

COMBINATION OF GIFT AND IVF/ET

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SUMMARY

This is a report on a successful twin pregnancy obtained by the combination of GIFT & IVF. Centres carrying out Assisted Reproduction in our country and not having facilities for cryopreservation could possibly obtain better success rates by combining the two techniques, utilizing those gametes and embryos that are morphologically having good potential. However, the number to be transferred should be restricted in view of the risk of multiple pregnancy. In future when combining these techniques our protocol will be to transfer 2 gametes by GIFT and 2 by IVF & ET.

INTRODUCTION :

The extracorporeal fertilization of oocytes and the transfer of pre-embryos in a mammalian system was first reported in 1959. (Thibault 1988). Since 1978, successful human in vitro fertilization (IVF) and embryo transfer and related techniques have been used all over the world. (Stephoe and Edwards 1978).

At its inception the primary medical indication for IVF was irreconcilable tubal damage or destruction. Pelvic endometriosis, pelvic adhesive disease, anomalies of the reproductive tract, male factor infertility, immunologic disorders and unexplained infertility are now emerging as other indications. (Crainger 1989).

Gamete intrafallopian tubal transfer (GIFT) was first introduced Richardo Asch. (Asch et al

1984) GIFT has been applied to most categories of infertility previously treated by IVF except tubal infertility. It is also applicable if ovum pick-up by the fimbria is deficient as in endometriosis and unexplained infertility. In oligospermia, GIFT promotes interaction of a concentrated fraction of spermatozoa with the oocytes within the natural environment of the ampulla. The passage of sperm through the hostile cervix in cases of immunologic infertility is avoided by GIFT. Although GIFT shortens the exposure time of the gametes to in vitro conditions and is more physiological with higher pregnancy rates, fertilization is not documented as in IVF and in the absence of a pregnancy it is not known whether fertilization occurred or not.

Pronuclear stage tubal transfer and tubal preembryo transfer (PROST and TPET), also called ZIFT (Zygote intrafallopian tubal transfer) are offshoots of IVF and GIFT. (Devroey 1986) As in IVF, fertilization occurs in vitro till

the pronuclear stage, but like GIFT, these preembryos are transferred to the fallopian tubes. ZIFT was developed to document fertilization in patients who otherwise fulfill the criteria for GIFT. ZIFT has several advantages over GIFT in that potential for early preembryonic development can be evaluated. The use of ZIFT however entails exposure to anaesthesia on two occasions and two surgical procedures, a day apart. Although development till pronuclear stage is documented, further cleavage and division is not known and this is specially important in male factor infertility and in the presence of seminal antibodies where division may get arrested or may be delayed. (Clarke et al 1985).

The combination of GIFT and IVF has been practiced in the United States in selected cases. (Medical Research International 1990, Medical Research International 1991.) We report on our initial attempts of combining the techniques of GIFT and IVF, with resulting delivery of twin girls at 37 weeks of gestation. We have since then selectively performed the procedure on two other occasions with one more ongoing pregnancy which is a twin gestation currently ongoing at 20 weeks.

CASE STUDY :

Mrs. R.S. & Mr. A.S.K. were married for 6 1/2 years. The female partner had mild pelvic endometriosis with patent fallopian tubes. She was treated medically with Danazol on two occasions. The male partner had asthenospermia, leukospermia and antisperm antibodies in semen. Initial treatment had been with antibiotics and prednisolone. These were followed by 5 cycles of ovulation induction and A.I.H.

The couple was referred to our unit for further evaluation and treatment. Computerised Semen Analysis (Parikh 1989) revealed a count of 84 mill/ml with 40% motility and only 8% progressive motility. Average velocity was 24 mic/sec (Normal = 25 mic/sec), Amplitude of lateral head displacement was 4.1 microns. (Mean - 2.26 mic.) Beat cross frequency was 4.1 htz

(Mean = 14.26 htz) and linearity was 5.1 (Mean = 6.05). There was persistent leukospermia (3 mill/ml.) The husband was offered antibiotics. Semen culture was repeated and semen was found free of bacteria. The couple underwent one cycle of superovulation and intrauterine insemination without success.

In view of the previous 6 cycles of ovulation induction and insemination, the couple was offered the procedure of GIFT. Controlled ovarian hyperstimulation was performed using the protocol of GnRH analogue in the luteal phase for pituitary downregulation. The ovarian stimulation proceeded with 225 iu. of pure Follicle Stimulating Hormone from day 2 to day 5 and 225 iu. of Human Menopausal Gonadotropin from day 6 onwards till 2 follicles greater than 17 mm in diameter were seen and the oestradiol levels reached 400 pg/ml per mature follicle. Then 10,000 IU of human chorionic gonadotropin was injected. Thirty four hours later oocytes were recovered by transvaginal ultrasound guided technique under general anaesthesia. Oocytes were graded according to the criteria of Veeck (Veeck 1986) and four oocytes with coronal dispersion, cytoplasmic maturity and cumulus mucification was isolated. Semen was collected directly in Ham's - F - 0 medium to dilute out seminal antibodies and sperm preparation was by the swim-up technique. 4 mature oocytes and 0.15 million motile spermatozoa were loaded into a GIFT cannula and transferred into the right fallopian tube by laparoscopy. Remaining oocytes were subjected to in vitro fertilization and inseminated with 0.1 mill. motile sperm per oocyte, 6 hours after the retrieval. The oocytes were screened 16 hours later for evidence of fertilization.

