

### Physiology Should be Supported with Evidence in Progesterone Administration for Threatened Miscarriage – Authors' Reply

Dear Editor,

We fully agree with Sotiriadis and Makrydimas<sup>1</sup> that only a large, randomized placebo-controlled trial could provide reliable information on the value of progestogens treatment in threatened abortion. However, the main aim of our study<sup>2</sup> was to compare serum hormonal profiles and urine progesterone-induced blocking factor (PIBF) concentrations between women with threatened abortion and women with normal pregnancy and to evaluate the impact of dydrogesterone supplementation on these parameters.

The impact of the conclusions drawn from our study could increase after inclusion of placebo-controlled or non-treated group. Alas, for ethical reasons we had no possibility to include a control group of untreated or placebo-treated threatened aborters. In Poland almost all women with clinical signs of threatened abortion are treated routinely by progesterone or progestogens. Progesterone application for women with threatened abortion needs no ethical approval in Poland. It would be very difficult to recruit a group of women with bleedings and uterine cramps early at pregnancy to whom no treatment had been introduced and enroll them to the study especially when second PIBF sampling was approximately 10 days after entry to the study.

Even without placebo-controlled group the conclusions from our study that dydrogesterone treatment of women with clinical symptoms of threatened abortion was associated with an increased PIBF production are justified. Initially, PIBF concentrations in urine samples of patients showing clinical symptoms of threatened abortion were significantly lower than in those of healthy pregnant women (453.3 pg/mL vs. 1057.94, respectively;  $P = 0.008$ ). As there was no difference between threatened aborters and controls in mean gestational age at the time of first sampling, this indicates that women with threatened abortion have significantly lower urine PIBF concentrations. After 10 days of dydrogesterone treatment PIBF concentrations of threatened aborters

significantly increased ( $P = 0.001$ ) to reach the level of healthy pregnant subjects of matching gestational age.

We believe that these data are important because they show that dydrogesterone treatment of women with clinical symptoms of threatened abortion could be associated with an increased PIBF production thus indicating one of the mechanisms by which dydrogesterone supplementation might improve pregnancy outcomes in humans. The results of our study<sup>2</sup> establish a possible mechanism for the protective effect of dydrogesterone in threatened abortion. In the Discussion we say that the results of our study *indirectly* suggest a beneficial effect of dydrogesterone treatment among threatened aborters. We also indicate the need for further well-designed studies evaluating the impact of progesterone supplementation among women with threatened abortion early at gestation on pregnancy outcomes.

### References

- 1 Sotiriadis A, Makrydimas G: Physiology should be supported with evidence in progesterone administration for threatened miscarriage. *Am J Reprod Immunol* 2005;54:240.
- 2 Kalinka J, Szekeres-Bartho J: The impact of dydrogesterone supplementation on hormonal profile and progesterone-induced blocking factor concentration in women with threatened abortion. *Am J Reprod Immunol* 2005; 53:166–171.

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