Dr Li et al. refer to two studies to corroborate their criticism. In the trial by Choksuchat et al., in which a comparison is made between oral versus vaginal misoprostol on cervical dilation when administered 12 h prior to diagnostic hysteroscopy (both procedures were found equally effective), time interval was not the subject for investigation (Choksuchat et al., 2006). The same conclusion applies to the study of Oppegaard et al. (2010).

Rationale for longer priming intervals may be based on pharmacokinetic studies, whereas we do not see any indication from the trials so far published that a new trial is needed. Therefore, we conclude that women undergoing IUD insertion do not benefit from misoprostol pretreatment, irrespective of the administration at longer priming intervals.

**References**


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**Premature progesterone rise and gene expression**

Sirs,

We read with great interest the article of Labarta et al. (2011). The authors examined the gene expression from endometrial biopsies taken during the window of implantation in oocyte donor cycles, and correlated these results with the serum progesterone (P) concentrations on the day of hCG administration. Currently, there is an ongoing debate about the definition of premature luteinization, or better defined as ‘premature progesterone rise’, as to where the threshold for premature P rise should be established.

In our group, we recently published a similar gene expression study (Van Vaerenbergh et al., 2011), in which we studied the endometrial gene expression profile on the day of oocyte retrieval in recombinant FSH-stimulated GnRH-antagonist cycles for IVF with embryo transfer in the same cycle. We correlated these results with the serum P concentration on the day of hCG administration. We analysed three groups of patients with different serum P concentrations on the day of hCG: a group with P below 0.9 ng/ml, an intermediate group with P from 1 to 1.5 ng/ml and a high concentration group with P above 1.5 ng/ml. These cut-offs were based on the recent literature (Venetis et al., 2007; Papanikolaou et al., 2009). In the present study by Labarta et al. (2011) two groups of patients were compared with P above or below 1.5 ng/ml. However, only one cut-off value was taken into account. In our comparison between three groups, a small difference in gene expression between the first two groups was found. However, the gene expression profile from patients with high progesterone concentration (>1.5 ng/ml) was significantly different from the patients in the other two groups. These results were also confirmed with principal component analysis and hierarchical clustering, where a separate cluster for patients with high progesterone concentration (>1.5 ng/ml) was found. In this way, we confirmed the threshold of 1.5 ng/ml, as suggested in recent literature (Papanikolaou et al., 2009; Bosch et al., 2010), at the molecular level.

Moreover, we could conclude that the early elevation of progesterone on the day of hCG administration seems to have an instant effect on the endometrial gene expression, measurable as early as the day of oocyte retrieval, about 36 h later. The present study of Labarta et al. (2011) observed this effect on the gene expression as well, however later in the cycle, in the window of implantation. The added value of our study is that we could analyse the gene expression in an IVF cycle with embryo transfer. Although, we only have limited sample numbers, the correlation with clinical pregnancy can be made. This is not possible in oocyte donor cycles.

Both studies can explain the impairment of endometrial receptivity in the presence of elevated P and the lower ongoing pregnancy rates, as has been found in recent literature (Bosch et al., 2003, 2010).

**References**


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