Distress level in men undergoing intracytoplasmic sperm injection versus in-vitro fertilization

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The purpose of this study was to compare the psychological reactions of men undergoing intracytoplasmic sperm injection (ICSI) (n = 18) or in-vitro fertilization (IVF) (n = 22). Men monitored their psychological reactions daily for one complete treatment cycle from the first day of down-regulation until the outcome of treatment was known (approximately 52 days). The results showed that ICSI patients reported marginally more distress on the days prior to retrieval than the IVF patients. Other than this difference the pattern of results indicated that the psychological reactions of men undergoing ICSI or IVF were similar and that there was no need to manage these patients differently during treatment. However, ICSI patients may benefit from some reassuring comments on the days prior to retrieval when they showed more anticipatory anxiety.

Key words: infertility/intracytoplasmic sperm injection/in-vitro fertilization/psychology/stress

Introduction

We here present the first report on the psychological reactions of men undergoing intracytoplasmic sperm injection (ICSI) compared with those involved in in-vitro fertilization (IVF). Several hypotheses can be made concerning treatment reactions in these two groups of patients. First, one might hypothesize that men undergoing ICSI would experience more distress during treatment than men undergoing IVF. This is because of the general finding that men with male factor diagnoses report more distress about their infertility than men in couples with unexplained or female-only diagnoses. Nachtigall et al. (1992) found that men diagnosed with a male factor problem were more likely to report feeling stigmatized and to report a loss of physical potency and self-esteem than men from couples not diagnosed with this kind of problem. Connolly et al. (1992) also found that the initiation of the diagnostic investigation was associated with a decrease in negative feelings for all patients except men who were diagnosed with a male factor problem. These men reported more anxiety and more psychiatric distress than did the rest of the sample 7 months into the diagnostic investigation. Given that male factor diagnoses are, by definition, more common among ICSI patients while female-only and unexplained diagnoses are more common among IVF patients (HFEA, 1996), one might expect that ICSI patients would report greater distress during their treatment cycle than the IVF patients.

A second hypothesis is that the difference in distress between the ICSI and IVF patients would be most pronounced during the active stages of retrieval, fertilization and transfer when men produce the sperm sample and find out whether the oocytes were fertilized with their spermatozoa. One aspect of providing the sperm sample that men worry about is the possibility that they will not be able to perform under the pressure that exists at the time the sample is requested (McGrade and Tolor, 1981). In the case of the ICSI patient there is the additional worry that even if a sample is produced it may not be sufficient to fertilize the oocytes retrieved. In this sense, ICSI patients have more to worry about during the active stages of treatment than the IVF patients. Significant stress may, in turn, have a negative impact on sperm parameters at the time of treatment. Harrison et al. (1987) found a significant deterioration in semen quality when comparing samples produced some months before IVF compared to those produced at the time of IVF. It was suggested that the stress of initiating IVF contributed to the poorer sperm quality in the 10% or so of men affected. Similarly, Cui (1996) found that sperm parameters in non-human mammals were significantly poorer in animals housed under stressful conditions compared with those with normal housing conditions. The potential negative effects of stress may have greater implications for the ICSI patient whose sperm quality is already compromised.

In this study we test the hypotheses by comparing daily distress in men undergoing either ICSI or IVF. In addition, we also examined differences in daily optimism about achieving a pregnancy because it seemed possible that this variable would influence the level of distress reported during treatment. Previous studies have found that patients’ optimism changes as a function of new opportunities for pregnancy. Van Keep and Schmidt-Elmendorf (1975) and Blenner (1990) found that the initiation of treatment after discovery of infertility was sufficient to increase couples’ sense of hope for a pregnancy while Boivin and Takefman (1996) found a surge in optimism after embryos had been transferred in women undergoing IVF. It is possible that the renewed hope for a genetically related child that ICSI patients may experience may mitigate their distress level during treatment.
Materials and methods

