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Stem Cells Restored Ovarian Function and Folliculogenesis Following Cyclophosphamide-Induced Ovarian Failure in Rats

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ABSTRACT

Aim of the study

The aim of this animal study was to explore the therapeutic potency of mesenchymal stem cells (MSCs) transplantation for cyclophosphamide-induced ovarian damage in rats.

Methods

Sixty mature female rats were studied. Fifteen rats as a Control Group (Group I); 45 rats (the Study Group) were injected, by intra-peritoneal route, with cyclophosphamide (CTX) to induce ovarian failure. The study group was subdivided into 3 equal groups (Group II, III and IV). Male MSCs were injected intravenously into rats of Group II, while group III received PBS (Phosphate buffered saline) and group IV did not receive any injections. They were followed up for eight weeks by daily vaginal smear and biweekly serum estrogen (E2) and Follicle Stimulating Hormone (FSH). PCR was done to detect Sry gene expression.

Results

There was no statistical difference between group I and II as regards the mean FSH (3.60 ± 0.08 mIU/ml vs. 5.38 ± 0.31 mIU/ml; P=0.1, respectively) and E2 levels (69.71±1.26 vs. 53.5±0.93 pg/ml, P=0.2; respectively) at 8 weeks. Cytological and histopathological examinations showed resurrection of ovarian folliculogenesis in group II only. The (Sry) gene expression was detected within the ovarian tissues in group II.

Conclusions

According to our results, MSCs seem to have the power of recovering ovarian function both in its hormonal and follicular development abilities, in cyclophosphamide-induced ovarian damage in rats.

Keywords: stem cells, ovarian failure, rats, cyclophosphamide, ovarian function text, Follicle Stimulating Hormone, estrogens, cytology

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INTRODUCTION

Premature ovarian failure (POF) is a heterogeneous syndrome characterized by lack of folliculogenesis and ovarian estrogen production, associated with secondary amenorrhea and infertility in women under the age of 40 years.[1] The syndrome is represented in 1% of menopausal women[2-3], and in 0.1% under the age of 30 years.[4] POF may be idiopathic in 74-90%[5] or associated with genetic[6], metabolic[7] or autoimmune diseases.[8] However, iatrogenic causes following surgery, radiotherapy or chemotherapy are also recognized causes for POF.[4] Although fertility restoration is a significant concern for these women,ovarian failure is also associated with an increased risk of osteoporosis, cardiovascular disease and dementia.[9] Hormone deficiency can be overcome by hormone replacement with all its due concerns.[10] Nevertheless, the loss of fertility is a major health problem that affects these patients; currently no treatment is available that effectively restores fertility potential.[11]

Although return of spontaneous ovulation and conception has been recognized in women with POF[12-13], the use of donor eggs with assisted conception and/ or adoption is the only means of parenthood if spontaneous return of ovulation does not occur. These options are not accepted universally on moral, religious and social grounds. On the other hand, cryopreservation of ovarian tissues and/ or oocytes of patients before chemotherapy or irradiation for future fertilization should be offered before the start of treatment if future fertility is to be preserved.[14] Although early menopause frequently occurs in women with leukemia after chemotherapy, bone marrow transplantation has been linked to an unexplained return of ovarian function and fertility in some survivors.[15]

The aim of this study was to explore the therapeutic potency of MSCs (mesenchymal stem cells) transplantation on ovarian function and folliculogenesis for chemotherapy-induced ovarian failure in rats.

MATERIALS AND METHODS

This study was a prospective case control animal study in collaboration between National Research Centre of Cairo, Egypt (the Reproductive Health Research, the Medical Biochemistry