Relationship between psychological stress and semen quality among in-vitro fertilization patients

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The purpose of this study was to determine the relationship between psychological stress and semen quality among men undergoing in-vitro fertilization (IVF). We assessed psychological variables, including self-reported stress, and sperm parameters in a group of 40 men undergoing IVF for the first time at a pre-IVF sampling period (T1) and at the time of egg retrieval (T2). Thirty-one patients completed the study. Results indicated that total and motile sperm concentration, total motile spermatozoa, and lateral head displacement decreased significantly from T1 to T2 in a high percentage of participants. In addition, the perceived importance of producing a semen specimen increased significantly (P = 0.001) from T1 to T2, and this change was significantly correlated (P < 0.05) with diminished semen quality at the time of oocyte retrieval. No decline in the semen quality or increase in perceived stress at egg retrieval was observed at T2 in male factor patients (n = 7). This study provides evidence for a significant decline in semen quality of male IVF patients at egg retrieval and demonstrates an inverse relationship between semen quality and specific aspects of psychological stress.

Key words: in-vitro fertilization/male infertility/semen/stress

Introduction

Infertile couples experience a wide range of physical and emotional stress during their attempts to conceive a child. The impact of this stress can be devastating, particularly to patients undergoing more advanced and involved procedures, such as in-vitro fertilization (IVF) (Baram et al., 1988; Newton et al., 1990). While the effects of psychological stress on female IVF patients have been well studied (Harlow et al., 1996; Milad et al., 1998), comparatively little is known about the impact of emotional stress on the male partner. Concern over the female partner undergoing egg retrieval, the importance of providing an adequate semen sample, and the uncertainty of fertilization results are but a few of the stresses commonly experienced by male IVF patients. It is not known whether the impact of stress is manifested in terms of altered semen quality at the time of the IVF procedure.

Previous studies have indicated that stress has a negative impact on various parameters associated with semen quality, including sperm concentration, motility and morphology (Moghissi and Wallach, 1983; Bents, 1985; Giblin et al., 1988). A decline in the semen quality of patients undergoing IVF has similarly been shown (Harrison et al., 1987; Kentenich et al., 1992). Boivin et al. (Boivin et al., 1998) have recently demonstrated that men undergoing regular IVF and IVF with intracytoplasmic sperm injection (ICSI) exhibit similar levels of psychological distress. In these studies, however, the impact of psychological stress on semen changes observed in male IVF patients was not adequately measured.

The objectives of the present study were: (i) to identify changes in perceived stress and semen quality in first-time male IVF patients from a baseline analysis to the time of egg retrieval and; (ii) to study the relationship between psychological stress and semen quality in men undergoing IVF treatment. An additional purpose of the study was to determine whether environmental distractions associated with semen collection had a negative impact on semen quality.

Materials and methods

Patients and sampling periods

Forty of 118 (34%) male patients undergoing IVF for the first time agreed to participate in this study. First-time IVF patients only were included in the study to decrease the change of habituation to the semen sample collection process that would occur among men undergoing IVF repeatedly. Of these, 31 completed the study, eight subjects chose not to continue after the first sampling period. One patient’s cycle was cancelled before egg retrieval.

Each participant in the study signed a consent form approved by the hospital’s Human Research Committee. Each patient provided a semen sample and completed a one-page questionnaire to assess anxiety levels at the following times: 4–6 weeks prior to the IVF cycle (baseline sample; T1) and at the time of oocyte retrieval (IVF sample; T2).

Sperm handling and assessment

Semen specimens were collected by masturbation in a temperature-controlled setting at the hospital. Men were asked to adhere to a 48–72 h abstinence period. Specimens were collected in sterile cups and allowed to liquefy at room temperature for 30–45 min, at which time the samples were processed.

Semen volume was measured to the nearest 0.1 ml with a calibrated pipette. Specimens were also assessed visually in terms of colour, viscosity, and debris, and any abnormalities were noted. Undiluted
semen (5 µl) were placed in a Makler chamber and inserted into an automated semen analyser (Hamilton-Thorn, Danvers, MA, USA). Sperm concentration and quantity and quality of motility were assessed. Total motile spermatozoa (motile sperm concentration×volume) was calculated for each sample. Qualitative measures of sperm motility assessed included mean path, and progressive velocity, mean linear index, and mean lateral head displacement (LHD). In cases where the sperm concentration was <10^6/ml, a manual measurement was performed to assess semen quality. In these cases, 10 µl of diluted semen (1:20 with Ham’s F-10 + 0.4% bovine serum albumin) was placed on a haemocytometer for determination of total sperm concentration, motile sperm concentration and forward progression. An additional aliquot of diluted semen was used to assess sperm morphology according to World Health Organization standards (World Health Organization, 1980).

