GYNAECOLOGY

Factors Affecting IVF Implantation Rates in Patients with Tubal Disease

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ABSTRACT

Objective   To determine which types, severities and causes of tubal disease affect implantation rates with in vitro fertilization (IVF).

Design   Retrospective study.

Setting   Reproductive Biology Unit, The Royal Women Hospital, Melbourne, Australia.

Subjects   A total of 165 patients treated between 1985 and 1995 with IVF for tubal disease were studied. The hospital and doctors' records were surveyed and information coded for the following: site of tubal obstruction, size of hydrosalpinx, density of pelvic adhesions, causes of tubal disease and surgery performed for tubal disease.

   IVF was performed and surplus embryos were frozen. Implantation was defined as the presence of an intrauterine fetal heart on transvaginal ultrasound scanned four weeks after embryo transfer.

   Differences of implantation rates were compared by Chi-square tests and the significance of groups of factors affecting implantation rates were analyzed by multivariate logistic regression.

Results   A total of 1300 embryos were transferred and 52.7 % of these were frozen thawed embryos. There were 67 clinical pregnancies with 80 fetal hearts from a total of 680 transfers (9.9 % per transfer). The average implantation rate was 6%. The implantation rate was significantly higher in patients with cornual obstruction (10.6%) compared with the other patients (6%). Logistic regression analysis indicated that frozen pelvis and salpingectomy also significantly affected implantation rates.

Conclusion   Pelvic inflammatory disease did not appear to be the main adverse factor in reducing implantation rates of women with tubal disease. Cornual obstructions were associated with significantly higher implantation rates and these were also marginally higher with frozen pelvis and lower after bilateral salpingectomy.

Key words :   tubal disease, implantation rate, in-vitro fertilization

Uterine tubal disease is the most common indication for IVF.[1] It is often the consequence of pelvic inflammatory disease, endometriosis, tubal ectopic pregnancy or pelvic surgery performed for other reasons. We have found the implantation rates are lower in women with tubal disease than in patients with other causes of infertility and this has also been reported by other groups.[2] A negative impact of hydrosalpinx on success rates has also been found.[3] The aim of this study was to determine whether the type, severity or cause of tubal disease affect implantation rates after IVF.

Materials and Methods

Patients treated on the IVF program through the public clinic at the Royal Women's Hospital were studied retrospectively. The 165 patients with tubal disease commenced IVF treatment between 1985 and 1995; most of the IVF was performed after 1990. They had diagnostic pelvic assessments by laparoscopy, hysteroscopy, hysterosalpingogram or pelvic sonogram before IVF. The tubal disease was diagnosed from the presence of any of the following: tubal adhesions, tubal obstruction or hydrosalpinx.

All informations in the hospital and doctors' records were recruited for the analysis. The study included site of tubal obstruction (cornual, midtube of fimbrial), diameter of the hydrosalpinx (<0.5 cm, 0.5-1 cm and > 1 cm), and extent of pelvic adhesions (external to tube, peritubal or frozen pelvis). The causes of tubal disease were coded in two grades of primary and secondary causes including pelvic inflammatory disease, endometriosis, tubal ligation, and ectopic pregnancy. Tubal surgery performed was also coded: salpingolysis, salpingostomy and salpingectomy.

A variety of ovarian stimulation protocols were used over the time including clomiphene citrate, natural cycle, clomiphene plus human menopausal gonadotrophin (HMG), gonadotrophin releasing hormone agonist and HMG of follicle stimulating hormone (FSH) in short or long protocols.[2-7] Most oocyte retrievals were performed 36 hours after chorionic gonadotrophin injection by transvaginal ultrasound guided follicular puncture. Standard IVF procedures were then performed or ICSI if there was a significant sperm defect after July 1992. Embryos were cryopreserved in 1,2 propanediol and sucrose.[8] After 1990 no more than 2 high quality embryos were transferred at a time. Implantation was defined as the presence of an intrauterine fetal heartbeat on ultrasound scan four weeks after embryo transfer.

The effect of factors on the implantation rates were analyzed by Chi-square tests and maximum likelihood logistic regression analysis was used to detect the significance of groups of factors. Confidence limits (95%) for proportions were from Documenta Geigy Scientific Tables. P values of less than 0.05 were considered statistically significant.

Results

Table 1 shows the frequency of diagnostic procedures. All patients have had one or more test(s).

Table 2 shows general information about the patients. The age of the couple was similar to that of other IVF patients seen in the clinic. However, in contrast to other IVF patients without tubal disease, some had pregnancies although parity was not high. Associated sperm defects were present in 19% of patients whereas in the overall IVF program, 40% had a diagnosis of male factor infertility alone or combined with female factors. A total of 1300 embryos had been transferred after 332 IVF and/or ICSI cycles. More than half of the transfers were thawed cryopreserved embryos.

Table 3 shows the type and extent of tubal pathology. The pathologic findings were found more frequently on the left than the right tube. Hydrosalpinx were present in about one quarter of the tubes. Pelvic inflammatory disease was the most frequent primary cause of the tubal disease (Table 4). Surgery had been attempted in a number of patients but salpingectomy was the most common procedure.

