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ORIGINAL ARTICLE

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Fertility rates after hysteroscopic treatment of submucous myomas depending on their type

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Abstract The objective was too evaluate the pregnancy rate and the chance of term pregnancy following hysteroscopic myomectomy depending on the type of the myoma. Between February 2000 and October 2005, a total of 25 patients under 36 years of age (mean 30.1±5.8 SD) with a diagnosis of primary or secondary infertility and menstrual disorders due to submucous myoma underwent hysteroscopic myomectomy. The subgroups of the patients depending on the type of the myomas were: Type 0, 14 patients; type I, 7 patients; and type II, 4 patients. For the subgroup of patients with type II myomas there was a control group of 8 patients with infertility but without menstrual disorders who did not consent to undergoing operative hysteroscopic treatment and received expectant management. Mean myoma size was 22.6±14.7 mm, mean duration of the procedure was 28±17 min, and mean follow-up was 18±12.5 months. Menstrual pattern was reestablished in 84% of patients. Hysteroscopic myomectomy was associated with an increase in pregnancy rate: 57.1% for patients with type 0 myoma and 42.8% for patients with type I myoma. Patients with type II myoma, after hysteroscopic myomectomy, had a 25% pregnancy rate, while patients who received expectant management had a 50% rate. Delivery at term was achieved by 35.7% of patients with type 0 myoma, by 28.5% of patients with type I myoma, and by 25% of patients with type II myoma, after hysteroscopic myomectomy. Patients with type II myoma without menstrual disorders had a 37.5% term delivery rate receiving expectant management. Three patients had a spontaneous abortion during the first trimester (12%) and one patient had premature labor at 34 weeks' gestation (4%). Fertility rates appear to increase after hysteroscopic myomectomy of type 0 and type I myomas in previously infertile patients. In patients with type II myomas fertility rates did not increase, in contrast with patients with type II myomas who received expectant management. No difference in fertility rates was observed between patients with different types of submucous myomas after myomectomy, while the complication rate for these procedures is low. Patients' age and type of infertility (primary or secondary) are factors that do not affect fertility rates after hysteroscopic myomectomy.

Keywords Submucous myoma · Fertility · Pregnancy rate · Operative hysteroscopy

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Introduction

Fibroids or leiomyomas are benign encapsulated tumors made up of uterine muscular tissues. They are extremely common and are found in up to 80% of all women by the age of 50 years [1]. The incidence of myomas in infertile women without any obvious cause of infertility is estimated to be between 1 and 2.4% [2, 3].Only 5–10% of fibroids are estimated to be submucous [4], but they are often symptomatic. Common symptoms include menorrhagia, intermenstrual bleeding, and subfertility. Submucous fibroids are classified according to the European Society of Hysteroscopy as: Type 0 (complete intracavitary myoma), Type I (<50% of the myoma contained within the myometrium), or Type II (>50% of the myoma contained within the myometrium) [5].

Different theories have been proposed to explain the effects of myomas on fertility. It is generally accepted that the location of a fibroid is an important factor, with submucous, intramural, and subserosal fibroids implicated

in causing infertility in decreasing order of importance. Myomas may cause dysfunctional uterine contractility, which may interfere with sperm migration, ovum transport or nidation [2, 6, 7]. Myomas may also be associated with implantation failure or gestation discontinuation due to focal endometrial vascular disturbances, endometrial inflammation, secretion of vasoactive substances or an enhanced endometrial androgen environment [2, 8].

In order to evaluate the impact of the hysteroscopic resection of submucous myomas according to their type on subsequent fertility, we have tried to analyze the results of this procedure on fertility and pregnancy outcome under different conditions in which submucous myomas are implicated depending on their type.

Materials and methods

From February 2000 to October 2005, a total of 25 patients under 36 years old underwent hysteroscopic myomectomy for symptomatic submucous myomas. Indications were primary or secondary infertility with menstrual disorders (menorrhagia, menometrorrhagia, abnormal uterine bleeding).