**Stress questionnaire**

Psychological stress was measured in four ways. First, the Spielberger State Anxiety Inventory (Spielberger et al., 1970) (STAI), which is widely used for assessing state or acute anxiety, was completed by all participants after collection of the semen specimen. The STAI asks the subject to describe how he feels ‘right now’ by responding to 20 questions with a 4-point response format ranging from ‘not at all’ (score 1) to ‘extremely’ (score 4). Total scores range from 20 to 100 points. Higher scores indicate greater anxiety. Second, the Spielberger Stress questionnaire (Stress parameters)

There was a significant decline in total sperm concentration (39% reduction), motile sperm concentration (47% reduction), and total motile spermatozoa (48% reduction) in semen specimens produced at the time of oocyte retrieval (T2) compared with baseline levels (T1) (Table I). Lateral head displacement (LHD) of the sperm head, a qualitative measure of sperm motility derived from the automated semen analysis, was significantly reduced from T1 to T2. No differences were observed in other quantitative and qualitative sperm parameters measured at the two sampling periods, including semen volume and sperm morphology.

A comparison of individual patients whose sperm parameters increased, decreased, or did not change from T1 to T2 is shown in Figure 1. For the purpose of these analyses, no change in a sperm parameter was defined as a deviation of 10% or less from T1 to T2. Total sperm concentration decreased in 61% of the patients from T1 to T2 (Figure 1A). Motile sperm concentration in 65% (Figure 1B). Total motile spermatozoa decreased significantly at T2 in 71% of the patients from T1 to T2 (Figure 1B). Total motile spermatozoa decreased significantly at T2 in 71% of the patients and increased or did not change in 42% of participants (Figure 1D).

**Stress parameters**

Perceived importance of producing a semen specimen significantly increased from T1 to T2 (P < 0.001) (Table II). Ninety-four per cent of men indicated the highest response category for this question at the time of egg retrieval, compared with only 41% at baseline (T1). STAI scores and perceived stressfulness of providing a semen specimen did not change from T1 to T2, nor was there a difference in the perceived...
level of distraction due to environmental factors over the sampling periods (Table II).

No significant differences between T1 and T2 were found for general stress related to family, friends, work, home, or finances. These were single items with a 4-point scale of severity. Means for these items ranged from a low of 1.2 for stress related to relationships with friends to 2.7 for work-related stress. There were no significant differences in scores from T1 to T2. The amount of alcohol consumed in the week prior to collection was assessed in categorical format. Results indicated that, at T1, 27% of men abstained, 49% had 1–3 drinks per week and 24% had 4–10 drinks. At T2, 35% abstained, 23% had 1–3 drinks per week and 35% had 4–10 drinks per week. Six per cent of the subjects did not answer the question. In terms of over-the-counter medication use, subjects were asked if they had used any in the prior week: at T1, 56% said they had, and at T2, 39% said they had.

Correlations between stress and sperm parameters
To address the question of a possible association between the psychological variables and specific sperm parameters, two separate analyses were performed. To determine whether there was a correlation between the psychological variables (state anxiety, perceived stressfulness, perceived importance) and sperm parameters, Spearman’s correlation was applied to baseline samples (T1) only. Perceived importance of producing a semen sample was negatively correlated with both total sperm concentration ($r = -0.36, P < 0.02$) and total motile spermatozoa ($r = -0.32, P < 0.04$). STAI scores were negatively correlated with semen volume ($r = -0.39, P < 0.02$).

We were interested in whether changes in sperm parameters from T1 to T2 were associated with changes in psychological variables. These results are shown in Table III. Changes in perceived importance of producing a sample and STAI scores from T1 to T2 were significantly and inversely correlated with changes in several sperm parameters, including total sperm concentration, motile sperm concentration, and total motile spermatozoa. No correlations were found between perceived stressfulness and any of the sperm parameters measured.

