REPRINTED FROM:

IN VITRO FERTILIZATION AND ASSISTED REPRODUCTION

Proceedings of the
10th World Congress of in Vitro Fertilization
and Assisted Reproduction

Vancouver (Canada), May 24-28, 1997

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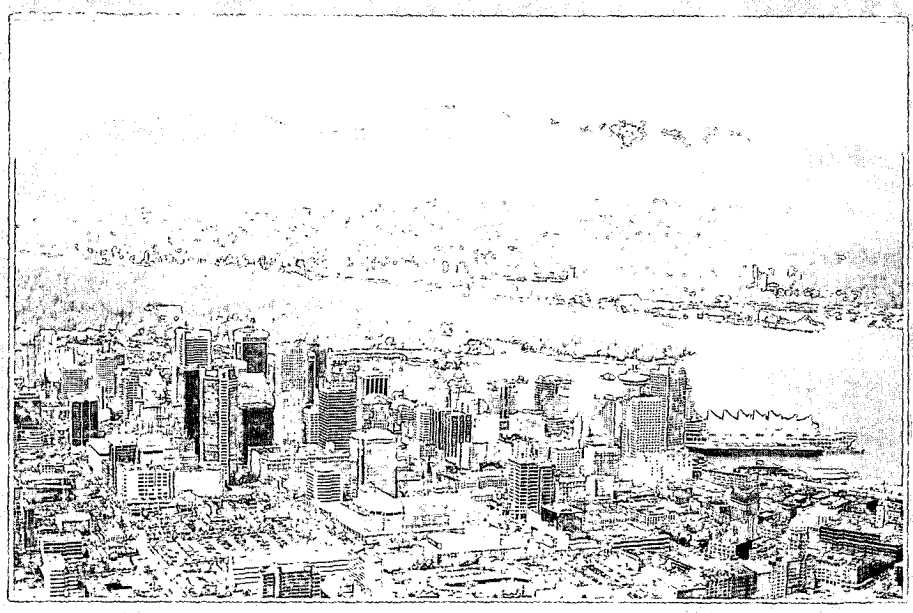

MONDUZZI EDITORE

INTERNATIONAL PROCEEDINGS DIVISION

10th World Congress on
IN VITRO
FERTILIZATION AND
ASSISTED
REPRODUCTION

Vancouver, Canada
24-28 May 1997

Pregnancy rates in women older than 43 following in vitro fertilization-embryo transfer (IVF-ET) with assisted ET

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SUMMARY

While world statistics demonstrate a poor prognosis for in vitro fertilization (IVF) success in older women, a more optimistic outlook in group of women age 40-43 having at least 3 embryos transferred with assisted hatching (AH) has been reported. The objective of the current study was to assess fertility potential following IVF-embryo transfer (ET) in patients 44 and over when AH and close sonographic monitoring of endometrial status were available. A total of 71 stimulation cycles were retrospectively reviewed. Only one clinical (and ongoing pregnancy) was achieved. Despite availability of AH, women age 44 and over have a poor prognosis for pregnancy when using their own oocytes. Therefore, donor oocytes should be recommended.

INTRODUCTION

The world data on in vitro fertilization (IVF) success in older women demonstrate poor pregnancy prognosis (SART, 1996; Hull et al, 1996; Fivnat et al, 1990). One previous study reported no deliveries in group of women age 44 or older utilizing their own oocytes (Bopp et al, 1995). This failure has been attributed to poor uterine receptivity or poor oocyte quality (Navot et al, 1991). The hypothesis of reduced uterine receptivity was undermined by the success of oocyte donation to women in their 40s and 50s (Check et al, 1994). But, oocyte quality manifested by high incidence of aneuploidy appears to be a critical etiologic factor (Munne et al, 1995).

However, in our center we experienced an adequate pregnancy rate (PR) (26.3% per transfer) following the transfer of at least 3 embryos and the use of assisted hatching (AH) in women age 40-43. The objective of the current study was to assess fecundity potential following IVF-embryo transfer (ET) in women age 44-45 and to measure the impact of AH and 3 day transfers under careful sonographic monitoring of the endometrial environment.

MATERIALS AND METHODS

Seventy-one consecutive stimulated ET cycles in women age 44-45 were retrospectively evaluated. Controlled ovarian hyperstimulation regimens included: short flare protocol, or clomiphene citrate (100mg x 5 days) followed by hMG (Shanis et al, 1995).

Cycles were cancelled before retrieval if there was a poor response to stimulation (less 3 mature follicles developed). Embryo transfers were deferred and all embryos cryopreserved if the patients were at risk for ovarian hyperstimulation syndrome or there was evidence of inadequate endometrial development, i.e., either the endometrial thickness was less than 10 mm or the homogeneous hyperechogenic echo pattern was observed (Check et al, 1991). Progesterone (P) supplementation in the luteal phase was 100mg oral P QID or 50mg P in oil IM BID.

Cycles were stratified by their use of assisted hatching (Cohen et al, 1990a). Prior to November of 1993, AH was not available. After 1993, patients had the option of using AH. Patients in the AH group were prescribed methylprednisolone and doxycycline. The corticosteroids were given to prevent the woman's immune system from attacking the embryo through the breach in the zona and the antibiotic was given to retard infection (Cohen et al, 1990b).

Assisted hatching using the zona drilling technique was performed using micromanipulation equipment from the Narishige Company (Nikon, Parsippany, NJ) as previously described (Check et al, 1996).

Pregnancy rates per stimulated cycle, retrieval and transfer were assessed. Furthermore, if the fresh transfer was deferred, adjusted PRs that included the results of the first frozen ET were evaluated. Clinical pregnancy was defined as evidence of a gestational sac in the uterus. Ongoing pregnancy was defined as pregnancy that successfully demonstrated a viable fetus on ultrasound after completion of the first trimester.

RESULTS AND CONCLUSIONS

A total of 71 stimulation cycles in women 44-45 years old were

performed. The cancellation rates before oocyte retrieval was 39.4% (28 cycles). Of the 43 oocyte retrievals, ET was cancelled in 37.4% (15 cycles).

There was only one pregnancy following fresh ET. This pregnancy resulted from the transfer of 5 fresh embryos without AH and successfully developed to delivery. No pregnancies were achieved following frozen ET. The PR per stimulation, retrieval, and transfer was 1.4%, 2.3%, and 3.6%, respectively.

Since many women are waiting until later in life to start families, it is important to examine the infertility treatment options available to them and to be able to advise them of their chance of success. Women aged 40 and over have lower PRs following IVF-ET, because they make less follicles and the oocytes have a higher percentage of aneuploidy. In a previous study we have been able to define a group of women age 40-43 responding well to stimulation, generating at least 3 embryos and undergoing AH who do have a good pregnancy prognosis following IVF-ET (Check et al, 1996). Nevertheless, the results of the current study are comparable to data reported by Bopp et al, (1995) and Hull et al, (1996) and are not optimistic for older women.

Although, AH was proved to be effective in overcoming the hatching deficiency in our previous experience, AH did not influence higher pregnancy in women 44-45. Probably this is mostly related to a high percentage of oocytes with aneuploidy (approaching 90%) and to a lesser degree a decreased number of mature oocytes following controlled ovarian hyperstimulation. Because of abnormal oocytes this older group of women attempting IVF-ET despite the low odds should have all of the embryos transferred.

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