Sample
The sample consisted of 18 men undergoing ICSI and 22 men undergoing IVF in a private fertility clinic in Sweden (Carl von Linné Kliniken, Uppsala). The ICSI group was significantly older (mean = 36.8, SD = 6.6) than the IVF group (mean = 33.2, SD = 4.6) \([t(38) = 2.05, P \approx 0.05]\). Both groups had been married for an average of 6.8 years ± 3.4 and had been infertile for 4.8 years ± 2.9. All men in the ICSI group had received a male factor diagnosis while the cause of infertility in most couples in the IVF group was a female-only factor (77.3%), with three cases of unexplained infertility and one mixed factor case. None of the ICSI patients had had a vasectomy, none of the patients had previous experience with ICSI and only one patient had undergone an IVF cycle. The pregnancy rate was also similar in the two groups with 40.9% (9) of IVF patients and 50.0% (9) of ICSI patients subsequently conceiving with treatment.

Materials
Prior to treatment men completed a short questionnaire designed to obtain demographic and medical information. They also completed the Swedish version (Collins et al., 1992) of an infertility reaction scale (Keye et al., unpublished observations) which was used to assess adjustment to infertility. Each of the 15 items was rated from 1 (disagree) to 7 (agree) with a high total score indicating poorer adjustment to infertility. Items concerned social pressures (e.g., ‘I avoid family and friends with children’), male role (e.g., ‘I am not a good husband’), extent of focus on childbearing (e.g., ‘I will do anything to have a child’) and the effect of infertility on sexual and other domains (e.g., ‘I am not able to respond sexually to my partner’).

During treatment, men completed the Daily Record Keeping (DRK) chart designed to assess emotional, physical and social reactions to infertility treatment (Boivin and Takefman, 1995). Only results obtained with the emotional subscale are presented in this paper. The emotional subscale consists of the positive item ‘optimism about pregnancy’ as well as a series of negative emotional reactions (e.g., nervous, tense). Patients indicated the extent to which they experienced each reaction daily on an analogue rating scale with a range of 1 (none) to 4 (severe). The negative emotional items were summed to create the ‘distress’ subscale. The psychometric properties of the distress subscale have been evaluated previously and have shown that the subscale is a reliable and valid measure of treatment distress. Internal reliability as measured in a number of studies has shown that Cronbach alpha is consistently above 0.87 (Takefman and Internal reliability as measured in a number of studies has shown that Cronbach alpha is consistently above 0.87 (Takefman and Takefman, 1992). The Cronbach alpha on the Swedish version (Collins et al., 1992) of an infertility reaction scale (Keye et al., unpublished observations) which was used to assess adjustment to infertility. Each of the 15 items was rated from 1 (disagree) to 7 (agree) with a high total score indicating poorer adjustment to infertility. Items concerned social pressures (e.g., ‘I avoid family and friends with children’), male role (e.g., ‘I am not a good husband’), extent of focus on childbearing (e.g., ‘I will do anything to have a child’) and the effect of infertility on sexual and other domains (e.g., ‘I am not able to respond sexually to my partner’).

Procedure
One to two months prior to treatment couples participated in an information afternoon at the clinic. During this time a complete description of the psychological study was provided and patients invited to participate. Of the 89 consecutive couples invited into the study, 40 (44.9%), completed all study materials and are included in this report. The remaining patients did not complete the study or are not included in the report for the following reasons: cancelled IVF protocol (18%), refused to participate or withdrew from the study (14.6%), incomplete study materials (10.1%) or withdrew from IVF (5.6%). A further 6.7% (6) of patients had not yet started their IVF cycle. There was no difference between patients who completed the study and those who did not, on number of years married \([t(88) = 0.49]\), years infertile \([t(88) = 0.43]\) or on adjustment to infertility as measured by the infertility reaction scale \([t(88) = 1.26]\).