Male factor subsample
Seven patients (23%) from the study group were classified on the basis of their baseline semen analysis as having a male factor infertility problem. All of these men were aware of their diagnosis prior to the study. No decline in total and motile sperm concentration, total motile spermatozoa, or lateral displacement of the sperm head from T1 to T2 was observed in male factor subjects (Table IV). In fact, total motile spermatozoa increased or remained the same at T2 in five of the seven male factor patients. In comparison, the semen quality of non-male factor patients decreased significantly from the baseline analysis to the time of oocyte retrieval ($n = 24$; Table IV).

No differences in STAI scores or stress levels from T1 to T2 were observed in male factor patients. In terms of perceived importance non-male factor patients reported a significantly higher level of perceived importance of producing a specimen at T2 than at T1; no such increase was found in male factor patients (Table IV). It is important to note, however, that perceived importance of the baseline analysis (T1) was signi-
The results of this study show that the semen quality of men undergoing IVF treatment for the first time is diminished at the time of oocyte retrieval and provide preliminary evidence of a relationship between psychological state and semen quality. Total sperm concentration, total motile spermatozoa, and quantitative and qualitative sperm motility decreased significantly at the time of the egg retrieval compared with pre-IVF baseline values. Moreover, individual comparisons of semen quality over the two sampling periods indicated that this phenomenon occurred in a high percentage of the study participants. Others have reported a similar but less dramatic decline in semen quality associated with IVF. Harrison et al. (Harrison et al., 1987) found sperm concentration, total sperm count, and motility to decrease slightly in 500 semen samples produced for IVF compared with those produced at the pre-IVF work-up. In a similarly designed study, Kentenich et al. (Kentenich et al., 1992) reported that sperm concentration decreased significantly at the time of oocyte retrieval in 36% of male IVF patients compared with that obtained from an earlier examination. These studies did not limit their samples to first-time IVF patients nor did they specifically measure anxiety.

While it has generally been assumed that semen quality is affected by psychological stress, there have been few attempts at assessing either the level or type(s) of stress impacting on male IVF patients. Most studies assessing semen quality in IVF patients have failed to measure directly the stress involved in such procedures (Harrison et al., 1987; Giblin et al., 1988; Pellicer and Ruiz, 1989). Kentenich et al. (Kentenich et al., 1992) used reported pleasantness and unpleasantness of specific events associated with IVF as experienced by the male partner, but did not attempt to correlate these feelings with changes in sperm parameters. In the present study, we evaluated specific psychological variables using cognitive appraisal and state anxiety immediately after subjects produced a semen specimen at the time of egg retrieval and provide preliminary evidence of a relationship between psychological state and semen quality. Total sperm concentration, total motile spermatozoa, and quantitative and qualitative sperm motility decreased significantly at the time of the egg retrieval compared with pre-IVF baseline values. Moreover, individual comparisons of semen quality over the two sampling periods indicated that this phenomenon occurred in a high percentage of the study participants. Others have reported a similar but less dramatic decline in semen quality associated with IVF. Harrison et al. (Harrison et al., 1987) found sperm concentration, total sperm count, and motility to decrease slightly in 500 semen samples produced for IVF compared with those produced at the pre-IVF work-up. In a similarly designed study, Kentenich et al. (Kentenich et al., 1992) reported that sperm concentration decreased significantly at the time of oocyte retrieval in 36% of male IVF patients compared with that obtained from an earlier examination. These studies did not limit their samples to first-time IVF patients nor did they specifically measure anxiety.

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Men in the present study were found to have moderately high levels of anxiety both when providing a pretreatment semen sample and when providing a sample on the day of oocyte retrieval. Although levels of state anxiety did not significantly increase between the two sampling times, the

