

PRINCIPAL PSYCHOLOGICAL DISORDERS ASSOCIATED WITH INFERTILITY

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Although infertility has some unique characteristics when compared to other chronic diseases (there are no associated symptoms, no physical limitations and there is no threat to survival), its diagnosis and treatment causes emotional disorders similar to those of other medical conditions. In this paper we review the nature, prevalence and process of such emotional disorders during the diagnosis of infertility and the treatment with assisted reproduction techniques. We emphasize the high interpersonal variability, the need to differentiate between emotional maladjustment and psychopathological disorder, and the existence of a high percentage of couples without emotional disorders or with adaptive resources to cope with infertility. Finally, we stress the need for further studies that would allow the identification of "high risk" couples.

Keywords: Infertility, psychopathology, emotional disorder, anxiety, depression

A pesar de que la infertilidad presenta una serie de peculiaridades en comparación con el resto de las enfermedades crónicas (no hay sintomatología asociada, no hay limitaciones físicas, no representa una amenaza para la supervivencia), su diagnóstico y tratamiento genera alteraciones emocionales similares a las de otras afecciones médicas. En este artículo, revisamos la naturaleza, la prevalencia y el curso de las mismas a lo largo del proceso de diagnóstico y tratamiento de reproducción asistida, resaltando la elevada variabilidad interindividual, la necesidad de diferenciar entre desajuste emocional y alteración psicopatológica, la existencia de un elevado porcentaje de parejas que no padecen dichas alteraciones o que disponen de los recursos adaptativos necesarios para superarlas y, por último, la conveniencia de profundizar en las variables que nos ayuden a detectar a las parejas de "alto riesgo".

Palabras claves: infertilidad, psicopatología, alteración emocional, ansiedad, depresión.

INFERTILITY: A CHRONIC ILLNESS

Chronic illness has a strong emotional impact on sufferers, as has been repeatedly shown by psychology professionals working in the care, teaching or research sectors of the field of health and illness. Various factors are behind the emotional reactions that occur, including the knowledge of suffering an irreversible condition, having to undergo life-long treatment (with its negative effects and inconveniences), the potential threat to one's survival, and limitations in one's everyday life.

The World Health Organization includes infertility in the category of chronic illnesses. However, it clearly has some features that distinguish it from other physical complaints: it does not affect the functioning of any organs, and hence does not impose any physical limitations on sufferers; there are no associated symptoms or pain; and there is no real danger or threat to life, so that couples can freely

choose whether or not to undergo treatment. Nevertheless, the clinical reality shows us that, in spite of this, couples with problems of infertility can have emotional reactions comparable even to those found in cancer patients (Domar, Zuttermeister & Friedman, 1993). It is not the goal of the present work to analyze the causes of such emotional reactions, but rather to focus on their nature, their prevalence, their course and the psychosocial variables that can modulate their appearance.

Nevertheless, before moving on to exploring these, we should consider some aspects that will put into context the significance and implications of our analysis. The first observation in this regard, which despite being obvious is also highly pertinent, is that people with problems of infertility do not constitute a homogeneous group. There are numerous personal and medical variables that affect the impact and consequences of infertility (see Llavona, in this same issue). Notable among these are sociodemographic variables, resulting in differences according to:

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- a) **Gender:** women find it more difficult to accept and adjust to the idea that a couple without children constitutes a family, and are more likely to have obsessive ideas about the gestation and conception of a child, with greater prevalence of anxious and depressive symptomatology.
- b) **Age.** In the area of assisted reproduction, time, or rather its passage, becomes a powerful stressor: couples are aware that as they get older biological fertility decreases, and consequently, as time goes on their stress levels increase (especially in the case of women) (Moreno-Rosset, Antequera, Jenaro & Gómez, 2008).
- c) **The presence of other children** acts as a buffer for emotional reactions to a diagnosis of infertility. However, this does not mean that couples with children who have difficulties in achieving another pregnancy may not also have negative reactions – which will be more intense if one of them is not the biological parent of the existing child or children.

