Article

Effect of inner myometrium fibroid on reproductive outcome after IVF

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Abstract

To evaluate the influence of inner myometrium fibroids (myomas) on the outcome of IVF cycles, a retrospective age-matched controlled study was performed at SISMeR Reproductive Medicine Unit. The study group included 129 IVF/intracytoplasmic sperm injection cycles in 75 patients with one or more intramural and/or submucosal fibroids, while the control group consisted of 129 cycles in 127 patients without fibroids. The two groups were similar for mean oestradiol concentration at human chorionic gonadotrophin administration (1205.16 ± 874 versus 1395 ± 821 pg/ml), mean number of transferred embryos (2.02 ± 0.4 versus 2.14 ± 0.6) and clinical pregnancy rate (34.9 versus 41.1%). Conversely, the implantation rate was significantly lower in the study group (18.0%) than in the control group (26.5%; $\chi^2 = 4.81$, $P < 0.05$), whereas the rate of spontaneous abortion demonstrated an opposite trend (40 versus 18.9%; $\chi^2 = 4.34$, $P < 0.05$). Further research should be aimed at classifying fibroids on the basis of their location, especially when they are positioned in the junctional zone of the myometrium. Whether this classification will be superior in predicting the impact of fibroids on the reproductive outcome should be elaborated in a large multicentric study.

Keywords: *abortion, assisted reproduction, fibroid, inner myometrium, reproductive outcome*

Introduction

The incidence of fibroids (myomas) in women of reproductive age is reported to be between 20 and 40% (Verkauf, 1992; American Society for Reproductive Medicine, 2001). Their presence could cause failure to conceive, but no scientific evidence supports improvement after the surgical removal of the fibroid. This was recently highlighted in a review (Donnez and Jadoul, 2002) reporting a pregnancy rate after myomectomy in infertile women varying between 10 and 80%.

A number of mechanisms by which fibroids could cause reduced fertility have been suggested and these include mechanical factors associated with the deformation of the uterine contour (for reviews see Verkauf, 1993; Wallach and Vlahos, 2004). This could interfere with sperm access to the cervix and uterine transport, distort or occlude the tubal ostia, or alter uterine contractility with consequent effect on normal sperm transport. An increased risk of spontaneous abortion has been attributed to augmented uterine contractions and growth or degeneration of fibroids. However, none of these potential mechanisms has been clearly demonstrated to adversely affect the outcome of the feto–maternal relationship, or to cause pregnancy wastage.

Factors influencing transport and fertilization are eliminated in assisted reproductive technologies and the evaluation of implantation and pregnancy rate and outcome have been investigated in retrospective and prospective studies.

Seven case–control trials published during the last decade have provided conflicting information regarding the impact of fibroids on these outcome measures. Two studies found that pregnancy rate is decreased when uterine leiofibromyomas cause deformation of the uterine cavity (Farhi *et al*., 1995;

Ramzy *et al.*, 1998). Two other studies (Eldar-Geva *et al.*, 1998; Stovall *et al.*, 1998) reported significantly reduced pregnancy and delivery rates after IVF in the presence of fibroids in the inner myometrium, despite the absence of uterine deformation. Accordingly, Hart and co-workers (2001) found that an intramural fibroid of 5 cm or less in size halves the chances of an ongoing pregnancy after assisted reproduction. On the other hand, Surrey and coworkers (2001) reported a significant decrease in the implantation rate in women younger than 40 years with intramural fibroids, but no significant difference in the live birth rate, while Check and colleagues (2002) found similar rates of implantation and delivery.

The purpose of this study was (i) to report the general outcome in assisted reproduction cycles performed by patients with fibroids in the inner myometrium and (ii) to discuss the current problems in evaluating the impact of uterine fibroids on IVF/intracytoplasmic sperm injection (ICSI) results.

Materials and methods

This retrospective case–control study was based on the analysis of the results generated by patients undergoing IVF/ICSI cycles at the SISMeR Reproductive Medicine Unit from 1996 to 2001. Before being referred to the assisted reproduction unit, patients underwent physical examination and vaginal ultrasound to evaluate the presence of uterine fibroids and signs of uterine cavity distortion. In suspected cases, hysteroscopy was performed.

The study included 129 treatment cycles performed in 75 patients with fibroids (study group) and 129 cycles in 127 patients without fibroids (control group) matched for age and cause of infertility. The study group also included 14 patients with recurrent fibroids after a previous myomectomy.