<p>| Table IV. Changes in sperm and stress parameters from T1 to T2 in male factor (MF; n = 7) and non-male factor (NMF; n = 24) patients |</p>
<table>
<thead>
<tr>
<th>Sperm/stress parameter</th>
<th>Patient type</th>
<th>T1</th>
<th>T2</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sperm concentration (×10^6/ml)</td>
<td>MF</td>
<td>24.8 ± 4.8</td>
<td>50.6 ± 13.7</td>
<td>0.063</td>
</tr>
<tr>
<td></td>
<td>NMF</td>
<td>139.3 ± 22.8</td>
<td>74.2 ± 10.4</td>
<td>0.003</td>
</tr>
<tr>
<td>Motile sperm concentration (×10^6/ml)</td>
<td>MF</td>
<td>7.0 ± 2.4</td>
<td>15.7 ± 8.8</td>
<td>0.128</td>
</tr>
<tr>
<td></td>
<td>NMF</td>
<td>97.4 ± 17.6</td>
<td>48.1 ± 8.7</td>
<td>0.002</td>
</tr>
<tr>
<td>Importance</td>
<td>MF</td>
<td>3.6 ± 0.2</td>
<td>3.7 ± 0.3</td>
<td>0.706</td>
</tr>
<tr>
<td></td>
<td>NMF</td>
<td>3.0 ± 0.2</td>
<td>3.9 ± 0.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Anxiety</td>
<td>MF</td>
<td>39.6 ± 2.7</td>
<td>38.7 ± 1.2</td>
<td>0.734</td>
</tr>
<tr>
<td></td>
<td>NMF</td>
<td>41.5 ± 2.0</td>
<td>43.2 ± 2.1</td>
<td>0.235</td>
</tr>
<tr>
<td>Stressfulness</td>
<td>MF</td>
<td>2.1 ± 0.3</td>
<td>2.0 ± 0.3</td>
<td>0.706</td>
</tr>
<tr>
<td></td>
<td>NMF</td>
<td>2.1 ± 0.2</td>
<td>2.1 ± 0.2</td>
<td>1.000</td>
</tr>
</tbody>
</table>

*Values are mean ± SEM.

Table V. Correlations between environmental distractions associated with semen collection and stress parameters at the baseline analysis (T1)

<table>
<thead>
<tr>
<th>Stress parameter</th>
<th>Environmental distraction</th>
<th>Rho (r)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>Presence of others</td>
<td>0.58</td>
<td>0.0003</td>
</tr>
<tr>
<td></td>
<td>Location of collection room</td>
<td>0.66</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>Noise</td>
<td>0.41</td>
<td>0.0009</td>
</tr>
<tr>
<td></td>
<td>Hospital atmosphere</td>
<td>0.50</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>Space limitations</td>
<td>0.32</td>
<td>0.046</td>
</tr>
<tr>
<td></td>
<td>Absence of wife</td>
<td>0.23</td>
<td>0.146</td>
</tr>
<tr>
<td>Stress</td>
<td>Presence of others</td>
<td>0.55</td>
<td>0.0006</td>
</tr>
<tr>
<td></td>
<td>Location of collection room</td>
<td>0.60</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>Noise</td>
<td>0.50</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Hospital atmosphere</td>
<td>0.54</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Space limitations</td>
<td>0.30</td>
<td>0.060</td>
</tr>
<tr>
<td></td>
<td>Absence of wife</td>
<td>0.34</td>
<td>0.032</td>
</tr>
</tbody>
</table>

*Significant correlations as analysed by Spearman’s correlation test.
mean scores for the sample indicated that the procedures involved in providing a semen specimen were relatively stressful. The mean scores at T1 (41.1) and T2 (42.2) were higher than those obtained by Dziegielewski and Tyler (Dziegielewski and Tyler, 1989), who assessed anxiety and semen quality in men first presenting for an infertility evaluation. Other reported scores for a basis of comparison are 42.4 for men undergoing a surgical procedure (Speilberger et al., 1970) and 43.6 for men who have been told they are HIV positive (Huggins et al., 1991). Moreover, the average score for non-psychiatric male patients is 35.7 (Speilberger et al., 1970). Therefore, although there was not a significant increase in reported anxiety state from the baseline assessment to the day of oocyte retrieval, the overall level of anxiety experienced by these men was clinically significant.

Two components contribute to the stressfulness of an event: the perceived importance of the event to the person (appraisal), and the person’s belief regarding how well they could cope with the event (coping) (Lazarus and Folkman, 1984). In the present study, the perceived importance of producing a semen sample increased significantly from pretreatment to the day of oocyte retrieval, indicating that the men were aware of the increased importance of providing the T2 sample. Moreover, the heightened importance of providing a specimen at egg retrieval was significantly and negatively correlated with the semen quality of men involved in IVF treatment. To our knowledge, this is the first definitive evidence linking psychological appraisal and semen quality among male IVF patients.

