

## RETROSPECTIVE ANALYSIS OF ASSISTED CONCEPTION TECHNIQUES: A THREE YEAR EXPERIENCE

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In this retrospective survey, we present the results of infertility treatment by various assisted conception techniques at the assisted conception unit, New Jeddah Clinic Hospital, Jeddah, Saudi Arabia. During a three year period from January 1990 to December 1992, a total of 249 treatment cycles were started in patients with long-standing infertility. There were 107 ovulation induction cycles carried out in patients with chronic anovulation and patent tubes and normal spermogram using rigorous ovulation induction therapy with intensive ultrasound monitoring. In 34 treatment cycles in patients with long-standing infertility and patent tubes, controlled superovulation (CSO) plus intrauterine insemination was carried out. In 30 treatment cycles, CSO plus sperm intrafallopian transfers (SIFT) were done. In the *in vitro* fertilization (IVF) and embryo transfer (ET) group, 73 oocyte pickups were carried out. Five gamete intrafallopian transfer (GIFT) procedures were done. A total of 54 pregnancies resulted from these treatments, giving an overall pregnancy rate of 21.6%. The highest pregnancy rate of 32.35% is seen in the CSO and intrauterine insemination (IUI) groups compared with a pregnancy rate of 13.3% in the SIFT, 20.56% in the ovulation induction and 20% in the GIFT. The pregnancy rate in the IVF/ET group was 22.2%/oocyte pickup and 30.8%/embryo transfer. *Ann Saudi Med* 1994;14(4):294-296.

Since the introduction of *in vitro* fertilization (IVF) and embryo transfer (ET) techniques in the treatment of infertile couples,<sup>1</sup> new techniques have been developed to achieve pregnancy utilizing IVF technology to treat patients with long-standing infertility. These procedures collectively called assisted reproductive techniques (ART) resulted in offering comprehensive tertiary service in many countries.<sup>2</sup> Patients with long-standing infertility were treated utilizing various assisted conception techniques (ART) depending on the etiology of their infertility.

### Material and Methods

During the period from January 1990 to December 1992, 249 treatment cycles were carried out (Table 1). The criteria for patient assignment to each treatment depended mainly on the underlying cause of the infertility. Patients with tubal damage will go for IVF from the start. Patients with chronic anovulation, normal spermogram and patent tubes will go for Intensive Ovulation Induction Therapy.

Patients with male infertility - unexplained infertility - who had patent tubes will be offered controlled superovulation (CSO) plus intrauterine insemination (IUI) or CSO plus sperm intrafallopian transfer (SIFT), first for

three cycles before proceeding to IVF or gamete intrafallopian transfer (GIFT). This also depended on patients wishes, as some patients with long-standing infertility would like to proceed directly to IVF or GIFT. There were 107 ovulation induction cycles in patients with chronic anovulation who had patent tubes. Normal spermogram was carried out with intensive monitoring using vaginal ultrasound follicle tracking.

Human chorionic gonadotropin (HCG) was given in a dose of 5,000 IU (HCG Profasi, Serono, Italy) when there were no more than three follicles with a mean diameter of the leading follicle around 17 mm to 20 mm. The patients were advised to have timed intercourse 36 hours after HCG.

The mean age of the above group of patients was 28.6 years (18 to 45). The mean duration of infertility was 3.7 years (1 to 15); 41.2% suffered from primary infertility and 58.8% from secondary infertility.

TABLE 1. Total number of treatment cycles in assisted conception procedure.

Procedure	Treatment Cycles	No. of Pregnancies	Pregnancy Rate
Ovulation induction	107	22	20.56%
CSO + IUI	34	11	32.35%
CSO + SIFT	30	4	13.33%
GIFT	5	1	20.00%
IVF	73	16	21.92%
Total	249	54	21.63%

CSO=controlled superovulation; IUI=intrauterine insemination; SIFT=sperm intrafallopian transfer; GIFT=gamete intrafallopian transfer; IVF=*in vitro* fertilization.

