Hysteroscopic resection of submucosal myomas in patients with infertility

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BACKGROUND: Submucosal myomas are associated with infertility, and may be treated by hysteroscopic resection. Improvement of the menstrual pattern after surgery has been examined and compared with pregnancy rate in a group of menorrhagic women with primary (n = 24) and secondary (n = 35) infertility. METHODS: The entire patient group (n = 59) was managed between January 1990 and September 1998. The submucosal myomas were intracavitary (n = 15), intramural class 1 (n = 34) and intramural class 2 (n = 10), and none was multiple submucosal myoma. The mean (± SD) age was 36.6 ± 4.6 years; mean myoma size was 24.5 ± 13.3 mm; mean duration of the procedure was 40 ± 23 min; and mean follow-up was 26 ± 18.8 months. Thirty-five patients had one or more associated infertility factors. RESULTS: An improvement in clinical symptoms was observed in 62% of patients. Sixteen patients (27%) conceived, and of these only six (10%) delivered at term. The pregnancy rate was significantly better when myoma was the exclusive aetiology of infertility (41.6%), and when the lesion was ≥50 mm in size (57.1%). CONCLUSIONS: Hysteroscopic myomectomy appears safe, and is effective in the control of menstrual disorders. However, the effect on infertility seems limited, particularly in terms of delivery rate. The advanced age of the patients may partly explain these results.

Key words: hysteroscopy/infertility/myomectomy/pregnancy rate/submucosal myomas

Introduction

Leiomyomas of the uterus are the most common solid pelvic tumours in women, and are present in ~20 to 25% of women aged 35 years. Leiomyomas are associated with infertility, the causal relationship in this regard appearing to be more evident for submucosal myomas. Indeed, leiomyomas represent an increasing medical problem in women attempting to conceive at a more advanced age, when the rate of development of these lesions is also increased.

In their submucosal localization, myomas can be treated exclusively using surgical procedures, and they may be accessible by operative hysteroscopy—the standard surgical approach. Several retrospective studies of small cases series were published during the 1990s (Donnez et al., 1990; Goldenberg et al., 1995; Giatras et al., 1999; Varasteh et al., 1999; Vercellini et al., 1999) demonstrating successful reproductive outcome after hysteroscopic removal of submucosal myomas in infertile women. Several hypotheses have been suggested to explain how submucosal myomas cause infertility or repeated abortions, but none is definitive. The aim of this retrospective study was to assess the pregnancy rate compared with the improvement of menstrual pattern in menorrhagic women after hysteroscopic resection of submucosal myomas performed in infertile patients.

Materials and methods

The study population included 59 patients who had been attempting to conceive for >2 years before hysteroscopic resection of submucosal myomas was undertaken. Preoperative diagnostic hysteroscopy and/or pelvic transvaginal sonography was performed in all cases to determine the size, number and localization of the lesions. The 59 women included in this series had no associated intramural or subserosal myomas. In all cases, sonographic evaluation of the myomas demonstrated a distance of ≥3 mm between the serosa and the myoma. The submucosal myomas were intracavitary (n = 15), intramural class 1 with largest diameter in the cavity (n = 34), and intramural class 2 (n = 10) (Donnez et al., 1994). No multiple submucosal myomas (class 3) were identified in this series of patients.

A routine infertility evaluation including at least serum concentration of FSH, LH and oestradiol on the third day of the cycle, hysterosalpingography and the partner’s semen analysis was performed in all subjects.

Twenty-seven of the women (46%) also complained of heavy menstural bleeding diagnosed on a pictorial blood loss assessment chart (Higham et al., 1990) for evaluating menstural flow.

