Clinical outcome after unilateral oophorectomy in patients with polycystic ovary syndrome

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The objective of this study is to report retrospectively on the clinical outcome of unilateral oophorectomy in 14 women with polycystic ovary syndrome who had undergone this treatment 14–18 years ago in our hospital for clomiphene citrate-resistant anovulation and long standing infertility or for severe hirsutism. The main outcome measures were menstrual cycle, pregnancy, hirsutism, testosterone concentrations, and premature ovarian failure. Unilateral oophorectomy restored regular menstrual cycles in 12 of the 14 patients. Thirteen years later, nine out of 12 patients still had regular menstrual cycles. Ten patients wished to become pregnant. Seven of them conceived spontaneously. Eleven patients complained of severe hirsutism. After unilateral oophorectomy, hirsutism regressed subjectively in six. Testosterone blood concentrations decreased significantly within the first year after unilateral oophorectomy in 11 patients. None of the women entered menopause within 14–18 years after surgery. Our results indicate that unilateral oophorectomy restores ovulatory function for many years in the majority of patients and does not result in premature ovarian failure. However, unilateral oophorectomy should not be recommended as a standard treatment for clomiphene citrate-resistant patients with polycystic ovary syndrome.

Key words: hirsutism/hormone status/menstrual cycle/polycystic ovary syndrome/pregnancy/premature ovarian failure

Introduction

In 1982, unilateral oophorectomy was proposed as a surgical treatment for ovulation induction and hirsutism in patients with polycystic ovary syndrome (PCOS) (Hamerlynck, 1982). In that study, unilateral oophorectomy resulted in restoration of ovulatory function in all 10 treated patients with PCOS; three out of five patients treated for primary infertility resistant to clomiphene citrate (CC) became pregnant within 1 year. Despite these encouraging results, unilateral oophorectomy was not accepted for the treatment of PCOS for three reasons. Firstly, it was felt that unilateral oophorectomy was unethical because it might lead to premature ovarian failure. Secondly, results of ovulation induction with gonadotrophins as well as results of in-vitro fertilization (IVF) improved. Thirdly, in 1984 laparoscopic electrocoagulation of the ovaries and in 1988 laparoscopic laser surgery of the ovaries were introduced as less invasive alternatives to bilateral ovarian wedge resection (Gjonnaess, 1984; Huber, 1988). The laparoscopic treatments proved to be highly effective in restoring ovulation in the majority of CC-resistant patients with PCOS (Kaaijk et al., 1995). However, restoration of regular ovulatory cycles in patients who do not conceive seems to be of short duration in the majority of patients (Armar et al., 1990; Gadir et al., 1990; Balen and Jacobs, 1994; Farhi et al., 1995).

Recently, we reported on the results of unilateral oophorectomy in three patients with PCOS who had been treated unsuccessfully with CC, gonadotrophins and IVF for many years and who had undergone unilateral oophorectomy for ovarian pathology (Kaaijk et al., 1997). Currently, 2–3 years after surgery, two of these patients are pregnant with their second child and the third patient, who had been exposed to diethylstilboestrol, still experiences regular ovulatory cycles. Unilateral oophorectomy, therefore, might have a long lasting effect on restoration of regular menstrual cycles.

To support this hypothesis, we evaluated the clinical outcome of unilateral oophorectomy in all patients with PCOS who were operated on 14–18 years ago in our hospital for treatment of CC-resistant anovulation and long standing infertility or for severe hirsutism.

Materials and methods

Data on menstrual cycle, fertility, changes in hirsutism and hormonal status of all patients with PCOS who had undergone unilateral oophorectomy as treatment for primary infertility or severe hirsutism were extracted from the records of our hospital; a total of 14 patients was operated on for these indications between 1978 and 1983.

Follow-up of these patients was accomplished by way of chart review. If the charts were not complete the patients were invited to visit our clinic. In this way, a complete follow-up was available in 12 patients. In two patients follow-up was limited to 1 and 2 years only.