It was interesting that male factor patients in the present study appeared to respond differently from normozoospermic patients. The perceived importance of providing a semen specimen by male factor patients did not increase, nor was there a decline in semen quality at the time of egg retrieval as was seen in the non-male factor patients. A possible explanation for this lies in the fact that the level of perceived importance in the male factor group was already elevated at T1 and remained high at T2. The male factor patients appeared to be keenly aware of the importance of their sample, even at the baseline sampling period as perceived importance remained high, semen parameters remained low. If perceived importance is associated with semen quality, then one would expect this relationship. The fact that some of the male factor patients exhibited a slight improvement in semen quality at T2 may reflect the degree of variability of semen samples within an individual patient (Cooper et al., 1991). These results are consistent with the recent finding of Boivin et al. (Boivin et al., 1998) that male factor patients undergoing IVF with ICSI report higher pre-IVF anxiety than normozoospermic men but that both groups’ anxiety is equally high during the actual treatment. Boivin et al. (Boivin et al., 1998) did not measure the correlation between psychological variables and subjects’ semen parameters, however.

Environmental distractions associated with the sperm collection rooms, such as the presence of others, noise, and the hospital atmosphere were often a source of dissatisfaction to our patients. The level of this dissatisfaction, however, did not increase at the time of egg retrieval, nor were these factors significantly distracting or stress-invoking to be associated with detrimental changes in sperm parameters. Thus, modification of the physical layout of a semen collection facility should be focused on patient satisfaction, but may not be particularly relevant to the quality of the semen produced.

The mechanism by which psychological stress could affect semen quality is unclear. The spermatogenic cycle in the human male is approximately 70 days (the time required for an undifferentiated spermatogonium to develop and mature into a motile sperm cell; Frishman, 1995). Given the sampling interval (T1 to T2) of 30–45 days in the present study, it is unlikely that increasing stress experienced as oocyte retrieval approaches exerts a direct effect on sperm production per se. Rather, effects of stress may be indirect in nature via the hormonal component of spermatogenesis. There is evidence that such a phenomenon may be related to hormonal changes observed in the male during stressful events. Testicular biopsies obtained from prisoners awaiting sentencing, obviously under extreme stress, revealed complete spermatogenic arrest in all cases (Steve, 1952). Milder forms of stress, such as that induced as a result of combat or surgery, have been shown to result in reduced testosterone concentrations in affected males (Kreuz et al., 1972). This may be a result of activation of hormones from the hypothalamic–pituitary–adrenal axis, which are known to be elevated in response to stress (Guyton, 1989). McGrady (McGrady, 1984) noted that social stress in animals was related to diminishing testicular function via changes in luteinizing hormone (LH) and testosterone. Cui (Cui, 1996) has demonstrated significantly lower semen volume and sperm concentration in a group of chronically stressed marmoset monkeys. These changes were attributed to lower concentrations of LH and testosterone (which were reduced in the stressed group). These changes appear to be mediated, according to Cui (Cui, 1996), by endogenous opioids in the hypothalamic–pituitary–adrenal axis. There is evidence for the role of opioids in blocking the inhibitory effects of stress on LH and testosterone by the administration of naloxone, an opioid agonist (Norman and Smith, 1992). Changes in LH and testosterone may further affect the sympathetic and parasympathetic systems in acute stress situations which directly affect testicular function and sperm quality.

The conclusions drawn from the present study are somewhat limited by the relatively small size of the sample. In addition, 23% of the participants dropped out of the study before completion. We believe that the drop-out rate was due to the sensitivity of the male IVF patients to issues regarding stress. Many of the participants seemed uncomfortable filling out the questionnaire, and it appeared that many of the men were attempting to minimize or mask any effects of stress related to the IVF procedure. This fact raises concerns regarding future subject recruitment and the necessity of obtaining more physiological indices to psychological stress. It would undoubtedly be beneficial to include certain hormonal measurements, such as urinary cortisol and plasma testosterone, in future studies involving stress and semen quality.

In conclusion, data from the present study showed a significant decline in the semen quality of IVF patients at the time of oocyte retrieval and provide evidence for a relationship between semen quality and specific aspects of psychological stress.
Further research is needed to determine whether either physical (frozen back-up semen samples) or psychological (relaxation training, guided imagery, or support groups) interventions would be helpful in reducing stress experienced by male IVF patients, with the potential benefit of minimizing stress-induced changes in semen quality.

References


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