Long-term psychological adjustment to IVF/ICSI treatment in women

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BACKGROUND: The aim of this study was to gain more insight into long-term psychological adjustment to IVF in women. METHODS: In a prospective cohort study, 298 women entering their first IVF treatment cycle (including ICSI) completed standardized psychological questionnaires before the start of the treatment, just after the last treatment cycle, and 6 months and 3–5 years after the last treatment cycle. The main outcome measures were state anxiety, depression and mode of adaptation to unsuccessful IVF. RESULTS: Anxiety and depression were found at follow-up to return to baseline levels following treatment not resulting in a live birth, after an initial increase during treatment. On the contrary, treatment resulting in a live birth was found to lead to a more positive long-term emotional status. Women who focused on new life goals as a mode of adaptation 3–5 years after IVF without a live birth showed lower levels of anxiety and depression compared with those who persisted in their attempts to get pregnant. CONCLUSIONS: Treatment that resulted in a live birth led to more positive emotional adjustment. In addition, most women who did not give birth to a child after treatment adjusted well psychologically. Positive adjustment was related to developing new life goals rather than persisting in attempts to get pregnant. Helping women to change life goals after abandoning treatment might have beneficial effects on the adaptation process.

Key words: adaptation/anxiety/depression/follow-up/IVF

Introduction

IVF treatment is physically and emotionally stressful. The unfulfilled desire to have a child and the consequent threat of permanent infertility were related to increased levels of anxiety and depression during IVF treatment (Verhaak \textit{et al.}, 2001). Numerous studies have been published on psychological aspects of IVF treatment. Until now, however, the long-term psychological consequences of IVF have rarely been investigated. An earlier study found that 6 months after the last unsuccessful treatment >20\% of the women showed clinical forms of anxiety and/or depression (Verhaak \textit{et al.}, 2005). It is known that a high level of depression shortly after the incidence of a stressor is a major risk factor for the development of a depressive disorder in the near future (Howarth \textit{et al.}, 1994).

On the contrary, cross-sectional studies have indicated that, in general, couples seem to adjust to their infertility (Freeman \textit{et al.}, 1987; Weaver \textit{et al.}, 1997; Leiblum \textit{et al.}, 1998; Hammarberg \textit{et al.}, 2001). A retrospective study indicated that the longer the time passed since the last IVF treatment cycle, the better the emotional adjustment (Baram \textit{et al.}, 1988). This is in line with the finding that the adjustment process normally takes about 2 years, after which most people seem able to adjust well (Janssen \textit{et al.}, 1997; Bonanno and Kaltman, 2001).

Positive adjustment to infertility was shown to be related to abandoning medical treatment and focusing on new life goals, whereas pursuing pregnancy was related to more negative adjustment (Van Balen and Trimbos-Kemper, 1994). This is in agreement with the longitudinal, qualitative study by Daniluk (2001) into emotional adjustment after unsuccessful fertility treatment, which indicated that ‘turning towards the future’ is an important aspect.

Because longitudinal studies on the course of the emotional response before, during and several years after unsuccessful treatment are non-existent, the question remains what happens to those women who did not succeed in getting pregnant. A longitudinal follow-up study could provide us with information about the number of patients developing clinical forms of anxiety and/or depression after treatment. Furthermore, it could provide insights into subsequent modes of adaptation. The aim of this study was therefore to gain a greater insight into the longitudinal adjustment of women in IVF. This could provide us with more information about the desirability of tailored support after IVF is abandoned.
Materials and methods

Sample
The data used were from women who came for the first cycle of a new IVF treatment (including 38% who underwent ICSI) at the Radboud University Nijmegen Medical Center in the Netherlands between 1998 and 2000. This group participated in a previous prospective follow-up study on the psychological aspects of IVF treatment. Of the 450 women contacted, 380 (84%) agreed to participate at the start of the previous study (T1). Participants were asked to complete questionnaires on psychological factors before the start of treatment (T1), after the last treatment cycle (T2) and 6 months after the last cycle (T3). Last treatment cycle was defined as not starting a new cycle, 1 year after the end of the previous cycle. Three to five years after T1, the 380 women who completed the T1 assessment were again invited to participate in a long-term follow-up assessment (T4).

All participants were guaranteed confidentiality and a separation of the questionnaire information on psychological, marital and sexual factors and their clinical management. Written informed consent was obtained from all participants.

Psychological measures
State anxiety was measured by means of the Dutch version of the State and Trait Anxiety Inventory (Spielberger et al., 1970), a scale that shows satisfactory reliability and validity. The inventory has 20 items that assess state anxiety; the score for each item ranges from 1 to 4, with higher scores indicating greater state anxiety. Total scores therefore range from 20 to 80. The threshold for clinical state anxiety was 48, which is 1 SD above the mean for the age-matched norm group of Dutch women (Vanderploeg et al., 2000).

Depression was measured by means of the short Dutch version of the Beck Depression Inventory (Beck & Beck, 1997). This scale is one of the most widely used, reliable and valid instruments for assessing intensity of depression and for detecting depression in the general population. The scores for each item range from 0 (low) to 3 (high). The threshold for clinical depression was a total score of 4.