Diagnosis of PCOS was based on menstrual cycle disturbances (oligomenorrhea or amenorrhea), elevated serum testosterone levels (>4.0 nmol/l), the absence of adrenal disease, and laparoscopic confirmation of polycystic ovaries.

In seven patients, the indication for unilateral oophorectomy was primary infertility. These patients failed to ovulate with CC in incremental doses up to 150 mg/day for 5 days during at least three treatment cycles. Three of these patients had been unsuccessfully treated with gonadotrophins. The remaining seven patients underwent unilateral oophorectomy because of severe hirsutism and menstrual cycle disturbances. The option of using an oral contraceptive for regulation of the cycle or a reversed sequential anti-androgen regimen...
for treatment of hirsutism had been rejected by these patients except for one patient who had previously been treated unsuccessfully with a reversed sequential anti-androgen regimen. Hirsutism was defined as excessive coarse hair on the face, the arms, the trunk and the thighs, and was assessed by a gynaecologist (J.H.). Possible drawbacks of unilateral oophorectomy were discussed with the patients and all patients gave their consent. A medical ethical committee did not exist in our hospital at the time of unilateral oophorectomy and approval was therefore not sought.

Unilateral oophorectomy was performed by laparotomy. In case of a difference in ovarian size, the larger ovary was removed. One patient showed extensive peritubal adhesions, only one tube being patent to dye. In this patient, unilateral oophorectomy was performed on the side of the blocked tube, in combination with lysis of the adhesions.

Histology of all removed ovaries showed a thickened ovarian capsule with multiple subcapsular cysts and a dense hyperplastic ovarian stroma.

**Results**

Table I summarizes the indication for unilateral oophorectomy, the age at unilateral oophorectomy, duration of infertility at the time of surgery, the hormone (testosterone, luteinizing hormone (LH) and follicle stimulating hormone (FSH)) concentrations of the patients before unilateral oophorectomy, the duration of follow-up, the age at present, the results concerning menstrual cycle and fertility, and the mean testosterone concentration in the first year after unilateral oophorectomy for each patient. Patients are numbered in chronological order of treatment.

**Menstrual cycle**

Following unilateral oophorectomy, menstrual cycles became regular (27–35 days) in 12 patients (85.7%) with biphasic body temperature charts and mid-luteal progesterone levels exceeding 20 nmol/ml in patients who wished to conceive. Nine patients menstruated regularly for at least 13 years.

Of the other three patients, one menstruated regularly after unilateral oophorectomy, but was lost to follow-up due to emigration 2 years after unilateral oophorectomy (patient no. 7), one relapsed to oligomenorrheic anovulatory cycles after 3 years and was additionally treated with CC and gonadotrophins (no. 3), and one relapsed to oligomenorrhoea after six regular cycles (no. 10). Five years after unilateral oophorectomy this patient became amenorrhoeic with FSH concentrations between 2.0 and 4.0 IU/l; she then started on oral contraceptives for cycle control.

In two patients the cycle remained irregular after unilateral oophorectomy. One patient remained irregular until 6 years after unilateral oophorectomy, after which she lost 40 kg weight and experienced regular cycles until the end of follow-up (no. 14). The other patient underwent hysterectomy in another hospital 1 year after unilateral oophorectomy because of persistent menorrhagia (no. 12).

**Pregnancy**

Six of the seven patients treated for primary infertility became pregnant during follow-up. Four patients conceived spontaneously at 2, 4, 6 and 12 months after unilateral oophorectomy (nos 5, 9, 4 and 8 respectively) and delivered four healthy babies. Patient no. 4 conceived again and delivered a second baby. Patient no. 5 conceived twice after delivery of her baby, but had two legal abortions, one for social reasons and one because of the onset of bowel cancer for which she had to be treated. The patient who showed extensive peritubal adhesions at surgery, conceived spontaneously 8 years after unilateral oophorectomy, but unfortunately miscarried (no. 13). One patient conceived through IVF–embryo transfer and delivered a healthy baby (no. 3).

