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The impact of ovarian cystectomy on ovarian response to stimulation during in-vitro fertilization cycles

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This study was carried out to investigate whether ovarian cystectomy interferes with follicular recruitment and the number of oocytes retrieved in an in-vitro fertilization (IVF) cycle. Patients who had previously undergone unilateral ovarian cystectomy (n = 90) and control patients (n = 90) with no history of ovarian surgery were included in our study. The parameters compared were the number of follicles recruited and the number of oocytes obtained from each ovary. In patients who had undergone surgery, the normal ovaries recruited a significantly higher number of follicles ($P < 0.001$) and yielded a significantly higher number of oocytes ($P < 0.001$) compared with the contralateral ovaries which had undergone cystectomy. In the control patients, no significant differences were identified between the left and right ovaries. These results demonstrate that ovarian cystectomy reduces follicle and oocyte numbers in ovulation induction cycles.

Key words: cystectomy/folliculogenesis/IVF/oocytes/ovaries

Introduction

Ovarian stimulation is universally used in protocols for in-vitro fertilization (IVF) and embryo transfer. It increases the number of follicles and oocytes so that there are more embryos to choose from for both fresh and frozen–thawed embryo transfers. The transfer of more than one embryo is thought to increase the chance of pregnancy (Edwards and Steptoe, 1983). A number of previous studies have analysed the ovarian response and outcome of IVF cycles in patients who have had a unilateral oophorectomy. To our knowledge, this is the first controlled study reporting the effect of previous surgery for benign ovarian cysts on ovulation induction in IVF and embryo transfer cycles.

Materials and methods

A total of 90 consecutive patients were studied (mean ± SD age, 32.40 ± 2.25 years) who had undergone unilateral cystectomy and who had no history of surgery on the contralateral ovary. The indications for surgery were simple cyst (n = 52), endometrioma (n = 36) and dermoid cyst (n = 2). A further 90 consecutive patients (mean ± SD age, 33.30 ± 2.24 years) who had not undergone ovarian surgery, matched for age and treatment method, were studied as a control group. The women in both groups underwent IVF and embryo transfer treatment between 1988 and 1994. A long down-regulation protocol using the gonadotrophin-releasing hormone (GnRH) agonist buserelin (Suprefact; Hoechst, Hounslow, UK), 500 μg s.c. daily, commencing on day 1 of the cycle, was used. When pituitary down-regulation had been achieved, as shown by the absence of ovarian activity and a thin endometrium, the administration of human menopausal gonadotrophin (HMG; Pergonal; Serono Laboratories, Welwyn Garden City, UK) was commenced. The dose of HMG was adjusted according to the patient's age (two ampoules/day at <35 years; four ampoules/day at 35–37 years; six ampoules/day at ≥38 years), basal follicle stimulating hormone (FSH) concentration and previous response. The woman's response was assessed using ovarian and endometrial ultrasonography from day 8 of HMG therapy. The dose of HMG was increased if there was a poor follicular response. When the mean diameter of the largest follicle reached 18 mm, 10 000 IU human chorionic gonadotrophin (HCG) were administered and the GnRH analogue stopped. Transvaginal ultrasound-directed oocyte recovery was performed 34 h later. Embryo transfer was carried out ~48 h after oocyte recovery. The cycle parameters compared were the number of follicles recruited and the number of oocytes obtained from each ovary. Paired t-tests were used for a statistical analysis of the data.

Results

In the study group, a significantly lower number of follicles (6.33 ± 5.22 versus 8.93 ± 5.14, $P < 0.001$) were recruited and a significantly lower number of oocytes (4.34 ± 3.80 versus 6.02 ± 4.11, $P < 0.001$) were collected from the cystectomized ovaries than from the normal ovaries (Table I). In the study group, a lower number of follicles (5.47 ± 3.69 versus 7.76 ± 5.89, $P = 0.032$) were recruited and a lower number of oocytes (3.71 ± 2.94 versus 5.50 ± 4.34, $P = 0.043$) collected from the ovaries that had had endometriomas removed compared with the ovaries that had had simple cysts removed (Table II).

In the control group, no significant differences in the number of follicles recruited and the number of oocytes retrieved were found when the left and right ovaries were compared (Table III).