Another group of factors affecting the impact of infertility concerns the nature of the problem and the characteristics of the treatment process. **Type of infertility** modulates the emotional impact on couples on receiving the diagnosis, with notable gender-related differences: men are found to be more affected when the diagnosis shows that they are the cause of the problem, whilst women’s reactions do not depend so much on its aetiology (Dhillon, Cumming & Cumming, 2000; Nachtigall, Becker & Wozny, 1992). But for both men and women, a diagnosis of idiopathic infertility, with its high levels of uncertainty, has a qualitatively different impact from the rest. The time the couple has spent involved in the process of diagnosis and treatment is related to the levels of frustration and tension

(Moreno-Rosset, Antequera, Jenaro & Gómez, 2008), as well as to the modification of adaptive resources. Obviously, the more time has passed since the diagnosis, the more cycles of treatment the couple will have gone through, each representing a new stressor, in which the couple experience both the hope of achieving their desired goal and the negative emotions associated with failing to do so. Accordingly, they modify their expectations and their coping resources.

Finally, in relation to the variables that make infertile couples a heterogeneous group, we should mention women that suffer multiple miscarriages (two or more in succession), who constitute a population with its own distinctive characteristics. Unquestionably, the experience of successive pregnancies that do not reach full term, with miscarriages that may occur in the early months, but also even as late as 6 or 7 months, generates greater emotional impact than the inability to conceive at all. We should not forget that for the couple, and especially for the women, the zygote that begins to divide is felt, imagined and experienced as her child, so that any miscarriage that occurs is a loss of “someone who might have been”. But it is also true that hope and positive expectations increase as the months of gestation go by, so that the sense of loss and subsequent reactions also increase with time.

It should be borne in mind that the reactions and emotional states of couples with problems of infertility are not static, but evolve and are modified as the treatment progresses through its different cycles. Thus, for example, the quality of the couple’s emotional state on carrying out the diagnostic tests is not the same as that of their state immediately after receiving the diagnosis. Likewise, their emotional state on commencing the treatment is different from the one they are in when it fails, or when it has to be started all over again... It is precisely the characteristics of this illness (which revolve around “the desire for the non-existent”), and of the treatment, that make the emotional reactions of these couples specific and different from those pertaining to other chronic illnesses. There emerges what could be called a “rollercoaster of emotions”, with negative and positive emotions coming and going in a short period of time. In other chronic illnesses we can generally distinguish different points of adaptation to the illness, which influence the incidence or reduction of emotional alterations: the first adaptation usually occurs six months after diagnosis, and the second after a year. But in the case of infertility each new treatment represents

Modulating variables of the impact of infertility	
1.- Sociodemographic characteristics	<p>Age: with increasing age, greater impact</p> <p>Gender: poorer adaptation among women</p> <p>Children: impact is less if the couple already have children</p>
2.- Illness and treatment characteristics	<p>Specific diagnosis</p> <p>Time spent trying with treatment</p> <p>Number of treatments undergone</p>
3.- Multiple miscarriages	

a beginning, and each failure, an end. Thus, the positive expectations, hope and optimism couples present when they begin treatment give way to worry, obsession and even near-hypochondria as they await the results, and to disappointment, sadness and frustration when the treatment fails. Such alternation of emotions is repeated with each treatment cycle, generating emotional wear and tear and a peculiar, idiosyncratic type of suffering in couples with problems of infertility.

In the development of Reproductive Psychology, emotional alterations in infertile couples have been understood not only as a consequence of the illness but also as a cause, especially in so-called idiopathic infertility (that which is present despite the fact that no functional problems can be found in the female or male reproductive apparatus). Work in this area is based on psychodynamic theory, developed within psychosomatic medicine and subsequently reformulated in terms of the theoretical principles of stress (Facchinetti, Demyttenaere, Fioroni, Neri & Gennazzani, 1992). The relationship between stress and reproductive capacity was already reported by Selye (1950), who observed the appearance of ovarian atrophy in rats that had been exposed to a range of stressors. However, and although the relationship between physical stressors (such as malnutrition or lack of exercise) and the reproductive function is considered to be well demonstrated, the role played by purely psychosocial stressors has still not been fully established, due in part to difficulties in distinguishing between cause and effect (Fassino, Piero, Boggio, Piccioni & Garzaro, 2002). And this despite the well-documented clinical observations pointing to the existence of such a relationship. A pertinent example is provided by the situation of couples that have undergone assisted reproduction treatment without success, and just when they are in the middle of the adoption process or already have an adopted child, they spontaneously manage to achieve pregnancy and have a biological child. Recently, Fassino et al. (2002) re-examined the notion of a personality (made up of dimensions closely associated with emotional alterations) that predisposes to infertility. Specifically, they claim that the triad made up of high levels of anxiety and depression and a tendency for the repression of anger predicts 97% of cases of functional infertility. Such results concur with the postulates of psychosomatic theories.

