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## LETTER

In reference to 'Strategies to manage refractory endometrium: state of the art 2016'



To the Editor

We appreciate the exhaustive review by Garcia-Velasco et al. on the management of refractory endometrium (Garcia-Velasco et al., 2016). We also appreciate being cited via three different publications in the section on granulocyte-colony stimulating factor (G-CSF). Unfortunately, however, the authors describe some of our results incorrectly and, therefore, also reach incorrect conclusions on the effectiveness of endometrial perfusions with G-CSF.

The authors correctly describe our first report on the subject involving four patients, in which we demonstrated significant endometrial expansion and pregnancies in women with chronically thin endometrium, resistant to more traditional treatments (Gleicher et al., 2011). They also correctly cite our second study, which was a prospective cohort study of 21 patients with chronically thin and resistant endometrium, which also demonstrated improvements in endometrial thickness (Gleicher et al., 2013). However, they misrepresent the results of our third study on the subject because they fail to note that this study, a prospectively randomized study, was performed in routine IVF patients; indeed, women with thin endometrium were excluded (Barad et al., 2014).

While the purpose of the first two studies was to demonstrate the ability of G-CSF to cause endometrial proliferation in women with chronically thin endometrium and, therefore, improve endometrial thickness, the primary goal of the third study was to determine whether G-CSF perfusion improved routine IVF outcomes. Since investigated women had normal endometrial thickness, further expansion was not necessarily expected and, indeed, was not found. The study, therefore, reported negative results not because endometrial thickness did not expand but because pregnancy rates did not improve. Indeed, in that study we specifically noted that the results obtained should not be interpreted as rejecting earlier claims of effectiveness of G-CSF in expanding endometrial thickness in women with chronically thin endometrium, resistant to standard treatments.

Yet, this is exactly the conclusion Garcia-Velasco and colleagues drew from our third publication, leading to their erroneous final conclusion that 'the only published RCT failed to show any impact on clinical outcome'. To test the effectiveness of aspirin on headache in patients who do not suffer from headache will, of course, demonstrate no therapeutic

effects of aspirin, even though aspirin is effective treatment in individuals with headaches.

The correct conclusion on the use of endometrial perfusions with G-CSF in women with refractory thin endometrium, therefore, should be that the best currently available evidence, which does not include randomized controlled trials (RCT), suggests that such treatment is effective in expanding endometrial thickness in this category of patient. Further RCT on the subject would be desirable but are unlikely, considering the clinical rarity of the condition.

## References

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