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In 34 treatment cycles, gentle controlled superovulation plus IUI was carried out in patients with patent fallopian tubes. The etiology of infertility included male factor, anovulatory plus male factor, unexplained, and polycystic ovaries (PCO).<sup>3-5</sup> The mean age of this group of patients was 30.0 years (18 to 43). The mean duration of infertility was 4.5 years (1 to 18); 54.3% suffered from primary infertility and 45.7% from secondary infertility.

In another 30 treatment cycles who had CSO, the washed prepared sperm were deposited in both fallopian tubes using a special catheter that is introduced transcervically either by tactile sensation or by ultrasound guidance. (Jansen Anderson, KJLTS 2000, Cook, Australia). This procedure is called SIFT.<sup>6</sup> The mean age of this group of patients was 27.7 years (18 to 39). The mean duration of infertility was 11.5 years (1 to 17); 72.7% suffered from primary infertility and 27.3% from secondary infertility. The controlled superovulation was achieved using the following protocol: 1. Clomiphene and human menopausal gonadotropins (HMG); 2. HMG alone; and 3. Suprefact long or short protocol and HMG.

*Criteria of ovulation:* In the above two groups of patients, ovarian superovulation was monitored solely by vaginal ultrasound. No E2 estimation was done. HCG was given when there were no more than three follicles with average diameter of the leading follicles around 17 mm to 20 mm.

IUI or SIFT was performed 36 hours later. If there were more than three follicles, the couples were counseled about the risk of hyperstimulation and multiple pregnancy and the cycle was canceled.

In the IVF and ET group, 73 oocyte pickups were carried out. The mean age of the patients was 29.9 years (20 to 40), duration of infertility seven years (2 to 18). A total of 54.4% suffered from primary infertility and 45.6% from secondary infertility.

*Superovulation in IVF and GIFT patients:* In this group of patients, superovulation was achieved with LHRH analogue - (Suprefact, Hoechst, United Kingdom) either as long protocol in the majority or as short protocol in a small group of patients.

In the long protocol, Suprefact was started on the first day of menses as nasal spray dose 200 µg q. 4 hourly or S.C. 0.5 mg b.i.d. All patients had a day two ovarian scan. Suprefact was given for two weeks to achieve pituitary down-regulation. Another vaginal scan was done to confirm ovarian suppression. No E2 was performed.

In the short protocol, Suprefact was started on the first day of menses in a similar dose as above and continued until the evening of HCG. Ovarian stimulation was started using HMG on the third day of menses.

HMG (Pergonal, Serono, Italy) dose was individualized depending on patient's age, day 3 FSH and LH, previous response to ovarian stimulation and the presence or absence of PCO.

In all patients, follicle tracking was done by transvaginal ultrasound. No E2 estimations were done and decision about HCG administration was solely taken on follicle size and number as seen by ultrasound.

*Oocyte retrieval:* This was scheduled 34 to 36 hours after HCG administration. Oocyte retrieval was performed under Valium 10 mg IV and Nubain 20 mg IV using ultrasound-guided transvaginal technique. In the GIFT<sup>7</sup> procedure, oocyte retrieval was performed as before but gamete transfer to the tube was performed by laparoscopy in four cases and transcervically guided by ultrasound using Jansen Anderson catheter in one case.

*Semen preparation for IVF and IUI:* Semen were collected on the morning of egg collection or IUI in a sterile container. Routine semen analysis was the method used to assess male fertility status. Male factor fertility is defined according to the World Health Organization (WHO) criteria (count 20 million, 50% motility and 50% normal morphology). Semen were allowed to liquefy for 20 to 30 minutes at room temperature. A routine semen analysis was done and sperm preparation was conducted as described below.

The sample was mixed with the same volume of Earl's balanced salt solution (EBSS media), centrifuged at 200 g for 10 minutes, the supernatant discarded and the pellet resuspended and centrifuged the same way as previously described. A 1 mL medium was gently layered over the final pellet and sperm allowed to swim up inside the incubator (37°C, 5% CO<sub>2</sub> in air) for one to two hours. The top layer was collected from the aliquot and final analysis was performed; this layer was used for IUI or IVF.