EMOTIONAL ALTERATIONS BEFORE THE DIAGNOSIS

At the time of being informed of the diagnosis, and almost regardless of the type of chronic illness in question, people tend to experience emotional alterations that have been interpreted: 1) as a normal reaction, 2) as a psychopathological condition, 3) as an anticipatory reaction of grief, especially in the case of those illnesses with a terminal prognosis, and 4) as another symptom of the morbid process. It is the first two of these possibilities that have aroused the most controversy. It is common to find references to the appearance of depression and anxiety disorders in seropositive, oncological and diabetic patients, those with cardiovascular alterations, and so on (Fisher, Thorpe, Devellis & Devellis, 2007; Oxlad & Wade, 2008; Pence, Miller, Gaynes & Eron, 2007; Power, Brown & Ritvo, 2008), as well as in the infertile (Castro, Borrás, Pérez-Pareja & Palmer, 2001; Moreno-Rosset, 2000; Verhaak, Smeenk, Evers, Kremer, Kraaimaat & Braat, 2007), but what varies from author to author is the consideration of these alterations, on the one hand, as depressive or anxiety symptoms constituting a reaction and of restricted duration, or on the other, as clinical alterations. For Ibáñez (1991), this situation is the result of having ignored the emotional component of depressive states and considered them solely in their psychopathological dimension: "In general, there has been a tendency to overlook the fact that depression, either as a syndrome or as a response to certain situations, is an emotion, or at least, has a strong emotional component. This oversight appears to have led clinicians to focus more on the analysis of pathological processes of depression than on its emotional components" (p. 40).

TABLE 2
CONSIDERATIONS IN RELATION TO EMOTIONAL ALTERATIONS
IN COUPLES IN ASSISTED REPRODUCTION

Considerations in relation to emotional alterations in couples in assisted reproduction
✓ Couples with problems of infertility do not constitute a homogeneous group
✓ The evolution of emotional alterations is determined, at least partly, by the evolution of the treatments themselves
✓ These alterations do not always fulfil clinical criteria that allow them to be considered as clinical entities. This has notable implications for psychological assessment and treatment
✓ There is a not inconsiderable group of couples who present no emotional alterations at all

Following this same line of argument, we consider the depressive and anxiety symptomatology that emerges in response to infertility diagnoses and assisted reproduction treatment to fit more appropriately into the concept of **emotional maladjustment** than that of psychopathological alteration (see, in this same issue, the work by Jenaro, Moreno-Rosset, Antequera & Flores). However, there is often confusion between the two terms in research on the issue. Thus, authors commonly refer to “depression” or “anxiety”, considering them as clinical entities, when they have been detected exclusively via questionnaires and self-report measures, designed for the assessment of the intensity or modifications of emotional alterations, and therefore lacking diagnostic capacity. And even then, when the scores obtained are compared with those of the normative population, they do not always yield statistically significant differences, or at least, they do not reach the cut-off point indicative of abnormally high scores, as Llavona stresses in this same issue. Hence the crucial importance of the recent creation in Spain of the DERA (Moreno-Rosset, Antequera & Jenaro, 2008), which assesses both the negative aspects of infertility (Emotional Maladjustment, *Desajuste Emocional*) and the positive ones (Adaptive Resources, *Recursos Adaptativos*); moreover, it is validated in infertile populations, removing the possible biases involved in applying instruments with standards obtained in the general population.

