International Seminar 7: From Bulgaria and China

4) The evolvement of work pattern in assisted reproductive technology
   —experiences from PUMCH

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Background The assisted reproductive technology, which achieves fertilization and early stage embryo development by artificial assisted technology in vitro, involves controlled ovarian hyper-stimulation, oocyte retrieve, semen processing, in vitro fertilization, cultivation of zygote, embryo transfer, embryo cryopreservation and thawing. IVF-ET procedure is costly and not covered by insurance. Meanwhile, it has limited pregnancy rate and no absolute guarantee for safety. As for the patients, they expect high chance of pregnancy at a cost as low as possible. The cost of IVF-ET distributes in the procedures of preparation, medicine and monitoring for COH, oocyte retrieve, cultivation in vitro, embryo transfer, embryo cryopreservation and thawing. The major cost occurs before the first transfer with fresh embryo. For the interests of patients, parameters used for evaluation the merit of ART centers should be cumulate clinical pregnancy rate in each oocyte retrieve cycle.

Parameters To ensure pregnancy rate as high as possible, each step of ART should offer a perfect result, especially the embryo survival rate after cryopreservation and thawing. Firstly, individualized COH strategies are beneficial to retrieve oocytes with high quality and right quantity. According to the patients’ ovarian reserve and complications (such as endometriosis), long-protocol, dual inhibitory protocol, ultra-long-protocol or mild stimulate protocol could be chosen for individual patient. Secondly, in the lab technology, besides strict quality control, we focus on the blastocyst culture and vitrification. So far, the clinical pregnancy rate in each fresh embryo transfer cycle has achieved 40%–50% and more than 60% in each frozen-thawed embryo transfer (FET) cycle. It is worthwhile to point out that the mean age of our patients were over 35 years old and 37% of them suffered from adenomyosis, reduced ovarian preservation or PCOS.

Evolvement of work pattern
[The first stage] Embryos were transferred at 8 cells stage in day 3, and all of the extra embryos were cryopreserved at the same day. Data from 106 cycles suggested that the clinical pregnancy rate in each fresh and frozen-thawed embryo transfer cycle were 27.3% and 24%, respectively. About 80% of patients who didn’t get pregnant at fresh embryo transfer cycle had cryopreserved embryos and more than 50% of these patients had more than 3 embryos. It could be calculated that the cumulate clinical pregnancy rate would be 48% for each oocyte retrieve cycle.

[The second stage] All of the embryos were cultivated to blastocyst stage in 5–6 days after oocyte retrieve. Blastocysts were transferred and the extra blastocysts were cryopreserved via vitrification. The patients who didn’t conceive in fresh cycle received frozen-thawed blastocyst transfer 3 months later. Data from 194 cycles showed that the clinical pregnancy rate in each fresh embryo transfer and frozen-
thawed embryo transfer cycle were 42.4% and 63%, respectively. However, 12.5% of the cycles were cancelled due to no blastocyst formation.

[The third stage] If the good embryos were less than or equal to 6, the blastomeres were transferred, the extra blastomeres were cultivated to blastocyst stage and then cryopreserved with vitrification. If the good embryos were more than 6, all of the embryos would be cultivated to blastocyst stage. In the fresh cycle, blastocysts were transferred and the extra blastocysts were cryopreserved via vitrification. The patients who didn't conceive in fresh cycle received frozen–thawed blastocyst transfer 3 months later. Data from 203 cycles demonstrated that the clinical pregnancy rate in each fresh blastomeres transfer cycle and fresh blastocysts transfer were 32% and 34.5%, respectively. The clinical pregnancy rate in each frozen–thawed blastocyst transfer cycle was 64.2%. However, the complex of work increased.

[The forth stage] The blastomeres were transferred in fresh cycles in day 3. The extra blastomeres were cultivated to blastocyst stage and than cryopreserved via vitrification. The patients who didn't conceive in fresh cycle received frozen–thawed blastocyst transfer 3 months later. Data from 511 cycles showed that the clinical pregnancy rate in fresh blastomeres transfer cycle was 37.5%. Blastocysts were obtained in 61.2% of oocyte retrieve cycles. About 52% of patients who didn't get pregnant at fresh cycle had cryopreserved blastocysts and 21% of the total cycles had more than 3 cryopreserved blastocysts (more than 2 times FET). The clinical pregnancy rate in each frozen–thawed blastocysts transfer cycle was 63%. It could be calculated that the cumulate pregnancy rate in each oocytes retrieve cycle would be approximately 70%.

Conclusions According to the experience from ART center of PUMCH, we concluded that fresh embryo transfer at day 3 in 8 cells stage will guarantee that most of the patients have at least one embryo transfer. Blastocyst culture of the extra blastomeres would make a good selection of the embryos which would reduce the amount of embryo frozen. Vitrification freezing technique ensures a good survival rate of frozen–thawed embryos, and increases the pregnancy rates of FET cycles.