An Evaluation of the Efficacy of In Vitro Fertilization with Intracytoplasmic Sperm Injection for Sperm with Low Hypoosmotic Swelling Test Scores and Poor Morphology

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Purpose: To corroborate or refute a previous study demonstrating that in vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI) is an effective therapy for infertility related to males with subnormal hypoosmotic swelling tests (HOST). The study would also determine if the copresence of poor morphology has any adverse effect on outcome.

Methods: Clinical and viable pregnancy rates and implantation rates were evaluated in a second series of patients. The data were further stratified according to whether the semen specimen demonstrated morphology using strict criteria <4% normal vs ≥4%.

Results: Clinical and viable pregnancy rates and implantation rates were 49.1, 45.3, and 23.4% for those with subnormal HOST scores and subnormal morphology vs 38.0, 34.3, and 22.5% for those with low HOST and strict morphology ≥4% ($p = \text{NS}$, chi-square analysis).

Conclusions: In vitro fertilization with ICSI is an effective therapy for infertility related to subnormal HOST scores. Poor morphology does not adversely affect the outcome.

KEY WORDS: Hypoosmotic swelling test; intracytoplasmic sperm injection; sperm morphology; strict criteria.

INTRODUCTION

One of the most daunting problems facing the clinician is that of finding a reliable diagnostic test to predict the fertilization potential of a given semen sample. The hypoosmotic swelling test (HOST) was believed to be an accurate, fast, and inexpensive prognosticator of poor fertilization potential of sperm when the HOST score was <50% (1,2). However the importance of this test was questioned when there was poor correlation demonstrated with subnormal scores and fertilization rates (3–7). However excellent results for predicting poor implantation of embryos

have been observed (8–10). Thus the HOST is unique in demonstrating that sperm may cause infertility by adversely affecting the ability of an embryo to successfully implant without any adverse effect on fertilization potential (9).

There have been several studies suggesting that strict morphology of <4% predicts poor fertilization potential in vivo following in vitro fertilization (IVF) with conventional insemination of oocytes with sperm (11–13). However there are some studies that do not agree that strict morphology <4% is very predictive of the subnormal male (14,15). In fact, a study comparing IVF outcome according to whether a male had only one semen parameter abnormal, i.e., motile density $10 \times 10^6/\text{mL}$, strict morphology <4% normal, and HOST score <50% found the normal controls with a clinical pregnancy rate of 25.7% per transfer, low motile density at 25.5% per transfer, low strict morphology at 44.4% per transfer but HOST score <50% with no clinical pregnancies (16).

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The studies showing that poor HOST scores did not correlate with poor fertilization potential did not include pregnancy rates in their reporting (3–7). However all studies to date that evaluated pregnancy rates with subnormal HOST scores have found very low fecundity (2,8,9,16). We then hypothesized that some sperm factor impairing the functional integrity of the sperm may be transferred to the zona pellucida by the supernumerary sperm that attach but do not penetrate (10). The hypothesis continues that these toxic factors are internalized by the zona pellucida and become part of the embryo and they then similarly impair the functional integrity of the embryo membrane thus preventing implantation (10). Support for this hypothesis was provided by the demonstration of a 49% pregnancy rate per transfer with sperm with HOST scores <50% following intracytoplasmic sperm injection (ICSI) (17).

The study presented here reevaluated a different group of patients from 8/98 to 8/01, to corroborate or refute the efficacy of ICSI for achieving pregnancies despite sperm with low HOST scores. In addition, the study would determine if the presence of sperm with subnormal HOST scores with the added abnormality of strict morphology <4% would impair the effectiveness of ICSI for overcoming HOST score abnormalities.

MATERIALS AND METHODS

General

Patients involved in this study were all undergoing IVF-ET with ICSI between 8/98 and 8/01. The criteria for inclusion was that the male partner exhibited a subnormal HOST score <50%. These men were subsequently divided into two groups based on normal or subnormal sperm morphology (≥ 4 or <4%).

Morphology

The sperm specimen was evaluated using strict criteria first described by Kruger *et al.* (18). For this study a normal morphology $\geq 4\%$ was considered normal. Staining procedure for all samples was uniform using a modified Diff-Quik protocol.

HOST

A 100 μL aliquot was introduced into a 1 mL hypoosmotic solution for 30 min as described by

Jeyendran *et al.* (1). All levels below 50% were considered subnormal (2).

Statistical Analysis

Following IVF-ET with ICSI, ultrasound analysis compared clinical and viable pregnancy rates between the two groups. Implantation rates between the groups were also examined. Comparisons between clinical and viable pregnancy rates and implantation rates were performed using chi-square analysis with $p < .05$ as significant.

RESULTS

The patients were divided according to abnormal strict morphology (group 1) vs normal morphology (group 2). All patients had HOST scores <50%.

Group 1 with both abnormal morphology and low HOST scores had 53 transfers with an average of 3.3 embryos per transfer. The clinical and viable pregnancy rates for this group were 49.1 and 45.3%, respectively. The implantation rate was 23.4% (Table I).

Group 2 with normal strict morphology and subnormal HOST scores had 137 transfers with an average of 3.1 embryos per transfer. The clinical and viable pregnancy rates were 38.0 and 34.3%, respectively ($p = \text{NS}$). The implantation rate for this group was 22.5% ($p = \text{NS}$) (Table I).

Table I. Pregnancy Rates for Patients with HOST <50 Based on Normal Morphology Using Strict Criteria

	Abnormal Morphology ICSI Low HOST	Normal Morphology ≥ 4 ICSI Low HOST
# cycles	69	236
# transfers	53	137
# ET	175	423
Avg. # ET	3.3	3.1
# pregnancies	29	58
# clinical	26	52
% clinical	49.1	38.0
# chemical	3	3
# ectopic	0	3
# implanted	41	95
% implanted	23.4	22.5
# viable	24	47
% viable	45.3	34.3
Mean HOST conceived	37%	39%
Mean HOST not conceived	41%	38%
Highest HOST	48%	49%
Lowest HOST	20%	12%

DISCUSSION

The data corroborated our previous findings that IVF with ICSI is an effective treatment for males with HOST scores <50% (17). The data also demonstrated that the additional burden of low strict morphology does not impair the success of ICSI when low HOST scores exist.

Although most studies of low strict morphology favored a significant impairment of pregnancy rates with conventional oocyte/sperm incubation (12–14,18–20), other studies showed that IVF with ICSI is a good technique to treat males with low strict morphology (21). Thus it is not that surprising that our data did not show that the combination of these two abnormalities would reduce the efficacy of ICSI.

Originally, we proposed to the institutional review board (IRB) a proposal to inseminate half of the retrieved oocytes from a given woman in the conventional manner and half by ICSI and to randomly transfer those embryos fertilized by conventional insemination and those by ICSI. Thus, we hoped that if the group with conventional insemination had poor pregnancy rates there would at least still be cryopreserved embryos left over fertilized by ICSI. However, the IRB stated that based on our previous studies showing extremely poor pregnancy rates with low HOST scores and conventional insemination (8,9,16), without any other studies refuting this claim, that it would be unfair to waste possibly half of a given woman's oocyte harvest. Furthermore they reasoned that fresh ET may be superior to frozen ET. Finally they argued that our previous data showed a very good success with ICSI (17). Thus the final decision was merely to attempt to corroborate or refute our previous finding of the benefit for ICSI for low HOST scores and at the same time to determine the influence of poor morphology on outcome.

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