But the scarcity of valid tests for applying to infertile people explains why researchers use the classic anxiety and depression questionnaires for assessing the consequences of the diagnosis and treatment of infertility, and do not tend to study positive aspects, such as psychological well-being. One study that assesses, together with the emotional repercussions, aspects of well-being and personality, is by Ardeni, Campari, Agazzi and Battista (1999); moreover, this study does refer to positive aspects in women receiving IVF treatments, as reflected in the following passage: “firmly anchored in reality, oriented toward the present and with a positive attitude to life; there are no signs of hypochondria or anxiety about their physical integrity. They do not display alterations in autonomy or in integration of the self, nor problems in social adjustment or communication. There are no depressive thoughts, but hopeful thoughts are present, with a balance between optimism and pessimism and adequate capacity for controlling their emotions.

They do not show feelings of distress in relation to the unknown”. Nevertheless, throughout their study, these authors analyze “anxiety” and its relationship with variables such as the diagnosis, the different treatment phases or the duration of the treatment processes.

Other studies (Oddens, Den Tonkelaar & Nieuwenhuys, 1999) compare anxiety or depression levels in infertile couples with those of couples with children, concluding that there are higher levels of depressed mood in the former. Similar results were found by Ozkan and Baysal (2006) when they compared anxiety levels in a sample of infertile women with those of a control group of women with children, finding that the infertile women scored significantly higher in anxiety. The same result was found in a Spanish population by Moreno-Rosset and Martín (2008).

Chen, Chang, Tsai and Juang (2004) explored the presence of psychiatric alterations (not only anxiety and depression) in couples attending an assisted reproduction unit. One of the principal contributions of these authors is their psychopathological exploration through a diagnostic interview, and not exclusively on the basis of participants’ scores on questionnaires. The results show that 40.2% of the sample presented at least one psychopathological disorder, and indeed, depression and anxiety conditions were those with the highest prevalence. Anxiety disorders were the most common (28.6% of the women in their sample), among which there was a predominance of generalized anxiety disorders (81.2%). Of comparable prevalence were mood disorders (26.8% of patients), 63.3% of which involved major depression, and the remaining 36.7% dysthymia. Another result worthy of note is the low percentage of women with psychiatric diagnosis who had sought help from mental health professionals (just 6.7%). This finding, indeed, has been highlighted in previous studies (Boivin, Scanlan & Walker, 1999). Even so, Chen et al. themselves acknowledge the possibility of cultural bias in their results, given the notable differences in the importance ascribed by the different societies to infertility.

Depression and anxiety have become clichés when we speak of the psychopathology that characterizes couples undergoing assisted reproduction. But it is also true that the published research on this topic focuses almost exclusively on the detection and study of these two kinds of alteration; few studies specify the precise moment of the psychological assessments (diagnosis, treatment phases,

results or repetitions of treatment). And of course, researchers only find what they are looking for. On performing the bibliographical search in the Medline, Serfile, CAB Health and PsycINFO databases (from 1980 to the present), the descriptors "infertility" and "psychopathology" yield 21 articles; the descriptor "personality disorder", 2 articles; "psychosis", 2 articles; "sexual disorder", 1 article; "eating disorder", 10 articles; post-traumatic stress disorder", 1 article; "anxiety", 134 articles; and "depression", 129 articles. We found no articles with the descriptors "dissociative disorder", "obsessive compulsive disorder" or "somatoform disorder".

EMOTIONAL ALTERATIONS DURING THE TREATMENT

Substantial technical and medical progress has generated high (and unreal) expectations among the general population about the effectiveness of assisted reproduction treatments. At a time in history in which it is possible to clone a human being, how can it not be possible to help healthy couples have children? This type of attitude, also shared by those attending assisted reproduction units, markedly increases expectations and contributes to treatments being seen as a panacea for satisfying the desire for a child. In the initial stages of diagnosis of the illness this belief helps couples to accept and adapt to the aggressiveness of the medical procedures and to their interference in private life and everyday reality. In fact, confronting the idea of one's inability to have a biological child is more disruptive and anxiogenic than the distress deriving from the treatment itself. The treatment thus becomes a kind of complement of the patients themselves, which increases their reproductive capacity and counteracts their feelings of "inferiority of the organ" (Ardenti et al., 1999). It has also been argued that advances in assisted reproduction treatments (such as the development of in-vitro fertilization with intracytoplasmic sperm injection (IVF-ICSI)) reduce levels of anxiety and even of depression in couples, since they increase perceptions of the potential for solving their problems and satisfying their yearning for paternity and maternity (Holter, Anderheim, Bergh & Möller, 2007)