All of the 25 patients of the study had been attempting to conceive for more than 2 years (range 2.2–3.8 years) before hysteroscopic resection of submucous fibroids. An infertility work-up preoperatively was performed on all patients including measurement of serum thyroid stimulation hormone (TSH) and prolactin (PRL) levels, serum concentration of FSH, luteinizing hormone (LH) and estradiol (E2) levels on the third day of the cycle, hysterosalpingography and partner's semen analysis, excluding other factors such as tubal or andrologic factors, and allowing investigation of the influence of submucous myomas on fertility. Preoperative transvaginal ultrasound was performed in all patients to define the size and location of the endometrial lesions and to exclude ovarian pathology. Infertility work-up was normal for all patients and submucous myoma seemed to be the only possible explanation for primary or secondary infertility. Patients with secondary infertility had at least one previous conception in their history. All patients complained of abnormal uterine bleeding, but only 18 of them (72%) had a history of iron deficiency anemia.

Diagnostic hysteroscopy was performed before operative hysteroscopy for exact localization and orientation of endometrial pathology. Patients were divided into three groups depending on the type of the submucosal myomas: (Type 0, n=14, Type I, n=7, and Type II, n=4). In addition, for patients with submucous myomas of Type I and mainly Type II, the thickness of the myometrium remaining between the deep edge of the myoma and the serous peritoneum was measured by transvaginal ultrasound and a safety margin of at least 1 cm was set. For the subgroup of patients with type II myomas there was a control group of 8 patients with infertility but without menstrual disorders who did not consent to undergoing operative hysteroscopic treatment and received expectant management. None of the patients in this study had two or more submucous myomas.

Antibiotic prophylaxis consisting of one injection of 1.5 g of cefuroxime was administered intraoperatively to all patients. Preoperative 2-month medical treatment with GnRH analogs was used in cases of submucous myomas over 3 cm (leuprorelin acetate or triptorelin 3.75 mg/month, intramuscularly). If the intramural part of the fibroids could not be completely resected, postoperative medical treatment with leuprorelin acetate or triptorelin (3.75 mg/month) was administered for 2 months. In these cases a control hysteroscopy after 2 months was performed to ascertain the normalization of the uterine cavity and the healing of the endometrium or to obtain a second complete resection. All women underwent hysteroscopic myomectomy under general anesthesia, using a rigid 27 Fr resectoscope (Richard Wolf, Knittlingen, Germany) with a 25° fore-oblique telescope.

The operative technique that was applied for Type 0 myomas is described by Hallez [9]. A combination of Mazzon [10] and Litta [11] techniques was applied for Type I and Type II myomas. The uterine cavity was distended with Purisole solution (sorbitol with mannitol) or 1.5% glycine solution. The distending medium was flushed at a flow rate of 250 ml/min and a pressure of 80–120 mmHg. A vacuum of −30 mmHg was applied for suction when necessary. Fluid balance was recorded by measuring the inflow and outflow fluid from the continuous flow resectoscope. Moderate fluid overload (fluid deficit >1,000–1,500 ml) was indicative of quick completion of the procedure. The procedure was terminated when the fluid deficit was 1,500–2,000 ml. Patients were fully counseled regarding the risks of operative hysteroscopy prior to the procedure.

Follow-up of patients was performed by repeat examination when indicated or by telephone questionnaire.

In this retrospective study, statistical analysis was performed using the X^2 test or X^2 test with Yates correction, and Fisher's exact test when the expected frequencies were small. The p value <0.05 was considered to be significant.

Results

A period of follow-up among the study population with a mean duration of 18±12.5 months (range 8–39.5 months) was recorded. The mean patient age was 30.1±5.8 years (range 23.5–35.5). Eleven patients had primary infertility and 14 had secondary infertility. The epidemiological characteristics of the patients are shown in Table 1.

The mean duration of the procedures was 28±17 min and the mean size of the myomas was 22.6±14.7 mm (range 8–46). GnRH analogs were administered in 6 patients (24%). The administration of GnRH was preoperative in 4 cases of Type 0 and Type I myomas and postoperative in 2 cases of Type I and Type II myomas. The latter two cases required a second intervention 2–3 months after the first operation to obtain complete resection.