Preoperative medical treatment was not used. All 59 women underwent myomectomy by operative hysteroscopy under general anaesthesia, using a rigid 26 Fr resectoscope (Karl Storz GmbH & Co., Tuttingen, Germany) and a 12° fore-oblque telescope. The uterine cavity was distended with 1.5% glycine solution (Uro 3000 Glycocoll 1.5%; Laboratoires Aguettant, 69006 Lyon, France). The
glycine was flushed at a flow rate of 250 ml/min and a pressure of 80–100 mmHg; a vacuum of ~30 to ~40 mmHg was applied for suction. Fluid balance was recorded by measuring the infused and drained fluid from the continuous flow resectoscope, taking into account the fluid lost during removal of the hysteroscope to collect the resected pieces of tumour from the operative field into a calibrated pouch. None of the patients suffered from fluid overload (>1000 ml) or electrolyte imbalance.

Complete resection was attempted in all subjects. The operative technique remained unchanged during the 9-year period of the study, although as the surgeons’ skill increased the number of repeat procedures needed to complete the resection was reduced.

Antibiotic prophylaxis consisting of one injection of 2 g amoxicillin + clavulanic acid was administered preoperatively to all patients.

Diagnostic hysteroscopy was performed 2 months postoperatively. If postoperative uterine synechiae were identified, they were lysed during the same procedure using the 30° fore-oblique telescope. For those patients with residual myoma(s), a second operative hysteroscopy was recommended (n = 15). The final follow-up of women was performed either in an ambulatory setting when the patients were re-examined (n = 41), or by telephone questionnaire (n = 18).

Statistical analysis was performed using the χ² test, the χ² test modified by Yates, and Fisher’s exact test when there were insufficient patient numbers

**Results**

Regular follow-up among the 59 women in the study was for a mean duration of 40 ± 24.6 months (range 18–120 months).

The mean patient age was 36.6 ± 4.6 years (range 26–45). Twenty-four patients (41%) suffered from primary infertility, the mean duration of infertility being 54.1 ± 43.2 months (range 24–240). Forty patients (68%) were nullipara, 12 (20%) were primipara, and seven (12%) were multipara. Thirty-five patients (59%) had one or more associated infertility factors, i.e. tubal factor (n = 13), male factor (n = 14) and others (n = 8). In addition to myoma(s), 19 patients (32%) had one more factor of infertility, and 16 (27%) had two more factors.

The mean duration of the procedure was 40 ± 23 min (range 15–65), the time being recorded between the onset of cervical dilatation and end of the resection.

No intraoperative complications were observed, and the immediate postoperative course was uneventful in all women; all were discharged within 10 h of surgery being performed.

The mean size of the myomas was 24.5 ± 13.3 mm (range 5–50). Resection was complete in 44 cases (75%), but incomplete in 15 cases and required a second intervention 3 months later, either due to the lesion size (n = 7) or to intramural class 2 (n = 8). Postoperative uterine synechie stage I or II were observed in five cases who had >50% intramural extension of the myomas. This complication was successfully treated in all five cases during the diagnostic hysteroscopy performed 2 months after the initial procedure.

Among the 27 patients who had heavy menstrual bleeding, a functional improvement occurred in 62% of the cases (n = 17) with a normal pictorial chart. Success in this regard was directly related to the size of the myomas: 78% had good results when the myoma was <30 mm compared with 14% when it was >50 mm (P = 0.0025), despite the absence of other intramural or submucosal myomas. Only six cases were observed where persistence of heavy menstrual disorder occurred.

Sixteen of the 59 patients (27%) conceived, the mean surgery–conception time span being 8.5 months (range 1 to 33 months). Eight of the 16 patients conceived spontaneously. Among 23 patients who required assisted reproduction techniques, eight conceived (ovarian stimulation with intrauterine insemination in three cases, and IVF in five).

Six of the 16 patients who conceived delivered at term, and eight had a spontaneous abortion. In the latter group, six women were aged >35 years, one woman had a tubal pregnancy, and one required a termination of pregnancy for fetal anomaly.

In the current series, there was no statistical difference in the pregnancy rate as a function of patient age (Table I), the number (one or two) of interventions for complete resection of myomas (27.3 versus 26.6%), or the type of myomas with regard to intramural extension. Two of the five patients with post-myomectomy adhesions that were lysed subsequently conceived.

