A comparison of follicular response of ovaries to ovulation induction after laparoscopic ovarian cystectomy or fenestration and coagulation versus normal ovaries in patients with endometrioma

In a comparison of follicular responses to controlled ovarian hyperstimulation (COH) between normal ovaries and ovaries previously treated by different laparoscopic techniques for ovarian endometrioma in 65 patients with unilateral endometrioma, laparoscopic ovarian fenestration and coagulation was performed in 24 cases (group 1) and laparoscopic ovarian cystectomy in the other 41 (group 2). In 16 patients with bilateral endometrioma (group 3), cystectomy was done in one ovary and fenestration and coagulation in the contralateral side. The results indicate that the response of ovaries to COH after laparoscopic ovarian cystectomy or fenestration and coagulation was the same and that there was no difference in response to COH between normal ovaries and those operated on by the laparoscopic techniques mentioned above. (Fertil Steril® 2007;88:507–9. ©2007 by American Society for Reproductive Medicine.)

In general, laparoscopic surgery has been considered the method of choice for the treatment of ovarian endometrioma. However, the best laparoscopic approach for endometrioma is still controversial (1–5). While two clinical studies have shown that postcystectomy ovaries could produce a number of follicles comparable to that of normal ovaries when stimulated with gonadotropins (6, 7), others have suggested that ovarian cystectomy in cases of endometriomas could be deleterious for residual normal ovarian cortex (8–10). Therefore, some investigators prefer to fenestrate endometriomas and follow up by burning the cyst wall using a laser or electrocoagulation (8). However, most of the above-mentioned investigations were retrospective studies, and in some the patients who had been operated on were compared with those who had not been operated on and who were being used as a control group, and this can cause bias. Also, there is no controlled base study in the literature that compares the response of ovaries to COH after different methods of laparoscopic surgery for endometrioma.

In a prospective randomized-design study, we compared the ovary that had been operated on (whether by cystectomy or fenestration coagulation) with the unoperated contralateral one of the same patients with respect to COH. In addition, in those patients who have bilateral endometrioma, the two different techniques were applied on either side to judge the results on each side after COH. From January 2002 to September 2005, 81 patients with infertility and ovarian endometrioma that was diagnosed by transvaginal ultrasound who were operated on by two different techniques of laparoscopy underwent ovulation induction with one single method at two universities and private hospitals. This study was approved by the Shiraz University of Medical Sciences Institutional Review Board.

Patients were divided into three groups: patients in groups 1 and 2 with unilateral endometrioma underwent fenestration and coagulation or the cystectomy technique, respectively. Group 3 patients had bilateral endometrioma, and ovarian cystectomy was done on one side, and fenestration coagulation on the other. The number of patients who were referred for COH after surgery was 24 in group 1, 41 in group 2, and 16 in group 3. The method of randomization for patients with unilateral endometrioma was computerized numbering.

Patients with bilateral endometrioma were selected for this study only if the sizes of their endometriomas were similar bilaterally. Those patients with endometrioma (≥3 cm) and infertility and no previous pelvic operation were included in this study only if other causes of infertility had been ruled out and if they had been referred for COH. No patient with a previous IVF cycle was chosen for this study, and all patients had a body mass index within the normal range.

The method of laparoscopy has been described elsewhere (11). All laparoscopic operations were performed by the first author. Endometriosis was classified according to the revised American Fertility Society (AFS) classification at the time of laparoscopy (12, 13). All patients had day 3 FSH assay before and one cycle after the operation, which showed normal ovarian reserve.

In this study, a total of 149 cycles were evaluated. Each patient had at least two COH cycles if pregnancy did not
occur in the first cycle. Controlled ovarian hyperstimulation was performed for all of the patients with the same method for at least 2 months after surgery. Clomiphene citrate (Iran Hormone, Tehran, Iran) was started in a 100 mg/daily dose from day 5 for 5 consecutive days of menstrual cycle; hMG (Menogon; Ferring, Mannheim, Germany) was injected from day 8 of menstrual cycle (2 ampules/day). Ultrasound follicular monitoring was performed from day 10 or 11 of each cycle, and when two follicles with an average diameter ≥18 mm were detected, ovulation was induced with 10,000 units of hCG, and 34–36 hours later, IUI with washed sperm was performed. The number of mature follicles with an average diameter ≥18 mm developed in each ovary just before ovulation or hCG injection was noted.

Each group was comparable in terms of age, duration of infertility, and type of menstruation. The average age was 24.4 years in group 1, 26.2 years in group 2, and 25.7 years in group 3. The average duration of infertility was 5.9 years in group 1, 5.1 years in group 2, and 4.6 years in group 3. There was no significant difference among the three groups in operative findings such as AFS score and size of endometriomas. These figures were, respectively, 43 and 3.6 cm in group 1, 45 and 4.4 cm in group 2, and 60 and 3.8 cm in group 3.