Results were analysed in terms of clinical pregnancies (defined as presence of a gestational sac with fetal heart beat), implantation rates and spontaneous abortions. These figures were related to size and number of fibroids by dividing the patients into subgroup A, with three or fewer fibroids, and subgroup B, having more than three fibroids.

In five patients with a negative outcome in the first assisted reproduction cycle, myomectomy was performed prior to further attempts. The reproductive outcome was analysed before and after myomectomy.

All patients received the same hormonal ovarian stimulation protocol after suppression with long acting gonadotrophin-releasing hormone (GnRH) agonists (Ferraretti *et al.*, 1996). Oocyte retrieval was performed 34–36 h after human chorionic gonadotrophin (HCG) administration and embryo transfer was programmed 2 or 3 days later. The extracorporeal phases have been previously described (Gianaroli *et al.*, 1996). Supernumerary embryos were cryopreserved and thawed in following cycles (Ferraretti *et al.*, 1999); these results were included in the present study giving cumulative data per cycle performed.

Statistical analysis

Comparisons were made by Student's *t*-test and chi-squared analysis 2 × 2 contingency tables when appropriate. $P < 0.05$ was considered as statistically significant.

Results

There was no statistical difference between study and control groups regarding mean maternal age (35.8 ± 4.9 versus 35.7 ± 4.8 years), mean oestradiol concentration at HCG administration (1205 ± 874 versus 1395 ± 821 pg/ml), mean number of embryos transferred (2.02 ± 0.4 versus 2.14 ± 0.6) and cause of infertility (**Table 1**). The mean number of fibroids diagnosed in the inner myometrium was 2.46 ± 2.8, with a mean diameter of 1.84 ± 1.4 cm (**Table 2**).

The clinical pregnancy rate per transferred cycle between the two groups was similar (34.9 versus 41.1%). However, the implantation rate was significantly lower in the study group compared with the control group (18.0 versus 26.5%; $\chi^2 = 4.81$, $P < 0.05$), while the rate of spontaneous abortions demonstrated an opposite trend (40.0% in the study group and 18.9% in the control group $\chi^2 = 4.34$, $P < 0.05$) (**Table 3**). Accordingly, the take-home baby rate per transferred cycle was higher in the control group (33.3%) compared with the study group (21.0%, $\chi^2 = 4.41$, $P < 0.05$).

The incidence of multiple pregnancies was 6.7% in the study group and 18.9% in the controls. Excluding patients with multiple pregnancies, the mean birth weight of the infants born was 2804 ± 689.5 g in the study group versus 3070 ± 498.6 g in the control group with a preterm birth rate in the study group of 33.3% (9/27) versus 18.6% (8/43) in the control group (not significant).

In the study group, 112 transfers were performed in patients with three or fewer fibroids (subgroup A) and 17 transfers in patients with more than three fibroids (subgroup B). The mean number of fibroids was 1.2 ± 0.5 in subgroup A and 5.7 ± 1 in subgroup B. The two subgroups were homogeneous in terms of mean maternal age (36.4 ± 5.1 versus 37 ± 2.7 years) and mean number of transferred embryos (2.0 ± 0.9 versus 2.6 ± 0.9). The rate of clinical pregnancies was 35.7% in subgroup A and 29.4% in subgroup B versus 41.1% in the control group, while the abortion rate was 35.0, 80.0 and 18.9% respectively (subgroup B versus controls: $\chi^2 = 6.28$, $P < 0.01$) (**Table 4**).

The results were evaluated according to the size of the fibroids (<1, 1–<3, ≥3 cm). In case of single fibroids, no statistical differences were noted in the rates of pregnancy (40, 37, 28%) or abortion (13, 13, 8%), whereas when multiple fibroids were present with a diameter ≥3 cm, the abortion rate was significantly higher compared with controls (80.0 versus 18.9%, $P < 0.01$).

In five patients with a mean maternal age of 39.5 ± 5.1 years, data pre- and post-myomectomy were analysed. The cause of infertility was tubal in two patients, ovulatory in two patients and male factor in one patient. Before myomectomy, five embryo transfers resulted in one spontaneous abortion, while after myomectomy, seven transfers resulted in four term pregnancies and one spontaneous abortion.