NATURAL OPTIONS IN AGED PATIENTS AND LOW RESPONDERS

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The first successful IVF treatment was performed by Steptoe and Edwards (1) in an unstimulated menstrual cycle. However, natural cycle IVF (NC-IVF) was replaced by IVF with ovarian stimulation (OS-IVF) yielding more oocytes and embryos available for transfer and consequently a higher pregnancy rate.

NC-IVF consists of monitoring the spontaneous cycle and retrieving a single oocyte prior to the spontaneous LH surge. The theoretical advantages of NT-IVF are:

minimal risk of OHSS and multiple pregnancies, no hormonal stimulation, less demanding physically, reduced cost , can be done in consecutive months, reduced aneuploidy rate, reduced endometrial estrogen stimulation and potentially better implantation. In recent years there is a renewed interest in NT-IVF because the IVF laboratory efficiency has markedly improved, making single embryo retrieval and transfer a realistic option.

Results of Pregnancy rates in good responders: Four Randomized Controlled Trial involving a total of 339 women comparing NC-IVF to stimulated IVF have been published. In spite of the small number of treatment cycles and variability in patient age, NC-IVF resulted in a significantly higher cancellation rate (27-70% vs 0-4%) and lower pregnancy rates per cycle (0-3.5%vs 13-23%).

The cumulative pregnancy rate of four successive natural cycles (46%) was found to be equivalent to to a single stimulated IVF cycle (2).

Pregnancy rates in poor responders: The application of NC-IVF as a treatment for poor responders was first suggested by Lindheim et al(3) and Bassil et al(4). In the latter publication 16 cycles of 11 patients were compared to their previous 25 stimulated cycles. The cancellation rate was 19% from (3/16) failure to find oocytes 15% (2/13) , failure of fertilization 45% (5/11), and a total of 6/16 ET's (37% of initiated cycles). 3 pregnancies occured (18% per initiated cycle) (one in a 40 year old and 2 in women < 35 years of age). Following this observation several other publications addressed this issue most of which were retrospective in nature. In the largest of these studies (5) , 294 poor responders in a previous OS-IVF cycle underwent 500 NC-IVF cycles . It was found that young poor responders did relatively well on NC-IVF with a pregnancy rate of 18% per cycle while women older >40 did poorly (5.8% pregnancy rate per cycle). Similar results were obtained in the only controlled trial comparing NC-IVF to microdose GnRH-a flare protocol.(6)

Chromosomal competence of embryos in NC-IVF compared to OS- IVF: The biological advantages of the natural cycle may provide a single oocyte of better quality and thus allow the transfer of a healthier embryo.

Recent studies using PGS have suggested that the proportion of aneuploidy in embryos is reduced by milder ovarian stimulation. Women <38 years of age undergoing conventional OS-IVF had a significantly higher rate of chromosomal abnormality (64%) compared with those undergoing a milder stimulation (45%). However, a 36% rate of aneuploidy was also found in young women undergoing NC-IVF suggesting that even without of exogenous stimulation chromosomal abnormalities of embryos still occurs.(7)

Conclusions: NC-IVF have a high cancellation rate of 30% and a low overall pregnancy rate, 10%, per initiated cycle. Young (<35 years of age) low responders have similar results to their normally responding counterparts in age undergoing NT-IVF (18 % per cycle), thus suggesting a protective role of age on oocyte quality. Low responders >40 years of age have meager results in NT-IVF (5% pregnancy rate per cycle) suggesting that the effect of age overshadows any other potentially beneficial effect.

References

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