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Research Article

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Evidence That Sperm with Zero Percent Normal Morphology Using Strict Criteria Is Not a Clinically Important Infertility Factor

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ABSTRACT

Almost 40 years ago sperm with <4% normal morphology using strict criteria was considered such a significant abnormality that the recommendation was to consider the use of donor sperm. Over the years it became clear that low percentage of sperm with normal morphology was not a very good predictor of male subfertility. Nevertheless, there is the possibility that when there is the absence of any sperm with normal morphology (with the exception of 100% globozoospermia), this may be a factor predicting male subfertility. However, just with natural intercourse correcting a female infertility factor 4 of 10 women (40%) delivered a live baby in just 21 cycles (19.0% live delivery per cycle. Through in vitro fertilization embryo transfer with intracytoplasmic sperm injection) (IVF-ET with ICSI) resulted in fifty-two of eighty-four women (61.5%) achieving a live baby in one hundred and six transfers (49.0% per transfer), this is the usual difference in success rates with natural intercourse vs IVF-ET partly related to only one egg released in natural cycles and generally two embryos transferred in IVF-ET cycles (1.92 in this study). Thus, zero% normal morphology should not be the sole reason for choosing IVF with or without ICSI.

Keywords: Strict Morphology of Sperm, Zero% Normal Morphology, Natural Intercourse, In Vitro Fertilization, Intracytoplasmic Sperm Injection

Introduction

One way to assess the value of a type of semen parameter as a potential factor leading to subfertility is to determine the ability of that sperm with that one abnormal semen assessment parameter to fertilize eggs with conventional in vitro fertilization (IVF). In 1988 Kruger et al using a new technique at that time to evaluate abnormal sperm morphology using strict criteria found that males with less than 4% of the sperm showing normal morphology despite other sperm parameters normal had an extremely poor fertilization rate of only 7.6% [1]. Since the egg using the conventional insemination technique is exposed to at least 50,000 more sperm than through natural intercourse, a logical conclusion would be that achieving a pregnancy with natural intercourse would be extremely unlikely if strict morphology showed less than 4% normal sperm. Furthermore, with the expense of IVF even 38 years ago, would IVF be worth trying despite such a low fertilization rate?

Thus, many infertility specialists were recommending the use of donor sperm intrauterine insemination (IUI) for even isolated sperm morphology issues. Intracytoplasmic sperm injections (ICSI), where one can choose a sperm with normal morphology and inject it into the egg, was not available as yet. Rather than follow the trend at that time to advise the use of donor sperm, we wanted to first do our own studies to see if conception was at all possible with sperm with an isolated morphology defect.

We thus determined the 6-month pregnancy rates in women where an abnormal female factor was identified and deemed correctable according to the percentage of sperm with normal morphology using strict criteria following intercourse at the proper time with normal follicular maturation prior to the LH surge (2). Using the <4% cut off there were 14 pregnancies in 28 women (50%) in 6 months [2]. Using <4% cut off there were 10/19 (53%) pregnant in 6 months [2].

New Jersey was one of the states that mandated insurance re-imbursement for in vitro fertilization-embryo transfer (IVF-ET).

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However, unless there was a clear-cut tubal abnormality or severe oligoasthenozoospermia several IUI cycles were required before reimbursement for IVF was allowed. We thus evaluated the efficacy of IUI according to 3 categories of sperm morphology using strict criteria: 0-4%, 5-14%, and 7>15% [3]. In this case, the pregnancy rate was calculated according to one cycle of IUI. Though the total motile sperm recovered for the IUI increased with each improved category of sperm morphology (13.4 million for <4%, 27 million for 5-14% and 50 million for 7>15%), the clinical pregnancy rates were similar 30% (28/91), 26% (71/268) and 20% (11/53). Thus, there was not even a trend for lower pregnancy rates with low percent morphology using strict criteria [3]. These data were published in 2002 ten years after the first study.

The objective of the present study was to compare the live delivered pregnancy rate (LDPRs) following IVF-ET with intracytoplasmic sperm injection (ICSI) versus natural intercourse where the male partner had zero percent normal morphology using strict criteria.

Materials and Methods

Couples with a minimum of one year of primary or secondary infertility were selected where the semen analysis x2 showed zero% normal morphology using strict criteria. The patients were given the option of IVF-ET with ICSI where we would choose the sperm with the least abnormal morphologic aspect (generally selecting tail defects rather than head abnormalities) or normal intercourse.

Of course, if there were fallopian tubal issues or severe oligasthenozoospermia the couple would choose IVF with ICSI. Some might choose IVF-ET with ICSI even if all other semen parameters were normal except for zero% with normal morphology depending on insurance coverage, finances, and previous infertility treatment.

