



TREATMENT OF SPERM WITH SUBNORMAL HOST SCORES WITH CHYMOTRYPSIN/VIABLE PREGNANCY AFTER IUI

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Men with low hypoosmotic swelling test (HOST) scores (<50%) rarely achieve a pregnancy with intercourse or conventional intrauterine insemination (IUI) or even IVF. The defect seems to be related to a toxic factor attached to the sperm that can be transferred to the zona pellucida, which ultimately interferes with implantation. A small case series showed optimistic pregnancy outcome with treatment of the sperm with low HOST scores with chymotrypsin. However, the live pregnancy rate in 90 subsequent IUI cycles in men whose low HOST scores were improved by chymotrypsin was only 3.3%. IVF with ICSI remains the only highly effective treatment of this disorder.

Keywords chymotrypsin, hypoosmotic swelling test, intrauterine insemination

The hypoosmotic swelling test (HOST) is a measure of the functional integrity of the sperm membrane [11]. A score of <50% correlates with extremely poor pregnancy rates (PRs) in non-IVF cycles [6]. Abnormally low HOST scores do not correlate with poor fertilization rates following IVF [1, 2, 4, 10, 15, 16]. However, HOST scores <50% do correlate very well with extremely poor implantation rates following IVF-embryo transfer (ET) [9, 14, 15].

There has been speculation that the poor implantation rates may be related to the transfer of some toxic factor to the zona pellucida by the attached supernumerary sperm [7]. Data supporting this hypothesis were provided by the demonstration of a very high PR following ICSI with semen specimens with low HOST scores, thus bypassing contact with the zona pellucida [8].

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A previous study, where sperm with low HOST scores were treated with the protein digestive enzyme chymotrypsin, showed a high pregnancy rate per IUI cycle (4/12, 33%) using sperm where the HOST score improved to >50% after such treatment [12]. The purpose of this present study was to either corroborate or refute these findings in a larger case study.

MATERIALS AND METHODS

Couples were selected with a minimum of 1 year of infertility and where the male partner had on initial testing a HOST score <50%. Couples were excluded if, after the male ejaculated into a chymotrypsin-galactose solution and the sperm subsequently processed, the HOST score remained <50%. Couples were excluded if there was a tubal factor problem or if the semen analysis showed < 5×10^6 /mL sperm concentration or normal strict morphology $\leq 4\%$.

Totals of 7.35 g sodium citrate and 13.5 g fructose were added to 500 mL of cell culture water. Additional cell culture water was added to make 1000 mL. The osmolarity read 150 ± 2 mOsm. After incubating the mixture for at least 30 min at 37°C, 100 sperm were observed with a phase-contrast microscope for tail swelling changes that were typical of a reaction in the HOST. Based on our previous study [6] scores <50% were considered abnormal instead of the 60% cutoff by reported by Jayendran et al. [11].

Galactose (0.1 M) and 5 mg of chymotrypsin was added to 5 mL Earle's balanced salt solution. The male partner then ejaculated into the solution. The enzymatic reaction was stopped after 10 min by adding bovine serum albumin [3, 13].

The semen was prepared by a 3-layer isoprep discontinuous gradient. The timing was 40 h after a spontaneous LH surge (detected by performing urinary LH kits every 5 h) or 40 h following 10,000 U hCG IM. Usually the oocyte was deemed released when IUI was performed by demonstrating the collapse of the follicle by sonography.

The female partner was evaluated by sonographic follicular maturation studies, serum estradiol and progesterone, and endometrial biopsy. Follicle maturing drugs and/or progesterone and/or hCG were given whenever appropriate.

RESULTS

Initially, there were 58 couples whose male partner scores were <50% after the HOST. Following treatment with chymotrypsin, 45 (77.4%) improved the HOST to >50%. Six couples chose to proceed immediately with IVF with ICSI, whereas 39 elected to try IUI with chymotrypsin-treated sperm.

There were only 2 viable pregnancies in the first cycle (5.1%) of these 39 women. There were 51 subsequent IUI cycles with only 1 viable pregnancy (2%). Thus, overall there were only 3 viable pregnancies in a total of 90 IUI cycles (3.3%).

DISCUSSION

The previous study of 12 patients with low HOST scores found encouraging results for both types of therapies: 2 of 4 choosing IVF with ICSI conceived (50% PR per patient and

per cycle) and 4 of 8 patients (50%) conceived with chymotrypsin treatment in 12 cycles (33% per cycle).

Evaluating the efficacy of IVF with ICSI for low HOST scores corroborated the initial optimism with a clinical PR per transfer of 49% and an implantation rate of 27% in 53 couples. However, unfortunately, the present study of 39 patients having 90 IUI cycles failed to corroborate that chymotrypsin treatment of sperm, even when it apparently improves the HOST score to >50%, is an effective treatment for men with low HOST scores. Whether the treatment offers any improvement over merely performing IUI without chymotrypsin treatment would require a prospective randomized study.

There are at least 2 mechanisms that one can hypothesize to explain why improving the HOST score to >50% did not result in a higher PR per IUI cycle [5]. If, in fact, the cause of reduced fecundity is a toxic factor transferred to the zona pellucida by the supernumerary sperm, these sperm could have reached the zona pellucida by intercourse. Also, the chymotrypsin treatment may negate to an extent the hypothesized toxic factor, enough to improve the HOST score to >50%, but not enough to eradicate it in all sperm.

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