The presence of infertility factors other than myoma(s) significantly reduced the pregnancy rate (Table II). The rate was higher in patients whose myomas was ≥50 mm in diameter (57%), compared with myomas of a smaller size (23% for myomas ≤30 mm, and 23.1% for those of 30–50 mm; Table III). Despite this clear trend, the difference did not reach

**Table I. Pregnancy rate and age of patients**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>No. of cases</th>
<th>No. pregnant</th>
<th>No. of deliveries</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>17</td>
<td>6 (35.3)</td>
<td>3 (50)</td>
</tr>
<tr>
<td>≥35</td>
<td>42</td>
<td>10 (23.8)</td>
<td>3 (30)</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages.

**Table II. Impact of infertility factors on pregnancy rate**

<table>
<thead>
<tr>
<th>Myoma factor</th>
<th>No. of cases</th>
<th>Total pregnant</th>
<th>No. of spontaneous</th>
<th>No. of pregnancies after ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myoma</td>
<td>24</td>
<td>10 (41.6)</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Myoma + infertility</td>
<td>35</td>
<td>6 (17.1)</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

*P = 0.037
ART = assisted reproduction technique.
Values in parentheses are percentages.

**Table III. Impact of myoma size on pregnancy rate**

<table>
<thead>
<tr>
<th>Myoma size (cm)</th>
<th>No. of cases</th>
<th>No. pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3</td>
<td>39</td>
<td>9 (23.0)</td>
</tr>
<tr>
<td>&gt;3–&lt;5</td>
<td>13</td>
<td>3 (23.1)</td>
</tr>
<tr>
<td>≥5</td>
<td>7</td>
<td>4 (57.1)</td>
</tr>
</tbody>
</table>

*P = NS.
Values in parentheses are percentages.
Hysteroscopic resection of submucosal myomas

Table IV. Summary of studies reporting on the reproductive outcome after hysteroscopic myomectomy

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of cases</th>
<th>No. of pregnancies</th>
<th>Pregnancy rate (%)</th>
<th>Delivery rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donnez et al. (1990)</td>
<td>24</td>
<td>16</td>
<td>67</td>
<td>67</td>
</tr>
<tr>
<td>Valle (1990)</td>
<td>16</td>
<td>10</td>
<td>62</td>
<td>50</td>
</tr>
<tr>
<td>Corson and Brooks (1991)</td>
<td>13</td>
<td>10</td>
<td>77</td>
<td>61</td>
</tr>
<tr>
<td>Hucke (1992)</td>
<td>14</td>
<td>4</td>
<td>28.7</td>
<td>–</td>
</tr>
<tr>
<td>Goldenberg et al. (1995)</td>
<td>15</td>
<td>7</td>
<td>47</td>
<td>40</td>
</tr>
<tr>
<td>Preuthipan and Theppisai (1998)</td>
<td>12</td>
<td>2</td>
<td>16.7</td>
<td>–</td>
</tr>
<tr>
<td>Giatras et al. (1999)</td>
<td>41</td>
<td>25</td>
<td>60.9</td>
<td>48.7</td>
</tr>
<tr>
<td>Varasteh et al. (1999)</td>
<td>36</td>
<td>19</td>
<td>52.8</td>
<td>36.1</td>
</tr>
<tr>
<td>Vercellini et al. (1999)</td>
<td>40</td>
<td>15</td>
<td>37.5</td>
<td>32.5</td>
</tr>
<tr>
<td>Current study</td>
<td>59</td>
<td>16</td>
<td>27.1</td>
<td>10.0</td>
</tr>
</tbody>
</table>

statistical significance, perhaps due to the limited number of patients in this series.

No specific data on the histological characteristics of the myoma as described previously (Nisolle et al., 1999) have been found in this series. In five cases (8.5%) recurrence of myoma was observed more than 2 years after the initial procedure, and a hysteroscopic resection was performed. None of these patients achieved a pregnancy.

Discussion

The relationship between leiomyomas and infertility and improvement of spontaneous fertility after myomectomy remains the subject of debate. The current results suggest a more modest benefit from hysteroscopic myomectomy compared with other published hysteroscopic and abdominal myomectomy series, though the advanced age of the present patients (36.6 ± 4.6 years) may partly explain this difference (Seoud, 1992; Goldenberg et al., 1995; Sudik et al., 1996).