Table 1 Patients' epidemiological characteristics

Characteristics	Statistics
Total number of patients	25
Age (mean)	30.1±5.8 years
Parous	9
Normal delivery	6
Cesarean section	3
Nulliparous	11
Previous uterine surgery[a]	8
Uterine size	6±2 weeks
Termination in the first trimester	5

[a]Includes dilatation and curettage or cone biopsy/conization of the cervix

Intraoperative or postoperative complications like uterine perforation and severe hemorrhage did not occur. Also, there were no cases of fluid overload or severe hyponatremia in the patients of the current study.

All 25 patients had menstrual disorders (menorraghia or menometrorrhagia or intermenstrual bleeding), and complete normalization of the menstrual status was observed in 21 (84%) of them and an improvement in the other 6 (16%).

In total, 12 of the 25 patients conceived (48%) and 8 of them delivered at term (32%). Three patients had a spontaneous abortion during the first trimester of pregnancy and 1 patient had premature labor at 34 weeks' gestation.

Patients' age is not correlated with pregnancy rate or the number of deliveries at term of patients in the current study, as is shown in Table 2. There is no statistical difference in fertility rates between patients of different ages (24–36 years) who underwent hysteroscopic myomectomy for submucous myomas of Type 0, I or II (X^2 and Fisher's exact test, p value not significant).

As is shown in Table 3, the pregnancy rate was higher in patients with primary infertility than in those with secondary infertility (63.6% vs. 35.7%), and the delivery at term rate was also higher in patients with primary infertility than in those with secondary infertility (45.4% vs. 21.4%). This difference did not reach statistical significance and the reason may be the small number of the study population (Fisher's exact test, p not significant).

The influence of myoma type on fertility rates is shown in Table 4. In patients with Type 0 myoma after hysteroscopic myomectomy, the pregnancy rate was 57.1%. In this subgroup of patients, deliveries at term (after the completion of 37 weeks of gestation) occurred in 35.7% of patients.

Table 2 Fertility rates and age of patients

Age (years)	Number of cases	Number of pregnancies (%)	Number of deliveries at term (%)
24–30	5	3 (60)	2 (40)
31–34	16	8 (50)	5* (31.2) *
35–36	4	1 (25)*	1 (25)*
Total	25	12 (48)	8 (32)

*p not significant

Table 3 Impact of type of infertility on fertility rates

	Number of cases	Number of pregnancies (%)	Number of deliveries at term (%)
Primary infertility	11	7 (63.6)	5 (45.4)
Secondary infertility	14	5 (35.7)*	3 (21.4)**
Total	25	12 (48)	8 (32)

*p=0.32 (not significant)
**p=0.30 (not significant)

Three out of seven patients with Type I submucous myomas conceived after hysteroscopic myomectomy (42.8%) and 2 delivered at term (28.5%).

One out of four patients with Type II submucous myomas conceived after the operation (25%) and delivered at 39 weeks (25%). In the control subgroup of patients with submucous Type II myomas who received expectant management the pregnancy rate was 50% and the rate of delivery at term was 37.5%. These percentages were higher in comparison to the percentages of the patients who underwent hysteroscopic myomectomy, but the difference was not significant. (X^2 ,Yates corrected, and Fisher's exact test, p not significant).

In addition, no statistical significant differences in pregnancy and in delivery rates were observed with regard to the type of submucous myomas after myomectomy (pregnancy rate after myomectomy in patients with Type 0 myoma in comparison to patients with Type I myoma, 57.1% vs. 42.8% (X^2, Yates corrected, p=0.87, the percentage of patients with Type 0, 57.1% vs. the percentage of patients with Type II, 25%, p=0.57, and comparison between patients with Types I and II myomas, 42.8 vs. 25%, p=1).

In this study, 12 of the 25 patients conceived (48%), and 9 pregnancies (75%) occurred during the first year. The mean operation to conception time span was 9 months (range 3 to 31 months).

Of the 12 patients who conceived, 10 conceived spontaneously and 2 patients who were over 35 years old conceived after ovarian stimulation with intrauterine insemination.

Eight of the 12 patients who conceived delivered at term, 1 had a premature labor at 34 weeks, and 3 had a first trimester spontaneous abortion (25%).