Five embryos were cryopreserved and 2 were allowed to develop further. Cleavage was noticed at 2 cell and 4 cell stage at 48 hours of retrieval. However, the 2 cell embryo showed fragmentation and granulation and hence the 4 cell embryo was transferred into the uterus 48 hours after oocyte retrieval.

The luteal phase was supported by 50 mg. of Progesterone in oil. Quantitative B-hCG 14 days after transfer was 184 m.i.u./ml. Transvaginal ultrasound performed at 6 weeks gestation revealed a triplet pregnancy. The pregnancy was supported by progesterone vaginal suppositories after 7 weeks of gestation. A repeat scan at 8 weeks showed 3 gestational sacs each of which demonstrated foetal heart activity. This was confirmed on abdominal scan. The pregnancy proceeded uneventfully. The patient was hospitalized at 35 weeks of gestation with pregnancy induced hypertension and oedema of feet. She was delivered at 36.5 weeks of gestation by caesarean section following spontaneous rupture of membranes. Birth weight of the babies was 2.1 kg. and 2.28 kg.

DISCUSSION:

IVF and GIFT are established techniques of alleviating infertility in selected cases (Leeton et al 1987, Asch et al 1988) We performed the combination of GIFT and IVF in a couple with male factor infertility, presence of seminal antisperm antibodies and pelvic endometriosis. Selection of subjects for this combined technique depends on several factors. GIFT was selected due to patent tubes and asthenospermia so that the gametes could be repositied in a natural environment. Supernumerary oocytes were fertilized in vitro, both the steps of fertilization and cleavage were documented in 2 embryos of which a healthy dividing embryo was transferred. The number of which a healthy dividing embryo was transferred. The number of gametes and embryos transferred was 5, as pregnancy rates increase with increased gametes or embryos replaced until 5 after which there is no advantage in replacing more (Penzias et al 1991) A double transfer has been recommended by several authors (Lewin et al 1989) for IVF/ET procedures. It has several advantages. Firstly it decreases the asynchrony between the endometrium and the embryos. Secondly it is thought that insertion of the transfer catheter may cause some degree of

decidualization of the endometrium which is helpful for implantation subsequently. The earlier implantation. In this case, the embryo from the IVF/ET procedure would be repositied in the uterus first and the gametes through GIFT would reach the endometrial cavity about 4 days after fertilization.

We preferred the technique of GIFT and IVF over PROST (pronuclear stage embryo transfer) to avoid anaesthesia twice and 2 surgical procedures as with PROST. With PROST the efficiency beyond the pronuclear stage is not known. This is more applicable in male factor infertility where fertilization and cleavage may be delayed or defective. Besides the pregnancy rate for IVF and GIFT combined (31%) compares favourable to PROST (27%) (Medical Research International 1991) Another advantage of the combination technique is that selection of the best gametes and the best embryos is possible and this improves pregnancy rates. This combination technique would be particularly useful if the oocytes obtained are of varying maturity, in which case only those which are mature may be transferred through the GIFT procedure. The remaining oocytes could be matured in vitro and the healthy preembryos transferred only optimum number of embryos and gametes (upto 4) as the incidence of multiple pregnancy would otherwise increase with no added benefit.

This is to our knowledge the first reported success of a pregnancy the IVF/GIFT combination method in India.

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HYPERKALCAEMIA: A COMMON ENDORINE
 THEBAG INFERTILITY

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SUMMARY

One hundred and thirty-eight (138) women with primary or secondary sterility were investigated for prolactin (PRL) elevation. An overall incidence of hyperprolactinaemia was found to be 24.7% in our study. Forty-two percent (31.2% of 302, 27.7% and 17.4% of women with raised PRL but galactorrhoea, secondary amenorrhoea, polycystic ovarian disease (PCOD), oligomenorrhoea and primary sterility respectively. Serum prolactin levels (7) along with PRL estimations were carried out in 19 primary sterility cases on day 7 after ovulation. Five of them (26.3%) had transient hyperprolactinaemia i.e. their prolactin level PRL was normal and raised PRL was elevated. From the present study we conclude that all females with primary or secondary sterility irrespective of their menstrual function should be screened for hyperprolactinaemia and those with transient or stress related hyperprolactinaemia might be considered for bromocriptine therapy.

to be associated with galactorrhoea, with disturbance of the menstrual cycle such as amenorrhoea, oligomenorrhoea and with both male and female infertility - including some testicular hypofunction. Evidence now suggest that elevated PRL levels may even play a role in premenstrual dysphoric disorder, PCOD and osteoporosis. Present study was undertaken to find out possible causes of PRL elevation and its association with menstrual disorders.

MATERIALS & METHODS :

One hundred and thirty eight females with a history of infertility were referred to our clinic for endocrine investigations. Of these 68 had

INTRODUCTION : Prolactin is unique among the anterior pituitary hormones in at least two respects : it is the only one under tonic inhibitory control by the hypothalamus and its actions are not limited to just one or a few physiologic events. (1980). As a result of this clinical abnormality we most likely to occur when there is loss of the inhibitory control and the consequences - while sometimes subtle - are apt to be seen in a wide range of clinical settings.

Attention in PRL levels in females are known to be elevated in the following conditions :
 1. Physiological elevation in pregnancy, lactation, and during the postpartum period.
 2. Elevation in response to stress, pain, and certain drugs.
 3. Elevation in response to certain endocrine disorders such as hypothyroidism, acromegaly, and Cushing's disease.
 4. Elevation in response to certain neoplasms, particularly of the hypothalamus and pituitary gland.