Although there are different types of assisted reproduction treatments, the majority of the knowledge acquired by reproductive psychology relates to the consequences for and adaptation of infertile couples that are receiving in-vitro fertilization (IVF) treatment – a

treatment that can be repeated over several years in cases of successive failures. The influence of such treatment on couples' emotional state not only appears in the long term: negative emotions can develop during the application of a single cycle of IVF. Thus, in general, negative emotions increase, relative to the basal level, during puncture for the extraction of oocytes and transfer of the embryo, and they increase even more when the cycle is unsuccessful. But if the woman does not have a sufficient number of mature ova for carrying out the puncture, so that the treatment cycle cannot be completed, then the anxiety and stress levels increase, even compared to those of the oocyte extraction and embryo transfer phase (Slade, Emery & Lieberman, 1997).

Numerous studies have confirmed high levels of anxiety after therapeutic failure, and the appearance of suicidal thoughts has even been reported in a quarter of women undergoing assisted reproduction treatment (Baram, Tourtelot, Muecheler & Huang, 1988). The greatest emotional impact occurs after the first treatment cycle, and may persist for weeks (Newton, Hearn & Yuzpe, 1990), though both the appearance of these alterations and their intensity are determined by individual variables, such as predisposition to anxiety or the presence of depressive symptoms prior to the treatment (Ardenti et al., 1999). Nor should we overlook the potential influence of the drugs on the emergence of depressive symptoms. This is what occurs, for example, with agonists of the hormones that release gonadotropine (used for reducing lesions to the endometrium and the pain associated with endometriosis through suppression of the ovarian hormones), whose use may generate depressive conditions in percentages ranging from 23% to 54%, mood swings in 60% and reduced libido in 61%. These depressive conditions are sometimes accompanied by anxiety, or even by psychotic symptoms (TAP Pharmaceutical Inc, 1995, Zeneca Pharmaceutical, Warnock, Bundren & Morris, 2000).

Once again it is necessary to highlight gender-related differences in emotional impact and psychopathological alterations as a consequence of treatment. Men maintain better levels of emotional equilibrium than women; indeed, some studies (Dhillon et al., 2000) have even failed to detect differences in levels of emotional well-being between men in insemination treatment and men whose partner is expecting a baby. In reality, it would seem that emotional maladjustment is more related to *the*

perception of threat to one's masculinity or feelings of failure in role-fulfilment than to the diagnosis or the treatment (Mahlstedt, 1994). But despite the low levels of emotional alteration presented by men with infertility problems, a relatively high percentage of them (between 24% and 33%) admit, after the unsuccessful application of a treatment cycle, that it would be useful to receive psychological help and support, suggesting that infertility treatment, regardless of its role as a trigger of psychopathology, constitutes a stressful event involving considerable investment of energy and constant effort to maintain one's emotional equilibrium (Holter et al., 2007).

As far as the effects of successive treatments are concerned, it has been found that as one process succeeds another and time passes, anxiety levels progressively decrease, probably because levels of uncertainty also decrease (Anderson, Sharpe, Rattray & Irvine, 2003; Berg & Wilson, 1991, Boivin et al., 1999).

Little information is available on long-term adaptation or the persistence of emotional alterations in couples that do not achieve gestation. Of considerable relevance in this regard is the work carried out by Wirtberg, Möller, Hogström, Tronstad and Lalos (2007), who interviewed 14 women who, 20 years after having undergone assisted reproduction treatment, did not have children. In reporting their results, the authors themselves remark on the intensity of emotions and the vividness with which, despite the time elapsed, the women remembered the assisted reproduction process. Curiously, the negative emotions were still present, together with the feeling of being "incomplete" and of some sense of social stigma, even though the impossibility of "being a mother" had been displaced by the impossibility of "being a grandmother".