The patients who agreed to participate completed pre-treatment questionnaires at the clinic at the end of their information session (1–2 months prior to treatment) and were then provided with the materials to complete at home during treatment. Couples were instructed to begin the daily charts on the first day of gonadotrophin-releasing hormone analogue (GnRHa) and to complete them daily until the beginning of menstruation or the pregnancy test (i.e., a total of mean = 52.8 ± 5.2 days). Daily forms were completed at night before going to bed and returned once a week in the stamped, pre-addressed envelopes provided.

The procedure for the provision of the sperm sample was the same for ICSI and IVF patients. On the day of oocyte retrieval patients were given a description of the medical procedures to be carried out that day and then given a choice to provide the sperm sample before or after the retrieval. Men were led to a private room away from the main areas of the clinic and asked to return the sample they produced to the laboratory staff. Men were informed of the results of the semen analysis before they left the clinic on the day of retrieval.

Patients carried out a home pregnancy test 21 days after transfer and provided the clinic with test results. Although both husband and wife completed the DRK, only the results for men will be presented in this paper with a complete report of gender differences to follow.

Data analysis
The daily distress and optimism scores for days of GnRHa, human menopausal gonadotrophin (HMG) and the waiting period were averaged to create stage scores as described previously (Boivin and Takefman, 1996). Distress and optimism scores were thus available for a baseline or pre-treatment period (i.e., GnRHa administration) as well as for nine stages in IVF: HMG, human chorionic gonadotrophin (HCG), day before and day of oocyte retrieval, day before and day of embryo transfer, week 1 of waiting, week 2 (i.e., day 8 to outcome) and outcome (i.e., beginning of menstruation or outcome of pregnancy test). The mean 17 days of GnRHa (mean = 17.19 ± 4 days) were considered as a pre-treatment period because the only intervention occurring during this period was self-administration of a nasal spray. Distress and optimism scores during treatment were then subtracted from baseline scores to create the change scores used in the subsequent analyses.

Distress and optimism were examined using two group (ICSI, IVF) × 9 (stage) analyses of variance (ANOVA) with stage as repeated measure. Because power formulas are not readily available for mixed ANOVA designs, it was necessary to estimate power for these analyses from programmes for between-subjects ANOVA and those for single group within-subjects ANOVA (Stevens, 1992). Based on these calculations (using: \[n = 40\], \[\alpha = 0.05\], effect size \(f = 0.25\), and moderate correlations between levels of the repeated measures), power for the ANOVA used in this study was estimated to be 0.81. Specific hypothesized differences were examined using one-tailed planned comparisons. Greenhouse–Geisser adjusted probability values were used where violations of sphericity or homogeneity of variance occurred.
Results

There was no significant difference \( t(38) = 0.89, P > 0.10 \) between the ICSI and IVF patients in terms of adjustment to infertility before treatment as measured by the Keye questionnaire. Moreover, there was no difference between groups on baseline distress \( t(38) = 0.87, P > 0.10 \) or baseline optimism \( t(38) = 0.37, P > 0.10 \) scores. ANOVA results for optimism also showed that the two groups did not differ overall during treatment \( F(1, 38) = 0.11, P > 0.10 \) or as a function of specific stages of treatment \( F(9, 342) = 0.75, P > 0.10 \).

Figure 1 shows distress change scores as a function of treatment stage for both the ICSI and IVF groups. In this figure, zero represents the point at which there is no difference between the distress level reported during treatment and the distress level reported during baseline (pre-treatment). Scores plotted above this zero line indicate that distress was higher during treatment, while scores plotted below this line indicate that distress was higher during the baseline period. Figure 1 shows a tendency for ICSI patients to report more distress during the 2 days that precede retrieval compared with IVF patients. That is, ICSI patients reported marginally more distress on the day of HCG \( t(38) = 1.30, P < 0.10 \) and the day before retrieval \( t(38) = 1.37, P < 0.10 \) than the IVF patients. However, distress level in the IVF group increased to that of the ICSI patients on the day of retrieval. Specifically, the increase in distress from the day before to the day of retrieval was not significant for the ICSI patients \( t(18) = 0.48, P > 0.10 \) but was found to be marginally significant for the IVF patients \( t(18) = 1.57, P < 0.10 \). Other than these differences, the pattern of distress was, for the most part, very similar in the ICSI and IVF groups across the treatment cycle. ANOVA results showed that the main effect of group \( F(1, 38) = 0.44, P > 0.10 \) and the group×stage interaction \( F(9, 342) = 0.02, P > 0.10 \) were not significant. However, the stage main effect was significant \( F(9, 342) = 5.96, P < 0.001 \) and post-hoc tests showed that for both groups distress was lowest at the time of ovarian stimulation and during the first week of waiting post-transfer.

