Letters to the Editor

Polycystic ovary-related miscarriage: should metformin be proposed to such frustrated women?

Sir,

We read with interest the work of Jauniaux et al. (2006) recently published in *Human Reproduction* on the evidence-based guidelines for investigation and medical treatment of recurrent miscarriages.

However, we found that too little importance was attributed by authors to polycystic ovaries (PCO) as a potential cause of miscarriage and that the lack of metformin in the table of recommended medical treatments was surprising.

Several works, starting from 2001, both retrospective and prospective, underscored the role of metformin in reducing the incidence of pregnancy loss in PCO patients. Jabukowicz et al. found a highly significant difference in patients’ abortion rate ($P < 0.001$) between treated versus untreated PCO. Notwithstanding the retrospective design of their study, this observation was obtained with a small number of women in each group (65 treated and 31 untreated, respectively), suggesting that the reduction in abortion rate with metformin administration may be very important. Other works have confirmed these data. With a PubMed search, we found at least 18 articles on metformin-PCO and abortion as key words; between these articles, at least five (Gluek et al., 2001, 2002; Jabukowicz et al., 2002; Palomba et al., 2005; Thatcher and Jackson, 2006) suggest that metformin is able to reduce miscarriage rate in polycystic ovary syndrome (PCOS). Remarkably, in Palomba’s work, metformin reduced spontaneous abortion in non-obese patients, also suggesting that overweight is not the only risk factor for miscarriage in such group.

Owing to the high incidence of PCO, about 5–10% of the general population and its relationship with miscarriage, we think that ultrasound and endocrinological evaluation to exclude PCO should be mandatory in all recurrent miscarriages. Owing to the particular psychological profile of these women—whose more frequent questions are ‘Why I miscarriage? What can I do to prevent abortion?’—the possibility to find a possibly correctable cause of miscarriage should not be undervalued by the specialist.

At present, the main mechanism by which metformin is able to prevent miscarriage is not clear, and several possibilities have been suggested (androgen reduction, insulin lowering, plasminogen activator inhibitor reduction and improved oocyte quality). We believe that a definitive conclusion on its efficacy may be reached only with a well-designed, sufficiently powered randomized controlled trial (RCT), with abortion as the main outcome criterion. However, we think that even today, because of the lack of teratogenic evidence and several literature evidences of clinical benefit from this approach, metformin administration may be more justified than no treatment in such women in our daily clinical practice. This approach perhaps may reduce the helplessness sensation of both physicians and patients approaching such a frustrating clinical problem as recurrent miscarriage.

References


Reply: Polycystic ovary-related miscarriage—should metformin be proposed to such frustrated women?

Sir,

We appreciate the interest of Dr Manno, Dr Tomei and Dr Marchesan in our ESHRE (SIGEP) publication on ‘Evidence-based guidelines for the investigation and medical treatment of recurrent miscarriage’ (Jauniaux et al., 2006). We are aware of several publications suggesting a possible beneficial effect of metformin in polycystic ovary syndrome (PCOS) patients.

PCOS is associated with a higher miscarriage risk in spontaneous pregnancies as well as in pregnancies after surgical treatment or induced ovulation with or without ovarian suppression. This is primarily related to obesity (Fedorchak et al., 2001) and...