Furthermore, four modes of adaptation were distinguished (according to Van Balen and Trimbos-Kemper, 1994):

(i) medical mode—still pursuing medical options in order to have a biological child of their own;
(ii) passive mode—not actively pursuing the desire, but still having the desire for a child;
(iii) alternative mode—pursuing other ways of having a child (e.g., adoption);
(iv) new goals—abandoning the desire to have a child and choosing other life goals.

Statistical analysis
Comparisons were made between women who gave birth to a child after the start of their IVF treatment (spontaneous pregnancies after the start of treatment were also included) and women who did not give birth. All statistical analyses were performed using the Statistical Package for the Social Sciences program (SPSS version 12.0). The course of anxiety and depression over time and differences in that course between women who gave birth to a child after their treatment and those who did not was examined using multivariate analysis of variance (MANOVA). Post hoc, one-way ANOVAs were performed to examine the course of anxiety and depression in women who gave birth to a child after treatment and those who did not. T-tests were used to compare women who gave birth and those who did not after treatment and to compare anxiety and depression at different times. One-way ANOVAs were used to compare anxiety and depression in women with different modes of adaptation.

This study was approved by the institution’s ethical committee.

Results
Of the 380 women who participated in the previous study, 298 (78%) completed an additional set of questionnaires 3-5 five years after treatment (T4). Sixty-four women (21%) already had a child before the start of the treatment. One hundred and ninety-three women (65%) gave birth to a child after IVF, and 105 women (35%) did not. A non-participation study (n = 82 of 380) showed a trend towards more non-responders (women who did not respond to T4) among women who did not succeed in giving birth to a child after treatment (χ² = 3.37; P = 0.07).

The mean age of the women was 33.4 years (SD = 4.1). Thirty-one per cent completed 10 years of education or less, 39% completed 11–14 years of education and 30% completed 15 years of education or more. All the women were part of a heterosexual couple at the start of the treatment. 96% were born in the Netherlands and 98% were Dutch. The causes of the fertility problems were as follows: female factor in 17% of the women, 39% male factor, 8% both male and female factors and 28% unknown.

After abandoning their treatment in the hospital where the study was carried out, 7% (n = 22) of the respondents went for treatment elsewhere; eight of them (36%) subsequently gave birth to a child. The options indicated were intrauterine insemination (IUI) with donor semen (n = 4), IUI with partner’s semen (n = 1), IVF at another clinic (n = 10), homeopathic medicine (n = 1), other medication (n = 1) and alternative medicine (n = 5), which included acupuncture, magnetism and ayurvedic therapy.

The course of anxiety and depression over time was studied using MANOVAs, comparing women who did and did not give birth after treatment. When only the pretreatment data (T1) and data from 3–5 years after treatment (T4) were considered, a significant interaction effect was found for time and birth, both for anxiety (F = 3.9; P = 0.05) and depression (F = 12.2; P < 0.01) (Table I).

In further analysing the effect, a significant decrease in anxiety (t = 2.6; P = 0.01) and depression (t = 5.0; P < 0.01) was found in women who gave birth to a child. The scores for anxiety and depression for women who did not give birth to a child did not differ significantly between pretreatment and 3–5 years after treatment.

A complete data set (T1, T2, T3 and T4) was obtained for 107 women; 68 women gave birth to a child after treatment and 39 women did not. The smaller sample size was because of

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<th>Table I. Anxiety and depression scores at pretreatment (T1) and follow-up at 3–5 years after treatment (T4) in women who gave birth after IVF and those who did not (n = 298; 193 gave birth after IVF; 105 did not give birth after IVF)</th>
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<tr>
<td>Pretreatment (SD)</td>
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<tr>
<td>Anxiety*</td>
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<td>Did not give birth after IVF</td>
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*Significant interaction effect time × birth: F = 3.9; P = 0.05.
*Significant interaction effect time × birth: F = 12.2; P < 0.01.
incomplete data at T2 and T3. Comparisons of anxiety and depression at T1 and T4 did not reveal significant differences between responders and non-responders at T2 and T3. The same was true for pregnancy rates.

The data are summarized in Table II. A significant effect over time was found for depression ($F = 3.2; P = 0.02$). No significant main effect for anxiety was found. Furthermore, a significant interaction effect on time x birth was revealed for both anxiety ($F = 3.5; P = 0.02$) and depression ($F = 4.5; P < 0.01$). More specifically, in this particular subgroup a significant decrease in anxiety was found in women who gave birth when comparing T1 and T2 ($t = 3.1; P = 0.03$), and significantly lower levels of depression were found when comparing T1 and T2 ($t = 2.6; P = 0.01$) and T1 and T4 ($t = 3.0; P < 0.01$). In analysing the women who did not give birth after treatment, higher levels of depression were found at T2 compared with T1 ($t = 2.1; P = 0.05$).