Discussion

The purpose of this study was to compare the distress level in men undergoing ICSI with that of men undergoing IVF. We expected that the men undergoing ICSI would experience more distress during treatment especially during the active stages of retrieval, fertilization and transfer than men undergoing IVF. However, we found that the ICSI patients reported more distress on the 2 days preceding the active stages of treatment while distress was the same for the two groups during retrieval, fertilization and transfer. This finding suggests that men undergoing ICSI experienced greater anticipatory anxiety than those undergoing IVF. As the two groups were treated in the same way during treatment, we can only suggest that the history of poor sperm quality made the process of providing the sperm sample and waiting for the results of fertilization and the transfer procedure somewhat more daunting for the ICSI patient. Whether this is due to the uncertainty of fertilization, feelings of physical inadequacy or some other reason needs to be determined by future research. However, it seems unlikely that these minor differences would have affected sperm parameters as has been found previously in men (Harrison et al., 1987) and non-human mammals (Cui, 1996).

Our hypothesis that ICSI patients would experience more distress throughout the treatment cycle was not supported either. Indeed, ICSI and IVF patients were similar in their adjustment to infertility before treatment and in their pattern of distress across the many days of the treatment cycle. These findings are inconsistent with those of previous studies which report more negative feelings about infertility and more psychiatric distress among men with a male factor diagnosis compared to men in couples receiving other diagnoses (Connolly et al., 1992; Nachtigall et al., 1992). The absence of differences in emotional reactions between the two groups may have been due to the fact that the ICSI patients were about to undergo a treatment that would circumvent their fertility problem. At the time of previous studies the only medical option available for patients with male factor infertility was donor insemination. As Connolly and colleagues (1992) stated, this option offered men the possibility of having a child and not, as ICSI does, the possibility of conceiving one. Hence the feelings of loss and hopelessness that would normally accompany a male factor diagnosis (Nachtigall et al., 1992) and which led to our hypotheses, may have been much less pronounced in our sample of men about to undergo their first ICSI cycle. Indeed this possibility was reflected in the fact that optimism about a pregnancy was the same in the ICSI and IVF groups both before and during treatment. Both groups of men also reported similar reactions to the outcome of treatment. As has been found previously (Slade et al., 1997), both ICSI and IVF
patients reported a significant increase in distress at the time of the pregnancy test suggesting they were similarly affected by the outcome of IVF.

We recognize that our study was carried out on a small sample and that firm conclusions must therefore await replication with a larger patient group. However, because statistical power was adequate and because of the multiple assessment points we feel confident that the trends observed in this study will be supported in future work. While the age difference may have been a contributing factor in the distress differences observed, this seems unlikely because the minor distress differences occurred only at specific stages rather than throughout the treatment cycle. Overall, the pattern of results would suggest that while ICSI patients tend to worry more before the active stages of treatment, both the ICSI and IVF patients experience similar distress on the actual days of retrieval, fertilization and transfer. Other than this difference the pattern of results indicated that the psychological reactions of men undergoing ICSI and IVF were similar and that there was no need to distinguish these patients on a psychological dimension during treatment. However, the ICSI patients may benefit from some reassuring comments on the days prior to retrieval.

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