For IUI, the prepared sperm were deposited high in the uterine cavity using Bourn Wallace or Frydman ET transfer catheter. For IVF, the prepared sperm were kept for capacitation until the time of insemination.

*Insemination and Fertilization:* After eggs were retrieved, the oocyte cumulus mass was carefully assessed under the dissecting stereoscopic microscope. The eggs' maturity was determined. The eggs were carefully rinsed in medium and transferred into 1 mL drops of culture medium supplemented with 10% maternal heat inactivated serum under liquid paraffin. They were then placed in the incubator. Forty hours after HCG, insemination was done with 100,000 to 150,000 motile spermatozoa for each egg.

Evidence of fertilization was confirmed after 18 hours from insemination by detection of two distinct pronuclei.

In the GIFT procedure, the transfer catheter was loaded with medium; then up to three eggs and finally 100,000 to 200,000 good motile spermatozoa. The mixture of oocytes and spermatozoa was gently injected into the tube.

ET was carried out 48 hours after egg collection. Selection for transfer was based on morphological characteristics of the embryo and the rate of cleavage. Three embryos of good quality at 2 to 4 cell stage were

transferred to the uterine cavity. Patients were given progesterone vaginal suppositories (Cyclogest) 400 mg daily for 14 days for luteal support.

### Results

A total of 54 pregnancies resulted from these 249 treatment cycles. These were all clinical pregnancies except for two biochemical pregnancies in the IVF group. The higher pregnancy rate of 32.35% was seen in the CSO and IUI group compared with a pregnancy rate of 13.3% in the SIFT, 20.56% in the ovulation induction and 20% in the GIFT group. The pregnancy rate in the IVF/ET group was 22.2%/oocyte pickup and 30.8%/embryo transfer.

In the male factor infertility, we had four pregnancies from 19 IVF cycles treated, pregnancy rate of 20.0%.

Ovarian superovulation in IVF and GIFT program was achieved using Suprefact long protocol in 56 treatment cycles and Suprefact short protocol in 20 treatment cycles. There were nine pregnancies in the long protocol and five pregnancies in the short protocol. The results of CSO and IUI are far better than depositing sperm in the fallopian tubes (SIFT).

A randomized controlled prospective study will be ideal in comparing the results of the two procedures.

### Discussion

IVF and ET have proved successful in the treatment of infertility due to tubal block. Its success in other forms of infertility in patients with patent tubes has also been documented.<sup>2</sup> This heterogeneous group includes those patients with unexplained infertility, mild endometriosis, and moderately reduced semen quality. However, IVF is labor-intensive, emotionally demanding and costly.

In the above group of patients who have no obstruction, monthly fecundity can be improved by gentle ovarian superovulation, thus increasing the number of eggs, together with IUI or SIFT,<sup>5,6</sup> thus delivering washed sperm near the site where fertilization takes place.

IVF is the cornerstone of ART and remains the standard treatment for infertility due to tubal obstruction or tubal

absence. It is also the most important definitive method available for proving the fertilizing capacity of the sperm.

Patients in this part of the world prefer to leave IVF as the last resort. The high pregnancy rate seen in our patients with CSO and IUI certainly raises a strong case for trying this rather simple, less costly treatment in patients with unexplained infertility, moderate to mild male subfertility and mild endometriosis or immunological infertility.<sup>4,5</sup> This treatment can be applied for a short time, e.g., three cycles, before proceeding to the more difficult complex IVF, GIFT.

In CSO and IUI, the average pregnancy rate per cycle is nearly 20% but falls shortly after three or four cycles and the cumulative rate is about 68% after six cycles.<sup>8</sup>

In conclusion, assisted conception techniques have given great hope to couples with infertility, particularly those with tubal disease, prolonged unexplained infertility, and endometriosis. Although the technology has made great advances, a lot has to be done to reduce cost and complexity and improve effectiveness.

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