Relevance of thrombophilia and impact of office hysteroscopy on recurrent *in vitro* fertilization failures: a case series

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Summary

The study evaluated the validity of office hysteroscopy (OH) in 51 infertile women and whether congenital or acquired thrombophilia is more prevalent in women with recurrent IVF failures.

Key words: In vitro fertilization; Thrombophilia; Hysteroscopy.

Introduction

Recurrent *in vitro* fertilization (IVF) failures have been attributed to either embryo quality or endometrial receptivity, but remain unexplained in most cases. Benign endometrial pathologies may have a negative effect on pregnancy rate. Congenital or acquired thrombophilia have been associated with recurrent IVF failures as well.

Office hysteroscopy (OH) allows a reliable visual assessment of the cervical canal and uterine cavity while providing the opportunity to perform treatment if needed.

Materials and Methods

Fifty-one infertile patients, who could not conceive naturally after one year of having regular unprotected sex and subsequently, had undergone two or more failed IVF cycles, and admitted to the Infertility Clinic of Istanbul University School of Medicine, were selected for this study. The authors performed OH as an outpatient procedure. When intrauterine pathologies were detected, treatment was performed immediately. Patients were screened for the presence of congenital or acquired thrombophilic factors (factor V Leiden, prothrombin G202010A mutation, protein C, protein S, antithrombin III, anticardiolipin IgM antibody, anticardiolipin IgG antibody, lupus anticoagulant, and homocysteine). Afterwards, they were followed-up for pregnancy outcome.

Results

OH revealed that 39 patients (76.5%) had a normal uterine cavity, seven patients (13.7%) had endometrial polyps, and five patients (9.8%) had intrauterine adhesions. Screening for the presence of congenital or acquired thrombophilic factors presented: 15 (29.5%) congenital, 11 (21.6%) acquired, and four (7.8%) unclear causes of thrombophilia (Table 1). Out of 51 patients, 49 attempted another IVF and two dropped out. In 49 patients, 14 (28.6%) were beta-human chorionic gonadotropin (βhCG) positive; clinical pregnancy was positive in 11 patients (22.4%); ten patients (20.4%) had live births. Four out of ten patients with live births had intrauterine pathologies detected and treated by OH which represented 33.3% of patients with intrauterine pathologies.

Discussion

The etiology of recurrent IVF failures is still unclear and probably dependent on multiple factors. Studies on the impact of congenital and acquired thrombophilia on IVF failures have provided inconclusive results. The common belief is that thrombophilia may cause recurrent implantation failures by impairing the initial vascularization process occurring at implantation, which is necessary for a successful pregnancy [1-5]. Some of the studies showed that at least one thrombophilic factor was positive in patients with recurrent IVF failures [2, 4-6]. The results in this study also indicated that at least one positive test resulted for congenital or acquired thrombophilia in nearly 60% of the patients that were screened for such factors. In a very recent study on inherited thrombophilias and adverse pregnancy outcome, the findings did not support a significant association between inherited thrombophilia and the pregnancy outcome [7]. On the other hand, as the present researchers indicated themselves, this study had a small number of patients in the subgroups (ten stillbirths and 16 placental abruption cases) and wide confidence intervals.

In a recent meta-analysis, women experiencing assisted reproductive technology (ART) failures suggested to be more frequently positive for factor V Leiden and antiphospholipid antibodies, although the evidence is inconclusive [8]. The findings in this study also indicated factor V Leiden as the most frequently seen thrombophilic factor in women experiencing IVF failures.

A normal uterine cavity is important for a successful IVF outcome. In the literature, it is generally argued that

Revised manuscript accepted for publication May 24, 2012

Table 1. — *Overview of thrombophilia screening*.

	N	%
Congenital thrombophilia factors		
Factor V Leiden	8	15.7
Prothrombin G20210A mutation	3	5.9
Protein C deficiency	1	2.0
Protein S deficiency	3	5.9
Antithrombin III deficiency	0	–
Acquired thrombophilic factors		
Anti cardiolipin lgM	9	17.7
Anti cardiolipin lgG	0	–
Lupus anticoagulant	2	3.9
Unclear thrombophilic factors		
Elevated homocysteine levels	4	7.8

an increased rate of intrauterine pathologies is found in infertility patients, albeit with varying results. Researchers that evaluated OH's relevance on patients who had recurrent IVF failures reported somewhat similar findings. In one study, 26% of 210 patients with recurrent IVF failures had intrauterine pathologies [6, 9]. In another similarly formatted study, 37% of 520 patients had intrauterine pathologies [10]. The researchers also recommended a routine usage of OH on patients with recurrent IVF failures. In a review on the role of OH in women with recurrent IVF failures, the authors concluded that the pregnancy rates increased when OH was performed, yet they also indicated the need for further studies [11]. The follow-up finding in this study revealed that patients with detected/treated intrauterine pathologies by OH, one-third had a live birth.

Conclusion

Ultimately, this limited study suggests that women experiencing recurrent IVF failures are more frequently positive for thrombophilic factors, yet this evidence is inconclusive. Additionally, although the usage of OH in patients with a history of recurrent IVF failures remains debatable, it may be a valid method due to the high detection/treatment rate of intrauterine pathologies that can adversely affect pregnancy rates. Nevertheless, further cohort studies with a larger sample size have to be carried out to confirm and support both findings.

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