When only the percentages of the group with clinically relevant forms of depression were considered, at pretreatment (T1) 12% scored above the threshold level; just after the last treatment cycle (T2) 20%; 6 months later (T3) 25%; and 3–5 years later (T4) 16%. When clinically relevant forms of anxiety were considered, the percentages were 13% at T1, 23% at T2, 20% at T3 and 15% at T4.

Ninety of the 105 women (86%) who did not give birth provided information about their mode of adaptation. The following modes of adaptation were indicated: medical mode 12% ($n = 11$), alternative mode 13% ($n = 12$), passive mode 38% ($n = 34$) and new goals 37% ($n = 33$). The mean anxiety and depression scores are summarized in Table III.

Significant differences in anxiety ($F = 10.1; P < 0.01$) and depression ($F = 9.1; P < 0.01$) were found between these different groups. Significantly higher levels of anxiety and depression (anxiety: $t = 4.53; P < 0.01$; depression: $t = 4.51; P < 0.01$) were found in the two groups still pursuing a desire for pregnancy (medical and passive mode), compared with the two groups of women who had abandoned their active pursuit of pregnancy (new life goals and alternative mode). These differences remained when women who already had a child before treatment were left out of the analyses (data not shown).

At T4, 19% ($n = 20$) of the women who did not succeed in getting pregnant already had a child before the start of the treatment. A comparison of anxiety and depression at follow-up (T4) between these women and the women who did not succeed in getting pregnant with their first child revealed more anxiety and depression in childless women ($F = 4.58; P = 0.03$ for anxiety and $F = 8.04; P < 0.01$ for depression).

**Discussion**

This study followed up a cohort of women who underwent IVF treatment.

The most striking result was that anxiety and depression were found at follow-up to return to baseline levels after an initial increase during treatment in women who did not give birth after treatment. Treatment resulting in a live birth was found to result in a more positive long-term emotional status. New life goals and already having a child before treatment started were found to be associated with lower levels of anxiety and depression.

A limitation of the study is the high drop-out rate at various stages during the treatment, which resulted in a limited complete data set. Furthermore, a drop-out analysis revealed higher levels of drop-out in women who did not give birth to a child. Despite these limitations, this was the first time a large cohort was studied before, during and after treatment. This enabled us not only to analyse the course of anxiety and depression, but also to investigate the women’s attitude to childlessness and possible further treatment after abandoning IVF.

Longitudinal follow-up studies, as indicated, are scarce. Cross-sectional follow-up studies of the emotional status of involuntarily childless women and women with children indicate no important differences between these groups (Weaver et al., 1997; Leiblum et al., 1998; Hammarberg et al., 2001). This is in line with the present longitudinal study, which shows...
no differences in the emotional status of the women before treatment started and several years after unsuccessful treatment. However, the women who gave birth to a child after treatment showed a more positive emotional status compared with the baseline. This indicates a positive effect of pregnancy and motherhood on emotional status for women with fertility problems. This is supported by studies in definitively childless women, who showed comparable emotional status but less life satisfaction than women with children (Singh and Williams, 1981; Leiblum et al., 1998).

The availability of psychological counselling services was indicated as being vitally important at times of distress. It was indicated that ongoing counselling should be part of having IVF treatment and that the clinic should contact couples between treatments, because only a small proportion of the women availed themselves of the counselling services beyond the initial mandatory counselling session. On the contrary, it was already known that the most distressed patients fail to initiate contact with counsellors (Boivin et al., 1999). There should therefore be a reassessment of each couple’s feelings and degree of psychological distress after each IVF cycle (Guerra et al., 1998). Couples should be made aware that unsuccessful IVF treatment is associated with increased levels of anxiety and depression after treatment (Baram et al., 1988; Verhaak et al., 2001) and that this is a normal response and the effect is still present 6 months after the last IVF cycle (Slade et al., 1997; Verhaak et al., 2005).

Furthermore, successful IVF was also found to be associated with increased levels of anxiety in comparison with women who had conceived naturally (Hjelmstedt et al., 2003). Levels of stress related to parenthood, on the contrary, were found to be equal whether women had conceived with or without IVF (Hjelmstedt et al., 2004). Although it was found that long-term emotional well-being was not affected by a live birth, ~15% of the women whose treatment did not result in a live birth reported clinical levels of anxiety and/or depression. A strong relationship was found between emotional distress and mode of adaptation, because pursuing a desire for pregnancy was found to be associated with higher levels of anxiety and depression.

The clinical implication of the findings of this study points in the direction of additional support at the time people are abandoning treatment. Persisting with treatment options seems to have a negative effect on adaptation to childlessness because of an enduring uncertainty that results in a lack of control (Daniluk, 2001). Clinicians could address the issue of abandoning treatment in their final consultations and inform patients about the emotional consequences of letting go their attempts to get pregnant. Indicating that grief is a natural response might help patients to understand their emotions. In addition, the prospect of most women adjusting well after several years might encourage women to give up treatment and focus on other life goals. However, psychosocial support during the decision process after IVF is still a relatively uncharted area. Further research is needed to shed more light on the process of leaving treatment and focusing on other life goals.

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References


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