

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 *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 *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 *et al.*, 1994).

On the contrary, cross-sectional studies have indicated that, in general, couples seem to adjust to their infertility (Freeman *et al.*, 1987; Weaver *et al.*, 1997; Leiblum *et al.*, 1998; Hammarberg *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 *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 *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 *et al.*, 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 their 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 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 ($\chi = 3.37$; $P = 0.07$).

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

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)

	Pretreatment (SD)	Follow-up (SD)	Univariate test
Anxiety ^a			
Gave birth after IVF	36.1 (8.9)	34.2 (7.6)	$t = 2.6$; $P = 0.01$
Did not give birth after IVF	37.7 (12.2)	37.7 (10.6)	Not significant
Depression ^b			
Gave birth after IVF	1.1 (1.5)	0.5 (1.3)	$t = 5.0$; $P < 0.01$
Did not give birth after IVF	1.3 (1.9)	1.5 (2.2)	Not significant

^aSignificant interaction effect time \times birth: $F = 3.9$; $P = 0.05$.

^bSignificant interaction effect time \times birth $F = 12.2$; $P < 0.01$.

Table II. Anxiety and depression scores in the group of women who completed the questionnaire at all times during and after IVF ($n = 107$; 68 live birth after IVF, 39 no live birth after IVF)

	T1: pretreatment (SD)	T2: just after treatment (SD)	T3: 6 months after treatment (SD)	T4: 3–5 years after treatment (SD)
Anxiety ^a				
Gave birth after IVF	36.2 (9.6)	32.8 (8.2) ^c	34.0 (8.4)	33.9 (7.5)
Did not give birth after IVF	36.9 (13.1)	39.8 (14.5)	40.3 (15.5)	37.1 (11.1)
Depression ^b				
Gave birth after IVF	1.2 (1.5)	0.7 (1.0) ^d	0.5 (0.9)	0.5 (1.5) ^e
Did not give birth after IVF	1.3 (3.9)	3.9 (3.4) ^f	2.6 (2.9)	1.7 (2.2)

^aSignificant interaction effect time \times birth: $F = 3.5$; $P = 0.02$.

^bSignificant time effect: $F = 3.2$; $P = 0.02$; significant interaction effect time \times birth: 4.5 ; $P < 0.01$.

^cSignificant decrease T1–T2: $t = 3.1$; $P = 0.03$.

^dSignificant decrease T1–T2: $t = 2.6$; $P = 0.01$.

^eSignificant decrease T1–T4: $t = 3.0$; $P < 0.01$.

^fSignificant increase T1–T2: $t = 2.1$; $P = 0.05$.

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 \times 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

Table III. Anxiety and depression scores according to mode of adaptation at follow-up after treatment not resulting in live birth ($n = 90$)

Mode of adaptation	n	Anxiety	Depression
Still pursuing pregnancy wish			
Persisting with treatment (medical)	11	44.2	3.8
Still longing for a child (passive)	34	42.7	2.1
New life goals			
New goals	33	32.1	1.5
Adoption (alternative)	12	34.8	0.4

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.

Acknowledgements

This work was supported by grant 28-3012 from the Health Research and Development Council, The Hague, the Netherlands. The authors thank all the couples who participated in the study and the co-workers at the hospital.

References

- Baram D, Tourtelot E, Muelcher E, Huang K (1988) Psychosocial adjustment following unsuccessful in vitro fertilization. *J Psychosom Obstet Gynecol* 9,181–190.
- Beck AT, Guth D, Steer RA and Ball R (1997) Screening for major depression disorders in medical inpatients with the Beck Depression Inventory for primary care. *Behav Res Ther* 35,785–791.
- Boivin J, Scanlan LC and Walker SM (1999) Why are infertile patients not using psychosocial counselling? *Hum Reprod* 14,1384–1391.
- Bonanno GA and Kaltman S (2001) The varieties of grief experience. *Clin Psychol Rev* 21,705–734.
- Daniluk JC (2001) Reconstructing their lives: a longitudinal, qualitative analysis of the transition to biological childlessness for infertile couples. *J Couns Dev* 79,439–449.
- Freeman EW, Rickels K, Tausig J, Boxer A, Mastroianni L and Tureck RW (1987) Emotional and psychosocial factors in follow-up of women after IVF-ET treatment. *Acta Obstet Gynecol Scand* 66,517–521.
- Guerra D, Llobera A, Veiga A and Barri PN (1998) Psychiatric morbidity in couples attending a fertility service. *Hum Reprod* 13,1733–1736.
- Hammarberg K, Astbury J and Baker HWG (2001) Women's experience of IVF: a follow-up study. *Hum Reprod* 16,374–383.
- Hjelmstedt A, Widstrom AM, Wramsby H, Matthiesen AS and Collins A (2003) Personality factors and emotional responses to pregnancy among IVF couples in early pregnancy: a comparative study. *Acta Obstet Gynecol Scand* 82,152–161.
- Hjelmstedt ARNM, Widstrom AM, Wramsby H and Collins A (2004) Emotional adaptation following successful in vitro fertilization. *Fertil Steril* 81,1254–1264.
- Howarth E, Johnson J, Klerman GL and Weissman MM (1994) What are the public health implications of subclinical depressive symptoms? *Psychiatr Q* 65,323–337.
- Janssen HJEM, Cuisinier MCJ and de Grauw CPHM (1997) A prospective study of risk factors predicting grief intensity following pregnancy loss. *Arch Gen Psychiatry* 54,56–61.
- Leiblum SR, Aviv A and Hamer R (1998) Life after infertility treatment: a long-term investigation of marital and sexual functioning. *Hum Reprod* 13,3569–3674.
- Singh K and Williams S (1981) Childlessness and family satisfaction. *Res Aging* 3,218–227.
- Slade P, Emery J and Lieberman BA (1997) A prospective, longitudinal study of emotions and relationships in in-vitro fertilization treatment. *Hum Reprod* 12,183–190.
- Spielberger CD, Gorsuch RL and Lushene RE (1970) *Test Manual for the State-Trait Anxiety Inventory*. Consulting Psychologists Press, Palo Alto.
- Van Balen F and Trimbos-Kemper TC (1994) Factors influencing the well-being of long-term infertile couples. *J Psychosom Obstet Gynaecol* 15,157–164.
- Vanderploeg HM, Defares PB and Spielberger CD (2000) *Handleiding bij de Zelfbeoordelingsvragenlijst: een Nederlandse bewerking van de Spielberger State Trait Anxiety Inventory* [Dutch Manual for the Spielberger State and Trait Anxiety Inventory]. Swets & Zeitlinger, Lisse.
- Verhaak CM, Smeenk JMJ, Eugster A, van Minnen A, Kremer JAM and Kraaimaat FW (2001) Stress and marital satisfaction among women before and after their first cycle of in vitro fertilization and intra cytoplasmic sperm injection. *Fertil Steril* 73,525–531.
- Verhaak CM, Smeenk JM, vanMinnen A, Kremer JA and Kraaimaat FW (2005) A longitudinal, prospective study on emotional adjustment before, during and after consecutive fertility treatment cycles. *Hum Reprod* 8,2253–2260.
- Weaver SM, Clifford E and Hay DM (1997) Psychological adjustment to unsuccessful IVF and GIFT treatment. *Patient Educ Couns* 31,7–18.

Submitted on March 5, 2006; resubmitted on August 9, 2006; accepted on August 14, 2006