One patient treated for primary infertility did not become pregnant. Persistent menorrhagia, as already mentioned, made her decide to have a hysterectomy (no. 12).
Three patients treated for hirsutism wished to become pregnant during follow-up. Patient no. 1 wished to become pregnant 7 years after unilateral oophorectomy. She conceived 2 months later. She conceived again spontaneously 3 years after the birth of her first child and had no further wish to become pregnant after the delivery of her second child. Patient no. 2 wished to become pregnant 5 years after unilateral oophorectomy, but did not conceive despite regular ovulatory cycles; diagnostic laparoscopy revealed bilateral tubal adhesions, which were not present at the time of unilateral oophorectomy; IVF–embryo transfer was unsuccessful. Patient no. 11 had a legal abortion 2 years after unilateral oophorectomy; 9 years after unilateral oophorectomy, she wished to become pregnant and conceived 4 years later; 1 year after birth of her first child she conceived again; however, intrauterine fetal death occurred at 34 weeks of amenorrhoea.

**Hirsutism**

Eleven patients had complaints of hirsutism before unilateral oophorectomy. Hirsutism regressed subjectively in six patients within the first months after surgery and remained so during follow-up (no. 1, 6–10). This regression was characterized by progressive slowing down of hair growth and by thinning and lightening of the hairs, which resulted in a reduction of shaving or depilating sessions. There was no disappearance of the terminal hairs in any of the hair sites except in patient no. 9 in whom hirsutism disappeared completely.

The five patients who did not notice any improvement of hirsutism were additionally treated with a reversed sequential anti-androgen regimen or with oral contraceptives. During these treatments hirsutism regressed, but discontinuation of the treatment showed an immediate increase in hair growth.

**Total testosterone serum concentration**

Data on testosterone concentrations before and after unilateral oophorectomy were available in 13 patients. Testosterone concentrations normalized in 10 patients within the first year after unilateral oophorectomy. In two patients, testosterone concentrations decreased but remained at a high level (nos 2 and 8). In one patient, testosterone concentrations increased after unilateral oophorectomy (no. 1). Testosterone concentrations in all 13 patients before and after unilateral oophorectomy were compared over a period of 3 years (Figure 1). Data from patients who became pregnant are included until pregnancy, and data for patients treated for hirsutism are included until they used oral contraceptives or a reversed sequential regimen.

Within the first year after unilateral oophorectomy, there was a significant (Mann–Whitney rank sum test, $P < 0.05$) reduction in circulating testosterone ($5.05 \pm 0.5$ versus $3.7 \pm 0.8$ nmol/l). After the first year, the mean testosterone concentration further declined but not significantly.

**Menopause**

The patients are presently 39–53 years old and none of them has entered menopause yet.

**Discussion**

This chart review reports on the clinical outcome of unilateral oophorectomy in patients with PCOS who had undergone this type of surgery between 1978 and 1983 in our hospital for long standing infertility or hirsutism. Although the number of patients is relatively small and the study is uncontrolled, the strength is that the follow-up is complete, apart from one patient who moved abroad.

The most interesting finding of this chart review is that unilateral oophorectomy restored regular menstrual cycles (27–35 days) and fertility for many years in the majority of patients. Although ovulation was not systematically evaluated in all 14 patients, ovulatory cycles were confirmed in all patients who wished to conceive.

An important finding is that none of the patients suffered from premature ovarian failure, indicating that the fear of this possible complication is probably not warranted.

Unilateral oophorectomy was not very effective in the treatment of hirsutism. Although some patients noticed a progressive slowing down of hair growth resulting in a reduction of shaving or depilating sessions, a quantitative method of scoring the hirsutism after surgery by a gynaecologist was not performed. This finding is in accordance to studies addressing the effect of bilateral ovarian wedge resection and laparoscopic ovarian surgery on restoration of ovulatory cycles. However, surgical treatment of one ovary in PCOS has been described earlier. In this study, unilateral laparoscopic ovarian diathermy was performed in four patients with PCOS resistant to CC (Balen and Jacobs, 1994). Postoperatively, three out of four patients ovulated, but within 4–6 months all patients were anovulatory again and none of the patients conceived, suggesting a transitional effect of unilateral laparoscopic ovarian diathermy on restoration of ovulatory cycles.

