

## EFFECT OF TREATING ANTIBODY-COATED SPERM WITH CHYMOTRYPSIN ON PREGNANCY RATES FOLLOWING IUI AS COMPARED TO OUTCOME OF IVF/ICSI

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Males with 100% of their sperm coated by antisperm antibody have a very small chance of achieving a pregnancy by intercourse or conventional intrauterine insemination (IUI). A previous study found that treatment of the sperm with the protein digestive enzyme chymotrypsin improved the efficacy of IUI. The present study was designed to corroborate or refute this previous study and compare efficacy to IVF with ICSI. This time the subjects were an even more difficult group with 100% of the sperm coated by autoantibodies.

**Keywords** antisperm antibodies, intrauterine insemination, protein digestive enzyme

It has been demonstrated that men whose spermatozoa are all or nearly all (>70%) coated by antisperm antibodies (ASA) will suffer clinically significant infertility [6]. Furthermore, when 100% of sperm have ASA attached, intrauterine insemination (IUI) completely failed to achieve pregnancies [4]. A previous prospective study found that treating naturally antibody-coated sperm with the protein digestive enzyme chymotrypsin prior to IUI significantly improved the pregnancy rates compared to sperm ejaculated into Earle's balanced salt solution medium containing 5% albumin [1]. Other studies have shown improved pregnancy results in the female partner of men with ASA following IVF with ICSI [3, 5, 7]. One of these studies showed that men with ASA > 70% suffered no adverse effect on outcome when ICSI was used [3]. Given the high cost and invasive nature of IVF with embryo transfer (ET), the question remains if this is the appropriate first treatment option for all couples with ASA.

The study presented here evaluated only those males whose sperm demonstrated 100% ASA by direct immunobead testing. The study intended to determine the relative efficacy and cost effectiveness of IUI with chymotrypsin-treated sperm vs IVF with ICSI.

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## MATERIALS AND METHODS

Patients were given the option of chymotrypsin treatment of sperm followed by IUI vs IVF with ICSI. Some began by choosing IUI but proceeded to IVF with ICSI if the IUI was not successful. For chymotrypsin-galactose treatment, 0.1 M galactose was dissolved in 5 mL of Earle's balanced salt solution and added to 5 mg of chymotrypsin [1]. The patient ejaculated directly into this chymotrypsin-galactose mixture. The semen immediately was mixed to break up the coagulum. Bovine serum albumin (30 mg/mL) was added to stop the enzymatic reaction before the sperm head separated from the tail [1]. For IVF with ICSI, the motile sperm was immobilized with an injection pipet in a drop of polyvinylpyrrolidone (Scandinavian IVF Science AB, Goteberg, Sweden) and then injected into the ooplasm of each oocyte. The injected oocytes were then placed in human tubal fluid (HTF; Irvine Scientific, Irvine, CA) and 10% synthetic serum substitute (Irvine Scientific) and incubated for at least 16 hours before evaluation for signs of fertilizations (2 pronuclei).

We initially proposed another study to refute or corroborate our previous one comparing outcome of chymotrypsin-treated sperm vs those who ejaculated into albumin, only this time exclusively for males with 100% of their sperm coated with ASA. Testing for ASA used the direct immunobead test [2]. Before seeking IRB approval, the study was first submitted to the Ethics Committee. The Committee rejected the study because they believed that the data from the previous study showed such a difference between chymotrypsin treatment vs controls that with an even more difficult group, those randomized to the untreated group would be unfairly biased. The treatment options were offered not as part of a randomized study but merely as two clinical choices.

Thus, this study was simply a retrospective review of outcome for patients choosing the less expensive, less invasive, but likely less efficacious method of IUI with chymotrypsin-treated sperm vs the more invasive and expensive, but likely more successful, option of IVF with ICSI in a group of female patients whose male partners demonstrated 100% of their sperm coated with ASA. The time period evaluated was from 6/99 to 3/02. The purpose of this retrospective review was to determine what is the relative likelihood of success as evidenced by achievement of pregnancy with these two methods in this difficult group of patients so that patients in the future would have more information to make the best choice for them taking into account financial, risk, and efficacy considerations.

## RESULTS/DISCUSSION

There was a significantly higher pregnancy rate per cycle with IVF with ICSI vs IUI with chymotrypsin treatment as expected ( $p < .057$ ) (Table 1). These results suggest ICSI is more than 2½ times more effective per cycle than IUI with chymotrypsin-treated sperm in men with 100% of their sperm coated with ASA. These data also suggest that patients in this group who attempt approximately 3 IUI cycles can expect a pregnancy rate of nearly 30%.

Couples, where the male partner has 100% of his sperm coated with ASA, who normally would have an extremely poor success rate following conventional IUI [4] can decide, based on these data, which treatment option best suits their needs. These data thus

**Table 1.** Comparison of two treatment modalities for males with 100% of their sperm demonstrating antisperm antibodies

	Chymotrypsin treated group (n = 17)	IVF with ICSI treated group (n = 25)
Number of cycles	47	38
Number of pregnancies	5	11
Pregnancy rate/cycle	10.6%	28.9%
Pregnancy rate/patient	29.4%	44%
Average number of cycles/patient	2.7	1.5
Miscarriages	0 (0%)	1 (9.0%)

confirm the outcome of a previous study where the pregnancy rate per IUI cycle with chymotrypsin sperm was 15% per cycle using a less impaired male group (requirement of ASA > 50%) [1]. An extensive scan of the World's literature suggests that the present study is the first one attempted to refute or corroborate the study from 2000 [1]. Based on the data by Francavilla, the achievement of successful pregnancies following IUI with untreated sperm, of which 100% were coated with antisperm antibodies attached, would be very rare [4].

## REFERENCES

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