into a trait whose phenotype would be ‘able to transmit a particular genetic disease’, although it can only be observed in the next generation if some children develop the condition. In that sense, it could be considered like a ‘very late onset disease’. Then, I agree when the author says that there are two categories of carriers: those carriers of an autosomic recessive disease who will only be burdened by the inherited mutation if later in life their reproductive partner is also carrier of a mutation on the same gene and those carrier of a recessive X-linked mutation whose sons will have one of two chances of inheriting the mutation and therefore to develop the condition. What separates the two situations is merely the likelihood of having children with the disease, that is, the likelihood of expressing the disease, in other terms, the penetrance of the condition. We are therefore considering the status of carrier like a very late onset disease with a very variable penetrance. The penetrance is very low for a carrier of an autosomic recessive disease such as cystic fibrosis: 1/100 [1/2 chance for the person to transmit the mutant allele, 1/25 that his/her partner is carrier (for a Caucasian) and 1/2 chance that he/she transmits it] and is high for carriers of X-linked recessive: 1/4, or 1/2 of the male infants.

Does the fact that we can assimilate, at least theoretically, the status of carrier with a disease make PGD acceptable? The French legislation—which must only be applied in France of course but can provide fuel for thought to everybody—states that PGD can only be carried out for severe, non-curable genetic conditions. From what we said, we cannot exclude severity: the disease will probably be severe; albeit for the affected grandchildren, it is however curable because it is more than likely that our patient’s children will have access to at least the same level of medical care that they themselves had and will in turn have the option of prenatal or preimplantation diagnosis which will ‘cure’ the disease. If we accept the postulate that carriers of today will have access to PGD, we are then no longer talking about the health of the grandchildren as stated previously but merely of the reproductive options of the carriers. Now the ‘disease’ characteristics shift from very late onset (grandchildren developing the disease) to late onset (moment of reproduction of the children), and the phenotype is no longer ‘developing the original condition’ but becomes ‘having to undergo prenatal diagnosis (PD) or PGD’. All of us know that neither of these procedures can be taken lightly, and they are both highly undesirable, but in the scale of a lifetime, the notion of ‘severity’ introduced previously can now be seriously questioned.

From this reflection, we can conclude that PGD of carriers can be assimilated to the diagnosis of a curable, mild, late onset disease with variable penetrance. Whether that penetrance is high (X-linked disease) or low (autosomic disease), such a practice is clearly prohibited by the French legislation.

To carry out PGD only for this purpose as in the given example of PGD for males, hemizygous for an X-linked disease such as haemophilia with the exclusion of all obligate carrier females seems intuitively unethical because the inconvenience would outweigh the benefit: the inconvenience is to undergo a highly invasive procedure such as PGD, and the benefit is to exclude a hypothetical risk to the offspring that can be avoided later on while doing the same procedure or perhaps even a much less burdensome one considering the likely progress in science in the next generation.

One question remains: Would it be more ethical to select unaffected embryos while in the course of realizing PGD for homozygous affected embryos? In my personal opinion, and in compliance with the French legislation, I think that the priority must be to avoid the ‘real’ disease, therefore to exclude homozygotes or hemizygotes and to maximize the chances of implantation. Among a cohort of ‘healthy’ embryos (unaffected and carriers), I believe that embryos with the highest developmental potential (best morphology) should be selected for transfer whether carriers or not. I would, however, find it acceptable to favour the transfer of non-carrier embryos given the choice among a cohort of embryos of equivalent morphology, especially because for the time being, cryopreservation of biopsied embryos is hugely unsuccessful. In that case, there is no inconvenience because PGD is already being carried out, and the benefit is to avoid the future burden and stress of PD/PGD to the individual being conceived.

Reference


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doi:10.1093/humrep/del237

Incorporating qualitative approaches is the path to adequate understanding of the psychosocial impact of polycystic ovary syndrome

Sir,

We reviewed the manuscript by Elsenbruch et al. (2006) with great interest. Using self-reported measures to characterize polycystic ovary syndrome (PCOS) patients at risk of psychiatric disease and to assess the impact of emotional distress on quality of life, the authors analysed the incidence of mental distress in women with PCOS. This topic is extremely relevant in the current clinical management of PCOS patients. By using the German version (Schmitz et al., 2000) of the Symptom Check List 90 (SCL-90-R) (Derogatis, 1983), the authors verified that only 22 of the 143 women studied had scores ≥63, indicating marked psychological distress and probable psychological/psychiatric illness.

