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Short communication

The effect of Coenzyme Q10 in Cisplatin induced myelosuppression in rats

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Introduction

Coenzyme Q10 (2,3 dimethoxy-5 methyl-6-decaprenyl benzoquinone - CoQ10) is a lipid-soluble antioxidant, vitamin-like quinone commonly known as ubiquinone or vitamin CoQ10 present in all tissues and membranes in the body. CoQ10 plays an important role in the mitochondrial respiratory chain, for synthesis of adenosine triphosphate (ATP). Further, it protects the phospholipids and the proteins in the mitochondrial membrane, from lipid peroxidation (Saini, 2011). On the contrary, Cisplatin, is an antineoplastic drug that is used for treating wide spectrum of human malignancies. However, its therapeutic outcome is limited due to development of nephrotoxicity and myelosuppression. Few mechanisms are involved such as generation of free radicals, inhibition of protein synthesis and lipid peroxidation of the membranes. One of the most important targets of Cisplatin are the mitochondrias, where it reduces the amount of ATP, and consequently increases the ROS species (Choy et al., 2015).

The development of new pharmacological/therapeutical approaches and using supplements that aim the same targets as the chemotherapy but in the opposite direction, becomes a game-changer recently. Several clinical studies provided evidence supporting the use of supplements in preventing of Cisplatin induced damage of the bone marrow cells (Lin et al., 2020; Sinha et al., 2015). Therefore, the aim of this study was to evaluate the influence of the supplementation with CoQ10 on the myelosuppression induced by the treatment with Cisplatin on rats.

Materials and methods

Materials

A "ready to use" Cisplatin solution (1 mg/mL) was purchased from Accord, Latvia and used as received. CoQ10 standard was supplied from Sigma-Aldrich, Germany. All other chemicals were of pharmaceutical/chemical grade and were used without further modifications.

Sample preparation of CoQ10 for i.p. *administration*

The weight of each rat was reevaluated before preparing the CoQ10 solution, and the dose was adjusted accordingly. CoQ10 powder was solubilized in saline solution (0.9% NaCl) containing 1% Tween 80 to prepare CoQ10 solution (5 mg/ml). Final solution was obtained after continuous mixing and heating (200 rpm, 65 °C, 15 min). Afterwards, ascorbic acid (0.1%) was added to maintain the antioxidant capacity of the prepared solution.

Obtained results were statistically analyzed using T test with significant level($p<0.05$), in XLSTAT (Statistical Software for Excel).

Methods

This experiment involved sixty male, normotensive Wistar rats (250-300 g), obtained from the animal house

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of Faculty of Natural Science and Mathematics, UKIM Skopje and kept in wire polypropylene cages under typical laboratory environment (temperature 25±2 °C and artificial 12 h light/12 h dark cycle). The rats were fed with animal standard pellet diet and water *ad libitum* and allowed to acclimatize 1 week prior to the study. The animals were divided in 4 groups, each one of 15 rats. Rats in group 1 (Cisplatin treatment) received Cisplatin 5 mg/kg *i.p* on the 4-th day of the experiment as a single dose. Rats in group 2 (Cisplatin/CoQ10 treatment) received Cisplatin 5 mg/kg *i.p,* on the 4-th day, and CoQ10 10 mg/kg *i.p,* for 11 days, each day of the experiment. Group 3 (CoQ10 treatment) included rats that received only CoQ10 10 mg/kg *i.p*, for 11 days, each day of the experiment. The rats in group 4 served as a control and received physiological solution containing Tween 80 and ascorbic acid, *i.p*. (Fouad et al., 2010). During the investigation, blood samples for hematological analyses (HGB, WBC, LYM, MON HCT, RBC, RDWa, MCH, MCHC, MCV) were taken from the tail of the rats, on day 2, day 6 and day 12 of the experiment.

Results and discussion

The CoQ10 group showed significantly increased levels for HGB, WBC, LYM, as well as decreased level for MON compared to the other three groups such as the Cisplatin group, the Cisplatin/CoQ10 group, and the control group. The control group also showed significantly increased HGB levels than the Cisplatin group, as well as with the Cisplatin/CoQ10 group. However, there was a negligible difference in HGB levels between the Cisplatin group and the Cisplatin/CoQ10 group. Significantly increased levels for RBC and MCV in the Cisplatin/CoQ10 group compared to the Cisplatin group were observed ($p < .05$). Increased RBC in the CoQ10 group compared to the Cisplatin group was noticed. HCT values were significantly increased in the CoQ10 group compared to the rest of the groups. However, there was an insignificant increase in HCT levels in the Cisplatin/CoQ10 group compared to the Cisplatin group. WBC levels for Cisplatin/CoQ10 were significantly elevated compared to the Cisplatin group. At the same time, there was a significant decrease in the levels for MON and LYM in the Cisplatin/CoQ10 group compared to the Cisplatin group. Significantly increased MCV levels in the Cisplatin/CoQ10 group compared to the Cisplatin group were found. The obtained results correlate with the results of other studies where CoQ10 supplement was used to improve the impaired hematological parameters (Kennedy et al., 2020). These results are pointing out the inevitable Cisplatin induced anemia and toxicity/myelosuppression and are in positive correlation with the results obtained in other studies examined the toxicity/myelosuppression of Cisplatin (Song et al., 2017).

Conclusion

Carried out experiments revealed that many supplements can protect Cisplatin-induced myelosuppression in rats. However, our data give an insight about the possibility of using a supplement e.g CoQ10, together with the standard medicine Cisplatin, in order to mitigate the toxic Cisplatin-induced consequences in the bone-marrow.

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