Discussion

Previous studies comparing patients with one ovary and two ovaries receiving IVF treatment have yielded variable results (Boutteville *et al.*, 1987; Dodds *et al.*, 1987; Penzias *et al.*, 1993). Animal studies have shown that there is a compensatory hypertrophy of the remaining ovary, which may be attributed to the stimulatory effect of the additional FSH that becomes available to the ovary after unilateral oophorectomy (Biggers *et al.*, 1962). Penzias *et al.* (1993) suggested that there may

Table I. Normal and cystectomized ovaries in the study group (n = 90) (values are means ± SD)

	Normal ovaries	Ovaries after cystectomy	P value
No. of follicles	8.93 ± 5.14	6.33 ± 5.22	<0.001
No. of viable oocytes[a]	6.02 ± 4.11	4.34 ± 3.80	<0.001

[a]Cumulus–oocyte complexes.

Table II. Simple ovarian cystectomies versus removal of the endometriomata in the study group (n = 90) (values are means ± SD)

	Endometrioma (n = 36)	Simple cyst (n = 54)	P value
No. of follicles	5.47 ± 3.69	7.76 ± 5.89	0.032
No. of viable oocytes[a]	3.71 ± 2.94	5.50 ± 4.34	0.043

[a]Cumulus–oocyte complexes.

Table III. Patients with no ovarian surgery (control group; n = 90) (values are means ± SD)

	Left ovary	Right ovary	P value
No. of follicles	8.72 ± 4.99	9.08 ± 6.40	NS
No. of viable oocytes[a]	6.44 ± 4.35	6.47 ± 4.79	NS

NS = not significant.
[a]Cumulus–oocyte complexes.

be a factor, which could be a member of the activin/inhibin family or an insulin-like growth factor binding protein, which places a ceiling on ovarian response in a dose-dependent manner so that a woman with two ovaries capable of producing a certain number of oocytes may continue to do so when one ovary is removed. Boutteville *et al.* (1987) showed that patients with two ovaries recruited a higher number of follicles and yielded more oocytes than patients with one ovary, but the pregnancy rates were not significantly different.

However, a more common problem in clinical practice is that of patients with previous ovarian surgery for the removal of ovarian cysts. It has been shown previously that ovarian surgery may lead to adnexal adhesions (Darling, 1982). Here, our study has shown that it also has an adverse effect on ovarian response to stimulation with gonadotrophins and thus upon the results of fertility therapy. Ovarian cysts are common but the majority are benign. So careful consideration should be taken before operating on ovaries in patients who may in the future wish to conceive. In a study by Herrmann *et al.* (1987), the predictive value of a non-malignant diagnosis for ovarian ultrasonography was 95.6%. They proposed that the sonographic reassessment of masses with patterns suggesting benign disease may be an alternative to immediate surgery. Ultrasound-guided puncture of ovarian cysts has been shown to be an alternative to surgery in selected cases (De Crespigny *et al.*, 1989). It has been recommended for unilocular clear cysts, but multilocular and echogenic cysts may need further evaluation. Recently, transvaginal colour flow imaging has been used to identify potentially malignant masses (Bourne *et al.*, 1989). The absence of colour (neovascularization) and a high pulsatility index were used to exclude invasive ovarian cancer.

In our study, 36 patients underwent cystectomy for endometriomata. Our results (Table II) suggest that the removal of endometriomata causes more damage to the ovaries than the removal of simple cysts. This should be borne in mind in the management of endometriomata. Because small endometriomata (<1 cm in diameter) are treated equally well by conservative surgery (Schenken and Malinak, 1982) and hormone therapy (Butler *et al.*, 1984), the latter would therefore seem more appropriate. However, growth of an endometrioma may irreparably damage ovarian function. So small endometriomata should be kept under review and surgery performed if growth is observed.

Previous studies have shown that baseline ovarian cysts have no negative impact on IVF cycles (Karande *et al.*, 1990). The routine aspiration of such cysts has not improved results (Rizk *et al.*, 1990). Our study shows that ovarian surgery for benign cysts significantly reduces folliculogenesis. The implications of our study are very important. Ovarian surgery should be avoided in those who wish to conceive in the future. If surgery is contemplated, patients should be counselled regarding the adverse effects of such surgery. If they require IVF treatment after ovarian surgery, higher doses of HMG may be needed regardless of their age, so that more embryos are available.

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