الإجهاد التأكسدي. تم إعطاء معدن الزنك قبل تعرض الإشعاع مرة واحدة يومياً بجرعة 10 مجم/كم/يوم لمدة أربعة أسابيع ثم تم زرع نخاع العظم في ذكور الجرذان بالحقن في الوريد الذيلي بعد ساعة واحدة من التشعيع بجرعة خمس جراي. أظهرت النتائج أن العلاج بالزنك أدى إلى تحسين مستوى الطاقة الحيوية في كل مؤشري الدم وحالات الجرذان وتقليل استجابة الجهاز المناعي. وفقاً لأبيد السيمينوسون في نك والثاني نرم الفين نوك انتيرليوكن2 وعامل النخر السرطاني وانخفاض أيضاً نسبة الخلايا الليفية في نخاع العظام وكذلك نسبة الخلايا الحية في هذه الخلايا الهدف في الدم وكذلك الانتيرليوكن2. أدى العلاج بزراعة النخاع إلى تحسين مستوى الطاقة من دون الزنكي في حوار الجرذان بالحقن في الوريد الذيلي بعد ساعة واحدة من المرض خمس جراي. أظهرت النتائج أن العلاج بالمعدن الزنك أدى الى تحسن مستوى الطاقة الحيوية في كل مؤشري الدم وحالات الجرذان ومتنازيل النخاع والخلايا الليفية في الدم وتقليل النخر السرطاني وانخفاض نسبة الانتيرليوكن2 وعامل النخر السرطاني وانخفاض نسبة المضادات الناجمة للأدوات الانتيرليوكن2. وتظهر الدراسة الدور الوقائي لعدن الزنكي في تحسين نخاع العظام المزروع الذي قد يرجع إلى تغذية المناعة المضادة بفعل الإشعاع مما يؤدي إلى تحسين الدفاعات الطبيعية ضد أعباء الأكسدة في الجرذان المشعومين بالإشعاع.