Comparison of the efficacy of treating sperm with low hypoosmotic swelling test scores with chymotrypsin followed by intrauterine insemination vs in vitro fertilization with intracytoplasmic sperm injection

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Summary

Purpose: To compare the efficacy of two treatments for sperm with low hypoosmotic swelling (HOS) test scores – intrauterine insemination (IUI) with sperm pretreated with the protein digestive enzyme chymotrypsin versus in vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI). *Methods:* The choice of patient therapy was optional. The pregnancy rates following two IUI cycles vs one IVF cycle with ICSI were then compared. The data were further stratified and compared according to the severity of the HOS score defect. *Results:* The more severe the HOS test defect the less likely for chymotrypsin therapy to work whereas the severity did not affect IVF with ICSI success. The use of IVF with ICSI was much more effective than IUI with chymotrypsin treatment. *Conclusions:* Though IVF with ICSI is much more effective, IUI is much less expensive. Couples should be presented with these data and be allowed to make their own choice considering risks and expense versus efficacy and speed of success.

Key words: Hypoosmotic swelling test; Chymotrypsin; Intrauterine insemination; Intracytoplasmic sperm injection.

Introduction

Males with hypoosmotic swelling (HOS) test scores < 50% rarely achieve successful pregnancy following intercourse, intrauterine insemination (IUI), or in vitro fertilization (IVF) using conventional insemination [1-4]. Treatment with the protein digestive enzyme chymotrypsin-galactose (CG) can improve HOS test scores to ≥ 50% and has been found to improve pregnancy rates both with IUI and with IVF with conventional oocyte insemination [5, 6].

Though a pilot study was very optimistic about the benefit of chymotrypsin treatment followed by IUI [5] a larger study, though allowing some pregnancies, did not have anywhere near the same success rate [7]. We considered the possibility that the results were marred by allowing intercourse which would enable sperm with the hypothesized toxic factor to attach to the zona pellucida, transfer the toxic factor and thus prevent embryo implantation by causing a functional impairment of the embryo membrane [8].

Intracytoplasmic sperm injection (ICSI) has been found to negate the adverse effect of fertilization of the egg with sperm with low HOS test scores [9]. The present study was conducted to evaluate and compare the effectiveness of IUI with CG treated sperm with low HOS scores (< 50%) and IVF with intracytoplasmic sperm injection (ICSI) where precautions were given about unprotected intercourse.

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Materials and Methods

A retrospective cohort study was performed on infertile couples (> 1 year) where the female partner had patent fallopian tubes by hysterosalpingography and was either ovulating or could be made to ovulate with follicle maturing drugs but where the male partner had an HOS test score < 50%.

The couples were asked to abstain from intercourse prior to ovulation. Only those couples having at least two cycles of IUI with chymotrypsin galactose (CG) or IVF with ICSI were included in the study. Couples were excluded if the HOST score did not correct to > 50% following chymotrypsin therapy.

Males in the CG group ejaculated into 5 ml Earle's balanced salt solution (EBSS) with 0.1M D(+)galactose added to 5 mg chymotrypsin. Following production, 150 mg BSA was added and the specimen was centrifuged for 20 min at 300 x g.

Pregnancy rates were determined by the range of the HOS test scores. Only live delivered pregnancies were counted as successes.

Results

The pregnancy rates for IUI with CG versus rates for IVF with ICSI stratified according to ranges of subnormal HOS scores are given in Table 1. Five women having IUI with CG conceived during their first cycle and four women conceived on their second cycle.

The live/delivered pregnancy rate per 2 IUI cycles was 9.7% (9/93) versus 33% (142/431) evaluating IVF with ICSI ($p < .001$, chi-square).

Table 1. — *Comparison of pregnancy rates following either intrauterine insemination with chymotrypsin-galactose treated sperm versus intracytoplasmic sperm injection according to five subnormal ranges.*

HOS test score (%)	Pregnancy rate with 2 IUI cycles	Pregnancy rate with 1 cycle of IVF with ICSI
< 20	0% (0/1)	50.0% (12/24)
20-29	0% (0/6)	36.1% (13/36)
30-39	3.8% (1/26)	30.1% (38/123)
40-44	10.8% (4/37)	36.2% (38/105)
45-49	17.4% (4/23)	29.4% (41/143)

Discussion

Despite the use of IUI with CG treatment on sperm with low HOS test scores to neutralize a hypothesized toxic protein that may transfer from sperm to zona pellucida, low pregnancy rates were still evident. However, the treatment does allow for a somewhat higher percentage of pregnancies per IUI cycle (5%), as compared with previous studies when caution against unprotected sex was not given (3.3%).

There was a trend towards higher pregnancy rates with IUI if the initial pretreatment HOS scores were not too far below 50%. Severity of HOS score does not affect pregnancy outcome following IVF with ICSI.

Generally speaking the expected pregnancy rates per cycle with sperm with low HOST scores following untreated IUI or intercourse or even IVF with conventional oocyte insemination is zero or close to zero [1, 3, 4]. Thus there appears to be a benefit to treating sperm with low HOS scores with CG prior to performing IUI if the couple prefers not to start out with IVF with ICSI, especially if the severity of the defect as manifested by the HOS test scores is not too severe. A 17.4% live delivery rate in two IUI cycles with CG treated sperm was achieved with HOS test scores of 45-49%.

Though very good pregnancy rates were achieved by pretreating sperm with low HOS test scores with chymotrypsin and then performing in vitro fertilization conventional oocyte insemination there probably is no advantage over just performing ICSI [6, 9].

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