Treatment preferences and trade-offs for ovulation induction in clomiphene citrate–resistant patients with polycystic ovary syndrome

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Objective: To investigate patient preferences and trade-offs for laparoscopic electrocautery of the ovaries relative to ovulation induction with recombinant FSH (rFSH) in patients with clomiphene citrate (CC)-resistant polycystic ovary syndrome (PCOS).
Design: Assessment of preferences and trade-offs in a randomized controlled trial.
Setting: Academic hospital.
Patient(s): Thirty-two CC-resistant patients with PCOS who had been randomly assigned to either laparoscopic electrocautery of the ovaries or ovulation induction with rFSH and 32 control patients with PCOS under treatment with CC.
Intervention(s): Preference for laparoscopic electrocautery relative to rFSH was established during an interview. Trade-offs between treatment burden and effectiveness were evaluated by varying hypothetical pregnancy rates after laparoscopic electrocautery until patients switched in their initial preference.
Main Outcome Measure(s): Preference for laparoscopic electrocautery of the ovaries; trade-off between burden and effectiveness of treatment.
Result(s): The majority of the patients would prefer electrocautery of the ovaries over ovulation induction with rFSH if both treatment strategies resulted in similar pregnancy rates. However, most patients were willing to trade off their preference for increased effectiveness: the percentage of patients who preferred electrocautery over rFSH sharply declined when the difference in hypothetical pregnancy rates was more than 5% in favor of rFSH.
Conclusion(s): Patients with polycystic ovary syndrome are well able to express an informed preference for laparoscopic electrocautery of the ovaries or ovulation induction with rFHS. Preferences are guided by features of the respective treatments but seem to be dominated by their effectiveness and safety. (Fertil Steril® 2005;84: 420–5. ©2005 by American Society for Reproductive Medicine.)

Key Words: Polycystic ovary syndrome, clomiphene citrate, laparoscopy, electrocautery, rFSH, pregnancy, patient preferences

Polycystic ovary syndrome (PCOS) is a common endocrine disorder characterized by two of the following three criteria; oligo- and/or anovulation, clinical and/or biochemical signs of hyperandrogenism, and polycystic ovaries (1). Infertility due to chronic anovulation is the most common reason for seeking treatment.

Approximately 20% of women fail to ovulate when taking clomiphene citrate (CC), the drug of first choice (2). For those who fail to ovulate with CC, the principal options include ovulation induction with gonadotropins or laparoscopic electrocautery of the ovaries.

It is generally assumed that ovulation induction with gonadotropins is a cumbersome treatment for patients, owing to the need for daily injections and intensive monitoring. Furthermore, ovulation induction with gonadotropins bears the risk of multiple follicle development leading to termination of the cycle or multiple pregnancy (3, 4). In contrast, electrocautery of the ovaries involves a single procedure with limited monitoring, and potential complications inherent to ovulation induction with gonadotropins are absent (5). Yet, as a surgical intervention, electrocautery carries a risk of complications, such as thermal damage of the intestines, bleeding from the ovary, and adhesion formation (6–10).

Both treatment options clearly differ in terms of the invasiveness of the intervention, the intensity of monitoring, and possible complications.

Over the past 30 years, an increasing emphasis has been placed on the provision of information to patients and on their participation in treatment decision making (11–13). In the field of reproductive medicine, however, patient preferences have only rarely been studied (14, 15). We therefore thought it important to study treatment preferences in women who participated in a randomized controlled trial and in a control group of women with PCOS treated with CC. In

Received June 18, 2004; revised and accepted February 9, 2005.
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0015-0282/05/$30.00
doi:10.1016/j.fertnstert.2005.02.026

this trial, the electrocautery strategy was found to be equivalent to ovulation induction with recombinant FSH (rFSH) alone, with ongoing pregnancy rates of 67% for both strategies (16). The major difference, however, was a lower number of multiple pregnancies in the group first treated with electrocautery and CC. In such a situation, a greater understanding is required of the relationship between risk, benefit, and the acceptance and comprehension of these factors by patients, whose preferences and views vary depending on their personal situation (11–13).