Emotional maladjustment not only constitutes a consequence of assisted reproduction treatments, but is also related to their degree of success. Thus, there is a concatenation of cause-effect relationships in which the treatments generate emotional alterations, which in turn influence the success or failure of the therapy. Diverse models have been developed for determining which variables predict the success of treatments, even if the majority of them include almost exclusively biological and medical variables, such as age, duration of the illness, previous gestations or type of infertility (Templeton, Morris & Parslow, 1996). Models rarely include psychological

variables, and there are contradictory results about which emotional state plays the most determinant role. Thus, Smeenk, Verhaak, Eugster, Van Minnen, Zielhuis and Braat (2001) conclude that although both depression and anxiety contribute to the prediction of pregnancy, anxiety has greater discriminatory power than depression, whilst Thiering, Beaurepaire, Jones, Saunders and Tennant (1993) consider depression to be a better predictor than anxiety. This disparity is probably a consequence of methodological biases (due to sample composition, the assessment instruments employed or the medical variables included). In our view, the determining factor is the phase of the treatment that the couple is going through.

In any case, there is sufficient evidence about the mechanisms through which stress affects fertility: indirectly, through alterations in sexual relations, or directly, through the autonomic nervous system, the endocrine system and the immune system (Johnson, Kamilaris, Chrousos & Gold, 1992; Meyerhoff, Oleshansky, Kalogeras, Mougey, Chrousos & Granger, 1990). More information on the relationship between stress and infertility can be found in the article by Campagne in this special issue.

EMOTIONAL ALTERATIONS DURING PREGNANCY AND REARING

Paternity and maternity constitute a period of inter and intra-personal changes, which can lead to the emergence of unexpected conflicts (Repokari et al., 2007). One of the most significant changes for the dynamic of the couple is the transition from dyad to triad (Perren, von Wyl, Simoni, Stadlmayr, Buergin & von Klitzing, 2003). Bearing in mind that the birth of a child brings with it, in all cases, a period of stress and adaptation, it is difficult to distinguish the emotional consequences that appear in couples who conceive thanks to assisted reproduction treatments from those present in couples who conceive naturally. It is common, moreover, for such couples to be in the older age bracket, and to have more than one child, and these factors set them apart from the mean populational profile. Thus, the symptoms presented by couples who have twins or triplets after assisted reproduction treatment do not differ significantly from those of other couples who have multiple births (Ellison & Hall, 2003). Also, as in the general population, multiple-birth mothers with antecedents of infertility present more depressive symptoms than infertile couples with a single child

(Glazebrook, Sheard, Cox, Oates & Ndukwe, 2004)

Miscarriages tend to occur in 20%-25% of couples who receive assisted reproduction treatment (Wilcox, Baird & Weinberg, 1999), a figure that increases in women over 35 or where previous miscarriages have occurred (Pezeshka, Feldman, Stein, Lobel & Grazi, 2000). Miscarriages constitute one of the most traumatic events in assisted reproduction treatments and in the experience of maternity and paternity. Couples suffering multiple miscarriages present high levels of depression and anxiety (Beutel, Willner, Deckardt, Von Rad & Weiner, 1996; Janssen, Cuisinier, Hoogduin & De Graauw, 1996), which persist over time (Broen, Moum, Bodtker & Ekeberg, 2005) and which increase vulnerability to the development of major depression (Bernazzani & Bifulco, 2003; Franche & Mikail, 1999).

Finally, we should like to stress the need to bear in mind the existence of couples who present adequate levels of adaptation to the infertility diagnosis and to assisted reproduction treatments, and who either experience no types of alteration at all or manage to cope with them successfully. It would therefore appear necessary to continue exploring the variables that can help us to identify couples who may be more at risk of suffering emotional alterations, and who should constitute a priority target for psychotherapeutic intervention.

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