This study, as most of the previous research on PCOS, has been overwhelmingly conducted within a medical or psychiatric framework and has failed to explore women’s own experience regarding the syndrome. Thus, we would like to discuss the methodological procedures, especially related to the limitation of purely quantitative instruments, to assess essentially subjective aspects.
PCOS is a heterogeneous condition, and its main symptoms such as infertility, menstrual dysfunctions, hirsutism and obesity can, by themselves, cause increased psychosocial stress. Thus, we believe that a non-specific assessment instrument is unable to correctly evaluate the psychological impact of the disease. It therefore becomes increasingly more important to incorporate the contemporary qualitative approaches aimed at understanding the significant processes and the meanings experienced by women faced with PCOS (Kitzinger and Willmott, 2002; Keegan et al., 2003). The complexity involved in the illness process and the aspects related to the symptoms of this syndrome point to the importance of psychosocial studies that incorporate individuals’ perspective into their social context. Moreover, it becomes necessary to develop assessment instruments specific for use in patients with PCOS, as exemplified by Guyatt et al. (2004).

Using mixed methodology, we have performed a pilot study via a cross-sectional survey to provide information on health-related quality of life followed by in-depth semi-structured interviews to collect qualitative information. This latter approach aimed at identifying and understanding the feelings produced by women with PCOS regarding their disease. Preliminary results indicate that obesity and infertility have been mainly responsible for the feelings of social avoidance and sadness observed in PCOS patients. We have also found that effects on physical appearance cause a significant negative impact on psychosocial well-being by influencing feminine identity, corroborating the results previously related to the significant processes and the meanings experienced by women faced with PCOS (Kitzinger and Willmott, 2002). Thus, we believe that incorporating qualitative approaches into PCOS studies could contribute significantly to understanding the psychological impact of the disease and could act as an important complementary strategy to traditionally used methodologies.

Reply: Incorporating qualitative approaches is the path to adequate understanding of the psychosocial impact of polycystic ovary syndrome

Sir,

We thank Drs Azevedo and Moreira for their comments on our article addressing emotional distress and the quality of life in women with polycystic ovary syndrome (PCOS) and would like to address and further comment on several interesting aspects that were raised:

(i) We agree that there are different methodological approaches to address the impact of the physical features characterizing PCOS (e.g., obesity, hirsutism, acne and alopecia), the hormonal and metabolic aspects (i.e., hyperandrogenism and insulin resistance) as well as the situational (e.g., infertility) concomitants of the diagnosis on emotional well-being and the quality of life in affected patients. Clearly, the interactions between the medical and psychological aspects of PCOS are exceedingly complex, which are at least in part due to large inter-individual differences in symptom constellation on the one hand, and individual coping strategies and the individual social situation on the other hand. Thus, we feel that different approaches are possible and in fact necessary to expand our yet limited understanding of the psychological aspects of PCOS. Mixed methodology combining quantitative and qualitative methods may reveal complementary results. We are looking forward to yet unexplored ways to characterize and, in the end, help these women cope with PCOS and its consequences.

(ii) Apparently, Drs Azevedo and Moreira come to similar conclusions as other groups using qualitative methods as to which factors are most important in the reduction of the quality of life in PCOS patients, namely obesity and infertility. With regard to the emotional consequences of these symptoms, the authors also describe findings which are similar to our own data, i.e., the feeling of sadness which in our set of measures is reflected by increased scores on the SCL-90-R’s scale depressiveness, and the feeling of ‘social isolation’, reflected by increased scores on the SCL-90-R’s scale ‘interpersonal sensitivity’ and a greater mean score on the visual analogue scale ‘fear of social contacts’ (Elsenbruch et al., 2003). Certainly, it is important in a clinical context to explore PCOS strictly on an individual basis, but for larger samples, quantitative measures are critical to generate results that can be generalized and are statistically interpretable. Especially in the context of treatment studies, it is exceedingly important to use quantitative measures to allow statistical assessment of treatment effects on psychological and quality-of-life measures as additional outcome variables (Hahn et al., 2006).

(iii) Indeed, we agree that it would be particularly important to incorporate and address aspects of the social context into future studies on the psychological sequelae of the diagnosis. For example, it is well known from other medical conditions that perceived social support is a critical determinant of patients’ vulnerability to life stress. Clearly, an effective social network providing instrumental but particularly emotional support is one of the most important coping strategies and acts as a stress ‘buffer’, and we would expect this to play an important role in the ability of patients to cope with the diagnosis of and

References


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doi:10.1093/humrep/del239