Because of the limited monitoring and absence of complications, such as multiple follicle development and multiple pregnancies after electrocautery, we anticipated that most patients would express a preference for this strategy if effectiveness were to be equal.

Because future trials comparing both treatment strategies might force us to update our knowledge about their effectiveness, in terms of ovulation induction and pregnancy rates, we also explored to what degree patients are willing to trade off their initial preference against differences in effectiveness.

MATERIALS AND METHODS

Patients

Patients included in a multicenter randomized controlled trial were invited to this treatment preference study. Eligible patients were those with chronic anovulation of World Health Organization type II (17) and polycystic ovaries not responding to CC. From February 1998 to October 2001, consenting patients had been randomly assigned either to a treatment strategy entailing laparoscopic electrocautery of the ovaries followed by CC and rFSH when anovulation persisted, or to ovulation induction with rFSH (follitropin α, Gonal-F; Serono Benelux, The Hague, The Netherlands). For this study, we only invited patients who were treated at the Academic Medical Center, Amsterdam (the trial coordination center).

Electrocautery was performed with an Erbotom ICC 350 Unit (Erbe, Zaltbommel, The Netherlands) and done with a bipolar insulated needle electrode. Clomiphene citrate was reintroduced when anovulation persisted or if the patient became anovulatory again. If patients remained anovulatory despite the maximum dose of CC (150 mg), ovulation induction with rFSH was started. Further details of the design and results of this randomized controlled trial have been reported elsewhere (16).

A control group of consecutive patients with chronic anovulation and polycystic ovaries undergoing ovulation induction with CC were also invited to the study. The rationale for choosing these patients as controls was that they were informed about their condition and that they were potential candidates for treatment with either electrocautery of the ovaries or ovulation induction with rFSH if they became resistant to CC.

Methods

Preferences for electrocautery relative to rFSH were studied in an interview. All interviews were conducted by the first author.

Participating patients were first informed about the purpose of the study. The descriptions of both treatments were in accordance with the information that they had received during the initial informed consent procedure. Participants received written information regarding the possible advantages and disadvantages of both treatments. Potential advantages of laparoscopic electrocautery of the ovaries compared with rFSH are no need of daily injections, less need for intensive monitoring, and minimal chance for complications, such as multiple follicle development and multiple pregnancies. The disadvantage is the need for surgery and thus the possibility of such complications as thermal damage of the intestines, bleeding from the ovary, and adhesion formation.

The chances of a pregnancy were set at 40% after electrocautery and 35% after ovulation induction with rFSH, according to data available in the literature at the time the study was initiated. After reading the treatment descriptions, the women were asked which treatment they would prefer. We asked them for the reason for their treatment preference. We then investigated whether patients were willing to tradeoff their preference for a difference in effectiveness by systematically varying pregnancy rates after electrocautery. If electrocautery was the initially preferred option, the pregnancy rate after electrocautery was systematically decreased by 5% increments until the patient's preference switched to rFSH. If rFSH was the initially preferred option, the pregnancy rate after laparoscopic electrocautery was set at 50%. We chose a maximum ongoing pregnancy rate of 50% because we did not expect the ongoing pregnancy rate to exceed 50% (3). When the patient's treatment preference switched to electrocautery, the pregnancy rate after electrocautery was systematically decreased by 5% increments until her treatment preference switched back to rFSH. The pregnancy rate threshold at which the women would prefer electrocautery over rFSH was registered.

In our randomized controlled trial, all women underwent a diagnostic laparoscopy to exclude women without patent tubes or with severe endometriosis and/or adhesions. It is possible that the perceived burden of rFSH is lower in a strategy not including this diagnostic laparoscopy. Therefore, the preference assessment procedure was repeated in a scenario without a laparoscopy preceding ovulation induction with rFSH. The pregnancy rate was varied in the same way as described above. We registered the rate at which participating women would prefer electrocautery over rFSH without a diagnostic laparoscopy.

After completion of the trial, the actual pregnancy rates after the electrocautery strategy and rFSH were found to differ substantially from those initially used in the preference assessment. In trial patients, the ongoing pregnancy rate after