In the past, myomectomy for associated infertility was performed via laparotomy (Garcia and Tureck, 1984; Smith and Uhlik, 1990; Verkauf, 1992). In one study, a pregnancy rate of 47% was observed in 17 women who had undergone abdominal myomectomy of a submucosal leiomyoma (Garcia and Tureck, 1984), while others (Smith and Uhlik, 1990) found a similar pregnancy rate of 50% in 32 patients after abdominal myomectomy for cases with myomas located at various sites of the uterus.

The reported reproductive outcomes of several studies of hysteroscopic myomectomy are listed in Table IV. Most of these series report much better results than those achieved in the current study. Moreover, the rate of spontaneous abortion is higher over 35 years as the longstanding infertility and the existence of other infertility factors in 35 cases of the present patient group. Nevertheless, the current results are similar to those reported in two small studies, namely a pregnancy rate of 16.7% in 12 women (Preuthipan and Theppisai, 1998) and a rate of 28.7% in 14 women (Hucke et al., 1992).

In the current study, 75% of the pregnancies occurred during the first year, with a mean surgery to conception time span of 8.5 months. This short delay of conception has also been observed by others (Rosenfeld, 1986; Verkauf, 1992; Goldenberg et al., 1995). It is therefore strongly recommended that patients attempt to conceive soon after the procedure.

Postoperative reproductive outcome is adversely affected by the presence of additional infertility factors. The pregnancy rate was 41.6% (with five patients at term) when the myoma was the only apparent cause, compared with 26.3% with the presence of one factor and 6.3% with two or more additional factors. The initial size of the myoma also influenced the pregnancy rate. Paradoxically, in the current study the rate was higher among those with larger myoma(s) (≥50 mm), but none of these patients had additional infertility factors. This observation is important; indeed, the large size of the myoma was in these cases the sole factor for infertility, and reinforced the fact that myomas could be a cause of infertility. Similar results were obtained in a myomectomy via laparotomy series (Sudik et al., 1996), while another group (Varasteh et al., 1999) reported similar findings when using hysteroscopy, with a cumulative pregnancy rate of 25% for myomas <20 mm, and 75% for those >30 mm. These results offer indirect proof that large myomas are a valid cause of infertility, mainly because of the mechanical distortion and the dystrophy that they cause.

Several groups (Narayan and Goswamy, 1994; Fahri et al., 1995; Eldar-Geva et al., 1998; Stovall et al., 1998) have suggested that submucosal leiomyomas were associated with a reduction in the efficacy of assisted reproduction technique cycles, but further investigation would be required to assess the impact of hysteroscopic resection of leiomyomas on subsequent fertility. Indeed, the effectiveness of myomectomy or infertility was never evaluated in these four studies. Evidence suggests that hysteroscopic resection of large submucosal myomas offers similar results to laparotomy in terms of reproductive outcome. Furthermore, this procedure offers better compliance and lower morbidity as it is associated with rapid recovery.

Hysteroscopic myomectomy appears to offer long-term improvement for those who had associated menstrual disorders; only 10% of the patients in the current series had an unsatisfactory outcome in this regard, with a pictorial chart above 150 (Higham et al., 1990). Some factors influence the success of the functional results, especially the size and number of myomas, with few good results when the myomas were
>50 mm, or when submucosal leiomyomas are associated with an enlarged uterus and/or intramural class 2 or 3 (Donnez et al., 1996; Hart et al., 1999). The absence of information about histological characteristics of myomas in the current series does not explain the recurrence observed in five cases (Nisolle et al., 1999).

In conclusion, the effect of submucosal myoma resection on infertility seems limited. Nevertheless, when patients have bleeding or pain associated with infertility, the hysteroscopic procedure provides a safe and efficient treatment modality, and may be beneficial for all symptoms. Patient age (<35 years), myoma size (>50 mm) and an absence of others infertility factors are the best prognostic factors for subsequent fertility.

References

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