The group choosing natural intercourse could be relegated to IVF-ET with ICSI if the post coital test performed at the proper time was inadequate. However, they were not included if they chose intrauterine insemination (IUI).

All couples received supplemental vaginal progesterone (commercial or compounded) in the luteal phase. To eliminate the confounding effect of age on pregnancy rates only women age 35 or younger were included. There were no restrictions related to diminished oocyte reserve (DOR) (serum anti-mullerian hormone i.e., AMH levels <1ng/nl) since we have found DOR does not significantly decrease pregnancy rates especially in younger women [4-6].

All embryo transfers used 3-day old embryos. Post coital tests were performed at the time that the follicle achieved an 18-24mm diameter with a serum estradiol (E2) >200pg/nl but before the LH surge [7-9].

Patients were all treated with vaginal progesterone (P) in the luteal phase whether they did IVF-ET or natural intercourse. For those doing natural intercourse follicular maturation defects or the luteinized unruptured follicle syndrome was corrected by treating either with clomiphene citrate, letrozole, small dosages of gonadotropins or human chorionic gonadotropins or leuprolide acetate [10,11].

Results

There were 10 patients who opted for natural intercourse. There were 4 live deliveries (40% per patient). There were 21 natural cycles evaluated and the live delivered pregnancy rate (LDPR) per cycle was 19.0%. There were eighty-four patients choosing IVF-ET with ICSI. Fifty-two women achieved a live delivery (61.8% per transfer). These pregnancies occurred in 106 embryo transfer cycles. Thus, the LDPR per cycle was 49.0%. The average number of embryos transferred was 1.92.

Discussion

Related to transferring 2 embryos with IVF-ET cycles and selection of the embryos with the best morphology versus just one egg releasing in natural cycles and selection of the embryos with the best morphology), most of our studies have similarly found a 2.5-fold increased LDPR per cycle compared to natural cycles. Indeed, 2.5 times 19.0% LDPR for natural cycles would be 47.5%, and thus very close to the 49.0% for IVF-ET with ICSI per cycle.

Most studies concluding that strict morphology <4% was very predictive of male sub-fertility made their conclusion based on poor fertilization rates with conventional oocyte insemination. The actual first publication was by Kruger et al in 1987 [12]. Many of the subsequent studies corroborated this level as a prediction of subfertility when strict morphology was <4% were IVF studies, but mostly from the same renowned group from the Jones Institute [1,13-17]. Other well-known well respected IVF centers in the early days of IVF reached the same conclusions [17,18].

Our group was one of the first groups to disagree that low percentage strict normal morphology predicted poor fertilization rates and thus was likely to be a significant subfertility factor [2,3]. However, subsequently today, the Society of Assisted Reproductive Technologies (SART) using statistics from IVF centers around the world agree that low percent normal morphology <4% using strict criteria has little or no predictability of poor fertilization rates with conventional oocyte insemination [18]. For a while after the invention of ICSI, IVF was suggested to be able to choose sperm with normal morphology to inject into the oocyte [18]. However, subsequently other studies found no advantage of doing ICSI over conventional oocyte insemination for isolated sperm abnormalities with sperm morphology [19-21].

ICSI in general may lower live delivered pregnancy rates if it is not needed [19]. Thus, if lower percentage sperm morphology has no subsequent negative effects on fertilization or pregnancy outcomes, then possibly performing ICSI to select a normal appearing sperm may even have a negative effect on pregnancy outcome. In fact, we have shown lower LDPRs with IVF with ICSI versus conventional oocyte insemination both with fresh and frozen embryo transfers [20,21]. ICSI may lower the LDPR because it is possible that the procedure may damage the egg in some way, or the sperm that is selected is not the one that the egg would have selected [20,21].

Whereas van Waart and Kruger (who developed the strict criteria morphology test) suggested that sperm with < 4% normal morphology predict subfertility, also with IUI our own studies disagree [22,23]. We did not even find that males with only 1% of the sperm having normal morphology resulted in a lower pregnancy rate than sperm > 6%. Even 0% normal morphology

using strict criteria had IUI pregnancy rates comparable to other percentages [24].

The real test to determine if even zero % normal morphology predicts sub fertility is to see if natural intercourse results provide adequate LDPRs despite 0% normal morphology using strict criteria. The 19.0% pregnancy rate per cycle was just as effective or more effective than IUI in the aforementioned study. The results of the present study indicate that even zero% normal morphology using strict criteria is not a reason to recommend IUI, conventional oocyte insemination with IVF, or ICSI [23,24].

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