Original Article

Assisted Hatching in Selected Groups of Patients: Does it make a Difference?

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ABSTRACT

Objective: The aim of the present study was to examine the effect of assisted hatching (AH) using zona-drilling techniques on pregnancy rate, miscarriage rate and multiple pregnancy rates, in a selected group of patients.
Design: A retrospective study.
Setting: The Lister Hospital Assisted Conception Unit.
Patients: Between July 1996 and December 2000, 141 patients were treated with AH prior to embryo transfer. The effect of AH was compared to a control group of 456 patients who underwent embryo transfer without AH during the same time period.
Intervention: Assisted Hatching.
Main outcome: Pregnancy rates, live births, single and multiple pregnancies and miscarriage rates.
Results: Patients who underwent AH were significantly older than the control group (37.23 ± 4.47 vs 35.74 ± 4.25 years: P = 0.001) and had significantly more previous cycles of failed IVF/ICSI (2.51 ± 1.44 vs 2.02 ± 5.72: P = 0.00). The pregnancy rates, live birth rates, the incidence of single and multiple pregnancies and miscarriage rates were comparable in both groups.
Conclusion: These results suggest that assisted hatching is not detrimental to health and may improve the outcome in patients with poor prognostic factors, resulting in rates of pregnancy comparable to that of the control group.

KEYWORDS: assisted hatching, poor prognostic factors, selected group of patients, zona drilling

INTRODUCTION

Despite recent advances in assisted conception techniques, implantation rates remain low. The underlying cause of this is still obscure. The full expansion of the blastocyst accompanied by the natural thinning of the zona pellucida (ZP) and successful hatching of the embryo by the dissolving of the ZP by a proteolytic enzyme secreted by the uterus, is an important event in the implantation process[1,2]. It has been suggested that exposure of oocytes and embryos to an artificial in-vitro environment may have a negative effect on the embryo's ability to undergo normal hatching and may explain the low rates of implantation following in-vitro fertilisation (IVF) and embryo transfer[3].

The assisted hatching of cleavage stage embryos was first attempted by Cohen *et al* in 1990 who performed the technique of partial zona dissection to open the ZP[3]. The benefit of AH has been controversial[5]. Literature reports show that only a selected group of patients will benefit from AH i.e., older patients (> 35 years), patients who have embryos with thickened ZP, those with elevated basal follicle stimulating hormone (FSH) levels, patients with repeated IVF failure and those with frozen embryos[5,6,7,8]. The few prospective controlled trials, which were carried out in this field, also demonstrated a clear benefit of AH, particularly in the case of patients with poor prognosis[4,7,10]. In vitro fertilization patients with repeated failed embryo transfers have been shown to have a poor prognosis for pregnancy[11]. Also, it has been proposed that advanced ovarian age is related to abnormal zona synthesis[3].

AH may be performed by making a small hole or a slit in the ZP either mechanically using partial zona dissection[4] or chemically using zona drilling with acid Tyrode's medium[12], enzyme digestion[13] or laser microbeams[14].

MATERIAL AND METHODS

The records of patients who underwent ICSI and IVF–ET (fresh cycles only) at The Lister Hospital between July 1996 and November 2000 were reviewed retrospectively. The patients were divided into two groups, the AH group and then non-AH group (control).

Patients for AH were selected on an individual basis. Selection criteria included: Age > 35 years, number of previous IVF/ICSI failure (≥ 2 attempts), infertility of ≥ 2 years and only patients in whom three embryos were transferred back into the uterus on day-3 of embryo transfer.

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All patients were given a comprehensive patient information sheet describing the procedure and written consent was obtained. The AH group were matched with the control group according their previous IVF/ICSI failure, duration of infertility, number of embryos transferred into the uterus per ET cycle and the day of embryo transfer. Ovarian stimulation and monitoring were carried out according to routine clinical protocols[15].

AH was carried out according to the protocol of Alikani *et al*[16] using an acid Tyrodes solution of pH 2.3-2.5. Micromanipulation procedures were carried out on the heated stage of an Olympus IX 70 inverted microscope, using Narishige hydraulic micromanipulators. A microneedle measuring 10-12 µm in outer diameter attached to a mouth suction unit was used. AH was performed on those embryos that had reached at least the 5-cell stage of development on the morning of day-3 (*i.e.*, the day of embryo transfer).

STATISTICAL ANALYSIS

Differences in the pregnancy rate, miscarriage and multiple pregnancy rates between the AH and the control were analysed using the Chi square test. Student's T test was used for comparing the means. P value of ≤ 0.05 was considered to be significant.

RESULTS

The clinical characteristics of the AH and the control groups are presented in Table 1. There was a statistically significant difference in the age as well as the number of IVF/ICSI failed attempts and duration on infertility (P = 0.001, 0.001, 0.05 respectively) between the AH and control groups.

Table 2 summarizes pregnancy outcomes in both the AH and control groups. There was no statistically significant difference between the two groups in relation to pregnancy, live birth (single), multiple pregnancy and miscarriage rates.

DISCUSSION

In this study, the well documented poor-prognostic factors i.e., increased maternal age and increased number of failed IVF/ICSI attempts were significantly higher in the study group compared to the control group. Their chances of pregnancy without AH would have been expected to be much lower than in patients with favourable prognostic factors. We found that after implementation of AH using ZP drilling, the pregnancy rate in such poor–prognostic group of patients is so improved

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