



Press release - International Federation of Fertility Societies

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Study shows melatonin almost doubles IVF success rate in women with poor egg quality

Poor egg (oocyte) quality is an important cause of female infertility. Low quality eggs may have several problems, for example they may not divide properly, or they may be missing certain chromosomes. Egg quality also declines with age, and certain medical conditions, such as Polycystic Ovary Syndrome, can lead to poor quality eggs.

New research presented at the World Congress of Fertility and Sterility in Munich has found that treating women with the hormone melatonin may help improve the egg quality in IVF.

A group led by Associate Professor Hiroshi Tamura (Yamaguchi University Graduate School of Medicine, Japan) measured the presence of the oxidizing agent 8-OHdG in follicular fluids. High levels of oxidising agents such as 8-OHdG is an indicator of poor egg quality. The group found that as melatonin concentration in the follicular fluids naturally increased, the level of 8-OHdG went down, leading the group to believe that melatonin was linked to the reduction of the stressing oxidising agents. Melatonin has known anti-oxidizing effects.

They confirmed this finding in mice, and noted that addition of melatonin seemed to reduce the damage to the egg caused by the presence of oxidising agents.

The group then initiated a trial with a group of women coming for IVF treatment at the Yamaguchi University Graduate School of Medicine. Women who had failed to become pregnant because of poor oocytes quality after one cycle of IVF were split into two groups; 56 women were given 3 mg of melatonin before the next IVF cycle, and 59 just received a standard IVF cycle without any melatonin.

The team found that melatonin treatment significantly increased intrafollicular melatonin concentrations, and significantly decreased the concentration of the damaging 8-OHdG.

The results of the study found that 50% of the eggs from women who taken melatonin could be successfully fertilised, as opposed to 22.8% in the control group. When the eggs were then transplanted into the womb, 19% (11 out of the total 56) of the women became pregnant, as opposed to 10.2% (6 out of total 59) in the control group.

Associate Professor Tamura commented

“Despite great advances in assisted reproductive technology, poor oocyte quality remains a serious problem for female infertility, and so far no practical and effective treatment for improving oocyte quality has been established. Our work show that

oxidizing agents can lessen oocyte quality, and that this can be countered by action of the hormone melatonin. In addition, our clinical trial shows that melatonin treatment improves oocyte quality, leading to a higher fertilization rate.

To our knowledge, our study represents the first clinical application of melatonin treatment for infertility patients. This work needs to be confirmed, but we believe that melatonin treatment is likely to become a significant option for improving oocyte quality in women who cannot become pregnant because of poor oocyte quality.

Our next step is to analyze exactly how reactive oxygen species harm the oocyte, and how melatonin reduces oxidative stress in the oocyte”.

Notes for Editors

This work is being presented as a poster on 15 September, during the 20th World Congress on Fertility and Sterility, which is taking place in Munich from 12-16 September, <http://www.iffs2010.com/>

The World Congress on Fertility and Sterility is organised by the International Federation of Fertility Societies (IFFS), which represents national fertility societies from all parts of the world. We have more than 70 member societies from all parts of the World. The IFFS website is <http://www.iffs-reproduction.org/>. The next World Congress will take place in Boston in 2013. We can assist with press comment on any assisted reproduction matters, especially in an international context.

PLEASE MENTION THE WORLD CONGRESS ON FERTILITY AND STERILITY OR THE IFFS IN ANY STORY

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Abstract

Influence of oxidative stress on oocyte quality and protective role of melatonin as an antioxidant

Poor oocyte quality is an important cause of female infertility. Reactive oxygen species (ROS) are produced within ovarian follicles, especially during ovulation process, and it is thought that increased ROS activity may be a cause of impaired oocyte maturation. Pineal hormone, melatonin, is detected in the human follicular fluid and melatonin is known as a potent free radical scavenger. This study was undertaken to evaluate the relationship between oxidative stress and poor oocyte quality and whether melatonin administration improves oocyte quality by protecting them from radical cytotoxicity.

Follicular fluid was sampled at oocyte retrieval [85 follicular fluids from 85 patients were enrolled] during in vitro fertilization and embryo transfer (IVF-ET) program. Intrafollicular concentrations of 8-OHdG (8-hydroxy-2'-deoxyguanosine) were determined as an oxidative stress marker, and Cu,Zn-superoxide dismutase (SOD), glutathione (GSH) and melatonin were determined as antioxidants. There was no correlation between SOD, GSH

and follicular growth. However, melatonin concentrations increased depending on follicular growth. Although SOD and GSH did not show any correlation with 8-OHdG, melatonin showed a negative correlation with 8-OHdG. It seems that melatonin is the most important antioxidant in the follicle.

Oocytes recovered from immature ICR mice were incubated in medium with hydrogen peroxide (H₂O₂) and melatonin. After 12 hrs incubation, oocytes with first polar body were defined as mature oocytes, and ROS formation in oocytes were detected using a ROS dye (dichlorofluorescein). Reduced percentages of the oocyte with first polar body caused by H₂O₂ were recovered by melatonin addition. Fluorescence intensity caused by H₂O₂ was significantly decreased by melatonin treatment. H₂O₂ inhibits oocytes maturation but melatonin counteracted oxidative stress caused by H₂O₂.

Women who failed to become pregnant in the previous IVF-ET (fertilization rate < 50%) took 3 mg tablets of melatonin in the next IVF-ET [115 patients were divided into two groups. In the next IVF-ET cycle, 56 patients were given melatonin treatment, 59 patients without melatonin treatment (control)], and fertilization rate and pregnancy rate were compared to the previous IVF-ET. The fertilization rate and pregnancy rate were improved by melatonin treatment [Fertilization rate was improved in melatonin treatment cycle (50.0%) compared with the previous cycle (20.2%). On the other hand, in 59 patients who were not given melatonin, the fertilization rate was not changed (22.8%) compared with previous cycle (20.9%). Pregnancy rate was higher in melatonin treatment cycle (19.6%; 11/56) compared with without melatonin treatment cycle (10.2%; 6/59)]. Intrafollicular melatonin concentrations were significantly increased and 8-OHdG levels were significantly decreased by melatonin treatment.

In conclusion, ROS have a toxic effect on oocyte maturation and melatonin may protect oocyte from ROS. Melatonin administration is likely to improve oocyte quality.

Note Some clarifying details have been added to this abstract, so it is slightly different from that in the programme book.