There were 67 clinical pregnancies with 80 fetal hearts detected by ultrasound from 680 transfers of 1300 embryos. The clinical pregnancy rate was 9.9% (95% CL 8-12%) per transfer. The fetal heart

implantation rate was 6.2% (95% CL 5-8%). Analysis of individual factors affecting implantation rates showed that cornual obstruction was significant by Chi-square analysis. The implantation rate (10.6%, 95% CL 7-16%) being significantly higher with this condition than with other causes of tubal disease. When other factors were taken into consideration by logistic regression analysis the implantation rates were significantly higher with frozen pelvis and significantly lower with bilateral salpingectomy. The other factors in the logistic regression model were gravidity, total fertilizations and previous IVF implantation as positive factors while number of treatment cycles, female age and embryo grade (the higher the grade the worse the embryo quality) were negative factors (Table 5).

Discussion

We found no effect of a variety of factors on implantation rates including type of stimulation protocol and whether fresh or thawed embryos were transferred. The implantation rate in the IVF program was the same with ICSI as with standard insemination in vitro.[6]

Pelvic pathology was found to be more on the left side than on the right side. It has been postulated that a higher frequency of damage to the left adnexa may result from the closeness to the rectosigmoid bowel.[9]

The higher implantation rates with cornual obstruction may be explained by false positive diagnosis as it has been reported this may occur in up to one fifth of patients.[10] On the other hand true cornual obstructions might promote intrauterine implantation.[11] In the early days of IVF, Steptoe suggested that operation that occlude the tubes of the uterotubal junction might be useful in preventing ectopic pregnancy which has a higher incidence after IVF in women with tubal disease.[12]

The finding of higher implantation rates with frozen pelvis may be explained by the fact that 43% of the patients with frozen pelvis had this developing after gynecological surgery and thus these patients may

have less tubal and uterine pathology to impair implantation.

The finding that salpingectomy had a negative impact on implantation rates in this group of patients may result from poor uterine perfusion.[13] Interestingly we could not confirm a negative effect of hydrosalpinx on implantation rates as reported by others.[3,14] However, because there were only 165 patients in the present study it is possible that such findings may be missed because of inadequate sample size.

These results indicate that women with severe tubal disease not associated with cornual obstruction or frozen pelvis from the post operative adhesions have reduced implantation rates explicitly. The impaired implantation does not appear to be explained by the cause of the tubal disease of whether or not hydrosalpinx are present. It is possible that the mechanism is related to other factors than the anatomical abnormalities. For example, antiphospholipid syndrome has been associated with organic pelvic disease. This requires further investigation. However, it is important because such a condition might be treated with heparin and aspirin.[15]

Overall, we conclude that pelvic inflammatory disease does not appear to be the main adverse factor in reduced implantation rates in women with tubal disease. Implantation rates were marginally higher with frozen pelvis and lower after bilateral salpingectomy. Patients with cornual obstructions have significantly higher implantation rates.

Table 1. Preivf pelvic assessment

Laparoscopy	81.2 %
Hysteroscopy	30.3 %
Hysterosalpingogram	21.2 %
Pelvic ultrasonogram	6.1 %

Table 2. Patient characteristics. Mean and standard deviation, number or percentage (n=165)

Female age	32 ± 4.5 years
Male age	34 ± 5.1 years
Gravity	1.9 ± 1.6
Parity	0.8 ± 1.1
Sperm defect (%)	19
IVF	294 cycles
IVF - ICSI	28 cycles
Number of oocyte retrievals/cycle	2.3 ± 1.5
Number of ET (fresh & thaw)	4.9 ± 4.5
Total embryos transferred	1300
Thawed embryos transferred (%)	52.7

Table 3. Tubal pathology (n=165)

Pathology	Right (%)	Left (%)	Bilateral (%)
Tubal obstruction			
Cornual (32/165)	34.8	39.4	25.8
Fimbrial (46/165)	34.8	44.6	20.6
Hydrosalpinx (63/165)	37.0	40.8	22.2
Adhesions			
Frozen pelvis (28/165)	37.8	42.2	20.0

Table 4. Causes and treatments

Causes	PID (%)	Ectopic Pregnancy (%)	Tubal Ligation (%)
Primary (136/165)	80.0	13.3	6.7
Secondary (29/165)	41.4	58.6	-
Surgery	**Right (%)**	**Left (%)**	**Bilateral (%)**
Salpingectomy (53/165)	35.7	36.9	27.4

Table 5. Logistic regression model of implantation rates

Factors	Coefficient (SE)	P-value
Number of cycles	-0.250 (0.052)	< 0.001
Gravidity	0.283 (0.081)	< 0.001
Cornual obstruction	0.65 (0.194)	0.001
Total fertilizations	0.044 (0.016)	0.007
Female age	-0.083 (0.032)	0.010
Previous implantation	0.563 (0.221)	0.011
Frozen pelvis	0.443 (0.214)	0.038
Salpingectomy	-0.887 (0.421)	0.035
Average embryos grade	-0.587 (0.243)	0.016

SE= Standard Error

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