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Stem cells shown to restore non-functioning ovaries

Around 1% of women under the age of 40 suffer Premature Ovarian Failure (POF). Which is a stopping of normal functioning of the ovaries in a woman younger than age 40. Women largely stop producing eggs and ovarian hormones. It used to be called premature menopause. Infertility is a major problem that affects these women and currently no treatment is available that increases fertility

Now for the first time, a group of researchers have been able to restore ovarian function to rats suffering from POF. This is an important development which opens the prospect of treating women with POF in the future. This work is presented at the World Congress of Fertility and Sterility, in Munich.

The researchers, led by Professor Osama Azmy (National Research Center, Cairo, Egypt) used embryonic rat stem cells (MSCs, see below for definition) to restore ovary function in the experimental rats.

They studied 60 mature female rats. The rats were divided into 4 groups.

- The first group (group 1) was the control group, which was given no treatment.

The rest of the rats, groups 2-4, were given a chemical to induce ovarian failure with 15 rats in each group.

- Group 2 had ovarian failure, but then was treated with MSC injections. Male Stem cells were used, so that the exact location of the stem cells could subsequently be detected by looking for the presence of a Y chromosome.
- Group 3 had ovarian failure, and was injected with a saline solution
- Group 4 had ovarian failure and was not treated

The researchers also monitored the levels of FSH (follicle-Stimulating Hormone) and 17 β estradiol, to see if hormone levels of the treated rats returned to normal.

Within 2 weeks, the rats in the experimental group had regained fully-functioning ovaries. After 8 weeks, the hormone levels of the rats in the treated group (group 2) were the same as those rats which did not have ovarian failure (group 1). The researchers were able to detect the presence

of the MSCs in the ovaries of the rats by confirming the local presence of a Y chromosome.

Professor Azmy comments

“This work shows that Mesenchymal Stem Cells can restore ovarian function. The treated ovaries returned to producing eggs and hormones, and we could detect the presence of the stem cells within the newly functioning ovaries.

What we have done is proven that we can restore apparently fully-functioning ovaries in rats. The next step is to look how these rats might reproduce, and to characterise the chromosomes of offspring following treatment. We have not yet reached the stage of producing offspring, and so we will need to understand if the baby rats will be genetically related to the mother, or to the donor of the stem cells.

This is proof of concept, and there is still a long way to go before we can apply this to women. Nevertheless, this work holds out the possibility that women with premature ovarian failure might be able to bear a baby of their own”.

ENDS

Notes for Editors

For more information please contact Professor Osama Azmy, MD, FRCOG, DFFP, e-mail osamaazmy@yahoo.com

For additional comment on this, or any other work presented at the World Congress, please contact Tom Parkhill, e-mail tom@parkhill.it or call +44 7509 215 465 (mobile).

This work is presented at IFFS 2010, which is the World Congress on Fertility and Sterility, Munich 12-16 September (<http://www.iffs2010.com/>). This is the official congress of the International Federation of Fertility Societies (IFFS).

PLEASE MENTION THAT THIS WORK IS PRESENTED AT IFFS 2010, THE WORLD CONGRESS OF FERTILITY AND STERILITY IN MUNICH

Background

Premature ovarian failure (POF) is when a woman's ovaries stop working before she is 40. POF used to be called premature menopause. However, POF is not the same as menopause. Some women with POF still have occasional periods. Premature menopause is when periods stop before age of 40. This can be natural or caused by surgery, chemotherapy or radiation.

Missed periods are usually the first sign of POF. Later symptoms may be similar to those of natural menopause.

Most women with POF cannot get pregnant naturally. Fertility treatments help a few women; others use donor eggs to have children. There is no treatment that will restore normal ovarian function. However, many health care providers suggest taking hormones until age 50. (from National Institute of Health website, <http://www.nlm.nih.gov/medlineplus/prematureovarianfailure.html>)

Incidence

According to the International Premature Ovarian Failure Association (<http://www.runmyclub.com/IPOFA/ClientFiles/English%20Fact%20Sheet.pdf>), between 1 and 4% of women suffer from POF - equivalent to between 250,000 and 1 million women in the USA alone.

MSCs; Mesenchymal Stem Cells

Mesenchyme, or mesenchymal connective tissue, is a type of loose connective tissue, located within the embryo . Cells derived from the mesenchyme are capable of developing into a variety of tissues.

ABSTRACT

Stem cells restored ovarian function and folliculogenesis in rats following induced Ovarian failure

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Introduction: Premature ovarian failure (POF) is a heterogenous syndrome affecting 1% of women below the age of 40 years and 0.1% before 30 years. Infertility is a major problem that affects these women and currently no treatment is available that effectively increases fertility. Mesenchymal stem cells (MSCs) represent a promising tool for new clinical concepts in supporting cellular therapy.

Aim: The aim of this experimental animal study was to explore the therapeutic potency of MSC transplantation for chemotherapy-induced ovarian damage in rats.

Materials and methods: This was a prospective case control experimental animal study. Sixty mature female rats were studied. Fifteen rats served as a control group (group I). 45 rats were injected by intraperitoneal cyclophosphamide (CTX). The study group was subdivided into 3 equal groups (group II, III and IV). Rats of group II were injected intravenously by male MSC, while group III by saline and group IV did not receive any injections. The rats were followed up for eight weeks by daily vaginal smear and biweekly E₂ and FSH levels to monitor the ovarian activity. PCR was done to look for sry gene expression and Y chromosome incorporation into the ovarian tissues. Two rats were sacrificed every 2 weeks for histopathological examination for the ovarian tissues.

Results: Ovarian failure was achieved in the study group by two weeks. The hypoestrogenic and hypergonadotropic state was reversed in the group that received MSC injection by the eighth week. There was no statistical difference between group 1 and 2 after 8 weeks of follow up as regards the mean serum 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) .

Also, cytological and Histopathological examinations showed resurrection of ovarian folliculogenesis and corpus luteum formation in group II and such changes were not observed in the other groups. The (*sry*) gene expression of the Y chromosome was detected within the ovarian tissues in group II.

Conclusions: stem cells have the power of recovering ovarian function both in its hormonal and follicular development abilities. Our work has proved that this principle is achieved mainly by incorporation of stem cells into the ovarian structure and not merely by the paracrine effect.