Effect of Cyclophosphamide on the Testis of Adult Male Albino Rat and the Possible Protective Role of Vitamin E: Light and Electron Microscopic Study

Thesis

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SUMMARY&CONCLUSION

Cyclophosphamide is a chemotherapeutic agent used in treatment of malignancy. Although its great success in treatment of tumors, it initiates a harmful effect on testicular function, thus reducing spermatogenesis and fertility.

The aim of the present work is to study the effect of different doses and different periods of administration of Cyclophosphamide on the testis and spermatogenesis in the adult male albino rat and to evaluate the possible protective role of vitamin E.

Ninety five adult male albino rats were used in the present study. The rats were divided into nine groups. Group I (control group) consisted of 15 rats. The other groups each consisted of 10 rats. Group II : received Cyclophosphamide I.P (70 mg/kg) and sacrificed after16 hours, Group III : received vitamin E (100 mg/kg) orally with Cyclophosphamide (70 mg/kg) I.P and sacrificed after16 hours , Group IV: received Cyclophosphamide (6 mg/kg) I.P once daily for 15 days, Group V: received vitamin E (100 mg/kg) orally with Cyclophosphamide (6 mg/kg) I.P once daily for 15 days), Group VI: received Cyclophosphamide (6 mg/kg) once daily for 30 days, Group VII: received vitamin E (100 mg/kg) with Cyclophosphamide (6 mg/kg) I.P once daily for 30 days, Group VIII: received Cyclophosphamide (6 mg/kg) I.P once daily for 50 days, Group IX: received vitamin E (100 mg/kg) orally with Cyclophosphamide (6 mg/kg) I.P once daily for 50 days.

The animals of each group were sacrificed at the end of the experiment by an overdose of ether and the testes were removed and prepared for histological and histomorphometric study.

The histological study revealed that cyclophosphamide creates obvious degenerative changes in the seminiferous tubules. These degenerative changes were directly proportional to the dose and duration of the drug administration.

The pathological changes were ranging from mild to sever degeneration of the tubules in the form of alteration in the general architecture of the seminiferous tubules, reduction in the height of spermatogenic cell mass, separation of the spermatogenic epithelium from the basement membrane and vacuolation of the cytoplasm of cells. Sever degenerative changes were noticed in the form of complete degeneration of the spermatogenic epithelium and it was replaced by exfoliated residual bodies in the lumen of the tubules and presence of multinucleated giant cells and formation of interstitial acidophilic exudate in between the tubules .

The electron microscopic study in the present work revealed marked pathological changes of the spermatogenic epithelium in rats received Cyclophosphamide in the form of degenerated and rarified cytoplasm, chromatin clumps attached to the periphery of the nucleus, ill defined nuclearenvelop. Some tubules showed marked separation of the spermatogenic epithelium from the basement membrane, small condensed nuclei, multiple cytoplasmic remnants and presence of multinucleated giant cells.

The histomorphometric study in the present work revealed significant reduction in the diameter of the seminiferous tubules, increased collagen fibers in the interstitial spaces and decreased optical density in rats received Cyclophosphamide.

Followig administration of vitamin E to the experimental groups there was obvious improvement in the histological picture of the testis in the form of restoration of the normal architecture of the seminiferous tubules, nearly normal spermatogenic cell mass, normal intertubular spaces, minimal acidophilic exudate and disappearance of the cytoplasmic vacuoles. Ultrastructural study showed restoration of the nuclear membrane of the cells, homogenous chromatin material and decreased vacuolation of the cell cytoplasm. The improvement was marked in groups III, V, VII which received Cyclophosphamide for short durations. But there was minimal improvement in group IX which received Cyclophosphamide for longer duration.

This noticeable improvement of the histological picture of the seminiferous tubules after administration of vitamin E could be explained by its antioxidant effect which protects the testis and the spermatogenic epithelium from the harmful oxidative stress caused by Cyclophosphamide.

It could be concluded that cyclophosphamide induced a harmful effect on the testis and spermatogenesis causing obvious degenerative changes in the histological picture of the seminiferous tubules and these changes are directly proportional with the dose and duration of cyclophosphamide administration. Such degenerative changes can be improved with co-administration of vitamin E with cyclophosphamide. So it is advisable to give vitamin E as an adjuvant therapy in patients receiving cyclophosphamide to protect and maintain testicular function and preserving their fertility.