An important issue is how the duration of restoration of regular menstrual cycles after unilateral oophorectomy relates to that after laparoscopic electrocoagulation of both ovaries,
which is at this moment the surgical treatment of choice in CC-resistant patients with PCOS.

Three studies report on the long-term follow-up after laparoscopic electrocoagulation of the ovaries (Gjonnaess, 1994; Naether et al., 1994; Merchant, 1996). Unfortunately, in these studies the majority of patients disappeared from the study, leaving just a few patients of the inception cohort accounted for. Therefore, the results of these studies, mentioned below, might very well be biased.

Merchant (1996) reports on laparoscopic electrocoagulation in 74 patients with PCOS. Only 29 patients out of 74 were evaluated 3 years after treatment. All these patients still menstruated regularly.

Gjonnaess (1994) reports on laparoscopic electrocoagulation of 252 patients with PCOS. Only 51 patients out of 252 were evaluated 3 years after treatment. All these patients still menstruated regularly.

Similarly, Naether et al. (1994) report on the long-term follow-up in 206 patients after laparoscopic electrocoagulation, with only 53 patients included in a follow-up longer than 3 years. However, the number of patients that still menstruated regularly at follow-up is not reported.

These studies at least show that some of the patients maintain regular menstrual cycles for >3 years after laparoscopic electrocoagulation. Furthermore, all three studies report on patients who conceived twice or more, showing a prolonged treatment effect of laparoscopic electrocoagulation in these patients.

As at present no studies on long-term clinical effect of laparoscopic electrocoagulation with a complete follow-up are available, studies with a short-term but complete follow-up are of interest. There are four such studies treating a total of 111 patients (Armar et al., 1990; Gadir et al., 1990; Balen and Jacobs, 1994; Farhi et al., 1995). Out of 82 of these patients who had regular ovulatory cycles after treatment, 46 (56%) had relapsed to oligomenorrhea within 15 months of treatment.

On the basis of these uncontrolled studies, we have the impression that unilateral oophorectomy restores the menstrual cycle for a much longer duration compared to laparoscopic electrocoagulation of the ovaries.

How removal of one ovary causes resumption of regular menstrual cycles and spontaneous ovulation in the contralateral ovary remains an enigma. The working mechanism of laparoscopic electrocoagulation of both ovaries, however, is also unknown. Postoperative endocrine alterations after laparoscopic electrocoagulation, including a decrease in concentrations of LH, androstenedione and testosterone, suggest that reduction of ovarian hyperandrogenism plays an important role in restoring normal menstrual cycles in patients with PCOS (Doneski and Adashi, 1995). Laparoscopic electrocoagulation of both ovaries probably lowers the intra-ovarian androgen milieu, causing loss of androgen-induced follicular arrest in both ovaries. Consequently, follicular development resumes, followed by ovulation. A similar decrease of intra-ovarian androgen production probably does not occur after unilateral oophorectomy, suggesting that unilateral oophorectomy possibly corrects the ovarian pituitary feedback with the remaining ovary by decreased serum androgen concentrations due to elimination of the other androgen producing ovary. The finding that unilateral oophorectomy restores regular cycles for many years in most patients might then be explained by the large volume of androgen producing tissue that is removed.

In conclusion, our data show that unilateral oophorectomy is effective in restoring long-term ovulatory function. Despite these encouraging results it is obvious that unilateral oophorectomy cannot be recommended today as an ethically justified surgical treatment to restore ovulation in CC-resistant patients with PCOS. Nevertheless, we think that unilateral oophorectomy, preferably performed laparoscopically, might be considered in CC-resistant patients with PCOS in whom all treatment regimens, including laparoscopic electrocoagulation or laser surgery of the ovaries, have failed.

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References


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