

THE ROLE OF OOCYTE VITRIFICATION IN AGED PATIENTS AND LOW RESPONDERS

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Introduction: According to previous reports, there is an association between the number of fertilizable eggs and the overall IVF outcome. Accordingly, a poor response (PR) in aged patients to gonadotropins may result in cycle cancellation, a reduction in the pool of embryos available for transfer or cryopreservation, and decreased pregnancy rates. The possibility of building a larger cohort coming from successive controlled ovarian hyperstimulation cycles (COH) may possibly contribute to alleviate the negative effects of PR in aged patients on the IVF outcome. Obviously, an efficient oocyte cryopreservation/storage program is essential for these purposes. Recent advances in oocyte cryopreservation have been reported using the vitrification technique. The aim of this study was to assess the value of oocyte vitrification in cases of PR in aged patients to COH.

Materials and Methods: This is a retrospective cohort study, with data obtained from 92 PR (≤ 5 oocytes) patients (age 38-44 years), who underwent successive controlled ovarian hyperstimulation cycles (COH) (1-5) before doing a ICSI-PGD.

Oocyte vitrification was performed by Cryotop® method. Analysis was performed using SPSS 12.0 statistical analysis software, two-tailed student *t*-test and χ^2 test were used to compare mean values and proportions respectively.

Results: 92 patients between age 38-44 years old have been analysed for ACUVIT PGD. These patients had accumulated vitrified oocytes (average of vitrified cycles $1,53 \pm 6,7$) from various cycles (1-5), in order to add them to a fresh cycle or not, and to do only one cycle of ICSI-PGD. A 56,5% of patients of ACUVIT have transfer and this is significantly superior ($p < 0,05$) to the percentage of transfers (37,1%) accumulated in fresh cycles after 1-3 cycles. Inside the ACUVIT group we have divided the sample, according to age, in two groups: 38-40 years (38 patients) and 41-44 years (54 patients). There has been no observation related to differences in fertilization, embryo development (day 2, 3 and blastocyste) and average embryos transferred in these two age groups. The rate of clinical pregnancy per ACUVIT cycle is 15,5% while the evolutive rate per cycle is 13,3%. There has been no observation related to differences in pregnancy rate, implantation and miscarriage between the two different age groups. In the control group we counted with 323 patients between 38 and 44 years who realise 1 to 3 cycles with fresh oocytes and which clinical pregnancy rate in the first cycle is 12,6% while the evolutive rate per cycle is 8,7%. Only 11,2% (31 out of 276 patients) of the patients who did not get pregnant in their first cycle, realised a second fresh cycle, without getting pregnant none of them and finally 0,8% of these patients (2 out of 31 patients) realised a third fresh cycle without getting pregnant.

The embryo development in the ACUVIT cycles has been analysed according to if the oocytes proceeded from a fresh cycle or a vitrified one and it has been observed that there do not exist differences between both groups respecting to fertilization rates (68,2% with fresh, 66,8% with vitrified oocytes) and embryo development (division rate on day 3: 86% with fresh and 87,3% with vitrified oocytes; percentage of development until blastocyste stage per day 3 embryo: 54,6% with fresh and 57,2% with vitrified oocytes). In conclusion we can say that the vitrification does not affect the development capacity of the vitrified oocytes. We did not observe neither significant differences in the number of biopsiated embryos (47% fresh and 52,95% vitrified), analysed (47,3% vs 52,6%) and informatives (47,8% vs 52,1%) and not in the number of normal embryos (20,8% vs 25,7%) or anormal (76,1% vs 67,7%) according to if the oocytes proceeded from a fresh cycle or a vitrified one. In conclusion we can say that the vitrification does not alter the potential of the vitrified oocytes in order to generate competent and chromosomically normal embryos.

Finally comparing within this group of aged patients the ACUVIT with fresh we can observe that the patients with ACUVIT have more transfers statistically significant compared to the fresh accumulated (56,5% vs 35,7%), and this difference is shown as well in the total of ACUVIT (38-44 years) like in the two groups of age (38-40: 65,8% vs 47% and 41-44 years: 50% vs 26%). The average of transferred embryos is also significantly higher in the ACUVIT total (1,4 vs 1,2) like for each group of age (1,4 vs 1,2 y 1,4 vs 1,1 respectively). The evolutive pregnancy rate per ACUVIT cycle is higher than with fresh accumulated (13% vs 8,7%) and this in the total of ACUVIT like in both groups of age (15,8% vs 12,8 and 11,1% vs 5,2% respectively) although the difference does not reach significant values which could be associated to N. In consequence, even if the differences statistically are not significant, we observe a tendency to present a higher evolutive pregnancy per cycle in ACUVIT. Also, the miscarriage rate is lower in these cycles (7,1%) than in fresh accumulated which achieve 19,5% even if the difference is not significant.

Conclusions: The establishment of a larger oocyte/embryo cohort in cases poor response in aged patients to COH by means of storing vitrified oocytes does not improve the pregnancy rate as compared with the cumulative pregnancy rate obtained with consecutive fresh cycles. However, all the patients who vitrified oocytes had the chance to obtain the 50.8% of pregnancy rate, whereas with consecutive fresh cycles only 9.2% had this opportunity, because of the high percentage of abandonment of the treatment. Moreover, the "accumulation" of oocytes to be used in just one insemination cycle in cases of PR, encourages patients to undergo their treatment with their own oocytes before setting for other alternatives like ovum donation.

We propose the ACUVIT like a valid alternative for the patients with an advanced age offering the possibility to get pregnant with their own oocytes before passing to Ovodon.