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Fertility treatment: Getting stressed about stress

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Fertility treatment is stress-generating. Couples experiencing such stress are further concerned with the possibility that stress, in itself, may compromise the chance of treatment success. An internet search using the terms 'fertility' and 'stress' retrieves countless hits supporting the concept of stress adversely affecting fertility.

In this issue, Cesta (1) and colleagues report a prospective observational study investigating the effect of stress on the success of IVF. The study quantified stress by women's self-reported stress levels, which was a subjective measure; supplemented by the measurement of salivary cortisol levels, which was an objective measure of stress. The authors assembled a prospective cohort ($n = 485$) starting fertility treatment. Female participants were given two varieties of questionnaires to estimate self-reported stress. There was no group not undergoing fertility treatment, so it is not possible to estimate the extent of increase in the stress related to fertility treatment from this study. However, the authors compared the success (embryo quality and clinical pregnancy rate) in subgroups of their cohort. There was a significant correlation between the scores obtained by the two questionnaires, but interestingly, the scores did not correlate with salivary cortisol levels. None of the stress measures correlated with success, regardless of the way success was measured.

Is there a correlation between stress levels and success in achieving a pregnancy?

Women trying for a baby believe that stress had a role in their inability to conceive. The biological connection is the effect of stress on the hypothalamo-pituitary-ovarian (HPO) axis interfering with ovulation. This is well established. Whereas this is valid for natural conception, it is not applicable to ART, as ovulation is not natural any more. The possibility of stress affecting implantation has also been raised, but this connection is not well-accepted. There is some evidence that cortisol may play a role in implantation (2). However, it is far from clear, because both high and low cortisol levels have been associated with increased likelihood of pregnancy in women undergoing IVF.

In a systematic review and meta-analysis of 3583 infertile women, Boivin et al. (3) reported that emotional distress before a cycle of assisted reproductive technology was not associated with treatment outcome (defined as a positive pregnancy test, positive fetal heart scan, or live birth). The results of the Cesta study largely support those of the meta-analysis. In the setting of ART, stress does not appear to influence success of the treatment.

Do interventions to reduce stress improve the chance of achieving a successful pregnancy?

The answer to this question is dependent on the answer to the first question. Conceptually, interventions to reduce stress can work only if stress negatively influences the chances of a successful fertility treatment in the first place.

Interpretation of published evidence which could be used to answer this question is not straightforward. Two published meta-analyses reported conflicting conclusions. The Cochrane review published in 2015 (4) was unable to answer this question due to the very low quality of published evidence. On the other hand, another systematic review and meta-analysis also published in 2015 (5), reported that psycho-social interventions improved psychological outcomes and could improve pregnancy success. In the latter report, it is interesting to note that the relative risk gradually drifts towards one (no effect) with each passing year of publication. One can only guess the possible reasons behind this observation. It may be that journals are increasingly willing to publish negative trials. The other possibility is that women participating in the control arm of an intervention trial may actively seek and use methods to reduce stress, thereby eliminating the differences between the two arms of the trial.

Interventions to reduce stress may well work if couples are trying for a pregnancy by natural means. Psychological stress can severely affect spermatogenesis, mainly as a result of varying testosterone secretion (6). Stress has been reported to affect treatment outcome one year later, and the effect on women is greater than men (7). It is inevitable that stress in one partner will influence stress levels in the other. It is not possible to randomly assign women going through ART to high or low level of stress, and observational evidence is all that can ever be available. Stress does not appear to adversely affect the outcome of fertility treatment using ART in view of the present study, and other studies published so far. This should reassure couples going through fertility treatment using ART to some extent, that the outcome is not influenced by the extent of stress that they are going through.

References

1. Cesta CE, Johansson ALV, Hreinsson J, Rodriguez-Wallberg KA, Olofsson JI, Holte J, et al. A prospective investigation of perceived stress, infertility-related stress, and cortisol levels in women undergoing in vitro fertilization: influence on embryo quality and clinical pregnancy rate. Acta Obstet Gynecol Scand. 2018;97:258–268.
2. Whirledge S, Cidlowski JA. A role for glucocorticoids in stress-impaired reproduction: beyond the hypothalamus and pituitary. Endocrinology. 2013;154:4450–68.
3. Boivin J, Griffiths E, Venetis CA. Emotional distress in infertile women and failure of assisted reproductive technologies: meta-analysis of prospective psychosocial studies. BMJ. 2011;342:d223.
4. Verkuijlen J, Verhaak C, Nelen WL, Wilkinson J, Farquhar C. Psychological and educational interventions for subfertile men and women. Cochrane Database Syst Rev 2016;3: CD011034.
5. Frederiksen Y, Farver-Vestergaard I, Skovgard NG, Ingerslev HJ, Zachariae R. Efficacy of psychosocial interventions for psychological and pregnancy outcomes in infertile women and men: a systematic review and meta-analysis. BMJ Open. 2015;5:e006592.
6. Nargund VH. Effects of psychological stress on male fertility. Nat Rev Urol. 2015;12:373–82.
7. Boivin J, Schmidt L. Infertility-related stress in men and women predicts treatment outcome 1 year later. Fertil Steril. 2005;83:1745–52.