The number of dominant follicles from diseased and normal ovaries in groups 1 and 2 were comparable. In the third group, there was no difference between ovarian follicular responses in both sides. Between the three groups, data were analyzed by the Kruskal-Wallis test, and no significant difference could be detected (Table 1). There was no statistically significant difference among the three groups with respect to pregnancy rates, which were 30% in group 1, 35.7% in group 2, and 28.2% in group 3 ($P = .681$). It is valuable to note that the pregnancy rate was determined after COH in all groups, and if we had observed the patients for a longer duration of time and more COH cycles, the pregnancy rates might have shown an increase and the difference could have been detected in the three groups.

There are different ideas about the association between the type of laparoscopic technique used and the pregnancy rates in infertile women. Most of these studies were retrospective and not randomized clinical trials. However, there are two prospective randomized controlled trials comparing cystectomy of endometrioma with fenestration and coagulation. The first study was a randomized controlled trial that demonstrated that the pain and subfertility caused by ovarian endometrioma were improved more by cystectomy than by fenestration and coagulation (14). Moreover, the second one showed that laparoscopic cystectomy of endometriomas is a better choice than fenestration and coagulation because the former technique leads to a lower recurrence of signs and symptoms and a lower rate of reoperation and a higher cumulative pregnancy rate than the latter (11).

The choice of using the right laparoscopic technique in the surgical management of endometriotic cysts for better response to COH remains controversial. The vascular system of the gonad is important in terms of its ability to respond to gonadotropin stimulation. That is why gentle and careful bipolar coagulation of the bleeders after stripping the pseudocapsule during cystectomy or after fenestration of the endometrioma is of paramount importance. Moreover, the surgeon should avoid coagulation of the remaining ovarian stroma and the ovarian hilus (7).

In a recent study, the response of ovaries of 40 women (132 monitored cycles) younger than 35 years of age who underwent cystectomy were compared with the response of uninvolved normal ovaries (6). In this study, reduced follicular response in natural and clomiphene citrate–stimulated cycles was reported but not in gonadotropin-stimulated cycles. In another retrospective investigation, 32 patients with unilateral ovarian endometrioma were previously treated with cystectomy and

### Table 1

Mean number of dominant follicles achieved during COH after using different methods of laparoscopy for treatment of endometrioma.

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of cycles</th>
<th>No. of follicles in postcystectomy ovaries*</th>
<th>No. of follicles after fenestration and coagulation</th>
<th>No. of follicles in normal ovary</th>
<th>$P^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
<td>3.2 ± 1.1</td>
<td>2.6 ± 1.6</td>
<td>2.8 ± 1.6</td>
<td>.15</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>2.9 ± 1.1</td>
<td>3.2 ± 1.7</td>
<td>3.2 ± 1.7</td>
<td>.88</td>
</tr>
<tr>
<td>3</td>
<td>39</td>
<td>3.05 ± 1.3</td>
<td></td>
<td></td>
<td>.42</td>
</tr>
</tbody>
</table>

*a Values are mean ± SD.

*b Data were analyzed by paired t-test.

underwent 38 cycles of COH. This study demonstrated that surgery for ovarian endometrioma may damage ovarian reserve. It potentially results in a poor ovarian response to COH, compared with the response of the contralateral normal ovary in the same individual (9).

Also, another retrospective study in 32 patients and 46 cycles showed that excision of the endometriotic cyst was associated with a significant reduction in ovarian reserve (10).

On the other hand, one study demonstrated that laparoscopic ovarian cystectomy of endometriomas does not affect the ovarian response to gonadotropin stimulation. In this study, 39 patients who underwent laparoscopic ovarian cystectomy were compared with 39 patients with tubal-factor infertility after IVF cycles (7). Another study supported this idea and showed that ovarian response to stimulation by gonadotropins was not reduced (15). Two other studies reveal that the number of mature oocytes in patients with endometrioma was the same between those who were operated on and those who were not (16, 17). In fact, the number of oocytes retrieved from the affected ovary was similar to the number retrieved from the nonaffected contralateral one (17). In our study, the response of ovaries after laparoscopic cystectomy to COH was comparable with the response of contralateral normal ovaries of the same patient in 70 cycles of COH (P=.88).

Because of these conflicts, it has been proposed that cystectomy be replaced by fenestration and coagulation of the inner wall of the endometriotic ovarian cyst. One study that compared ovarian response to gonadotropins in IVF cycles did not show any difference in the number of oocytes retrieved after different methods of laparoscopic surgery for endometrioma. However, operated ovaries were not compared with the contralateral normal ones (15). In our study, the responses of one ovary to COH after fenestration and coagulation and of the normal one in 40 cycles were the same (P=.15). There is no study that compares follicular response to COH in patients who had bilateral endometrioma and were treated with different laparoscopic techniques. In our study, there was no difference between ovaries that were operated on by the two different methods in response to 39 COH cycles in patients with bilateral endometrioma (group 3; P=.42).

Overall, there is no significant difference between the follicular response of diseased ovaries to COH in patients who underwent unilateral cystectomy or fenestration-coagulation compared with that of contralateral normal ovaries. In the group with bilateral endometrioma operated on by the two different methods, the response of ovaries to COH was the same. Therefore, it can be concluded that there is no difference between the two methods of laparoscopy regarding ovarian response to COH. However, more studies in a larger number of patients seem to be required to make a certain judgment.

REFERENCES