Table 4 Impact of myoma type on fertility rates

Type of myoma	Number of cases	Number of pregnancies (%)	Number of deliveries at term (%)
Type 0	14	8 (57.1)	5 (35.7)
Type I	7	3 (42.8)	2 (28.5)
Type II	4	1 (25)	1 (25)
Type II (control)	8	4 (50.0)*	3 (37.5)**

*p=0.52 (not significant)
**p=0.63 (not significant)

Two recurrences of submucous myomas 1 year after the initial operation (8%) were observed during the follow-up period in patients who did not achieve pregnancy (1 patient with Type I and 1 with Type II myomas). These patients had a second procedure to obtain complete resection and improve menstrual status. Histologic results of the specimens from the study population confirmed the hysteroscopic diagnosis in all cases.

Discussion

The benefits of hysteroscopic myomectomy of submucous myomas for improving the chance of pregnancy and chance of term delivery need to be evaluated by randomized controlled studies comparing hysteroscopic myomectomy vs. expectant management for women with submucous myomas. Also, technical factors such as the surgeon's skill and experience as well as techniques used surely play an important role. In the current retrospective study, we analyzed the impact of the type of submucous myomas on pregnancy and delivery rates.[1]

Several non-randomized studies have reported that after hysteroscopic myomectomy in infertile women, pregnancy rates vary from 16.7 to 76.9%, with a mean value of 45% [12–23]. Similar rates have been observed in our study with patients from the Type 0 and Type I submucous myoma groups (57.1% and 42.8% respectively). A lower percentage (25%) was observed for patients with Type II submucous myomas after hysteroscopic myomectomy in contrast to patients with the same type of myoma who received expectant management (50%), but this difference was not significant. In the current study delivery rates between 25 and 36% with a mean value of 29.7% were observed in patients with different types of submucous myoma, and the abortion rate was 25%. Comparatively, delivery rates in other studies vary from 10 to 48.7%, with a mean value of 33.4% [14, 19, 21–23].

The relationship between patients aged less than 36 years and fertility after hysteroscopic myomectomy has not been proven in our study. No correlation between age and fertility after abdominal myomectomy has been reported by others, while the most important correlation with subsequent fertility was the duration of infertility prior to myomectomy [24, 25]. In another study concerning subserous and intramural myomas was found that an age of more than 35 years and an association with other infertility factors decrease pregnancy rates [26]. Fertility rates were higher in patients with primary infertility in comparison to cases with secondary infertility in the current study, but this difference did not reach statistical significance. A systematic review of 11 cohort studies suggests that women with a submucous myoma have lower pregnancy rates compared with women with other causes of their infertility, and myomectomy was not associated with an increase in the live birth rate, but was associated with a higher pregnancy rate [27].

Our data suggest no difference in observed pregnancy and delivery rates according to the type of submucous myomas after myomectomy, and this has also been reported in the literature [17]. The bleeding symptoms disappeared in 84% of patients and hysteroscopic myomectomy offered long-term improvement in the menstrual pattern and patient satisfaction, as is also reported by others [28]. Appropriate selection of patients (with no multiple myomas and no deep myomas penetrating the uterine wall) is essential for the success of the procedures, which were performed as outpatient surgery in most cases. Depending on the size of the intramural part of a submucosal myoma, one- or two-step surgery was required and has been reported [29, 30], while GnRH agonists proved useful in reducing myoma size and expelling the myoma inside the uterine cavity, as has also been established elsewhere [31]. The recurrence rate of the procedure was 8% 1 year after the initial procedure, a percentage also observed by others [19]. Hysteroscopic submucous myoma resection seems to increase pregnancy rates in patients with Type 0 or Type I myomas. Myomectomy efficacy has not been statistically proven, but almost 75% of patients became pregnant 12 months after surgery.

In conclusion, the results of this study demonstrate that mainly intracavitary submucous fibroids measuring up to 3 cm (Type 0 and Type I) are effectively treated by hysteroscopic resection. Menstrual pattern is reestablished in most cases and fertility rates seem to increase after hysteroscopic resection of Types 0 and I but not Type II submucous myomas in previously infertile women with no other infertility factors. Patients' age (<36 years) and type of infertility (primary or secondary) seem not to affect fertility rates after hysteroscopic myomectomy. No statistically significant difference in fertility rates was observed between patients with different types of submucous myomas after myomectomy.

[1] Although control groups are needed for all different myoma types, we only had a control group for patients with Type II myomas.

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