Mono-HP-hMG in ovarian stimulation for ART is associated with a significantly lower incidence of premature progesterone rise compared to mixed FSH-HP-hMG: is hCG-derived LH activity protective?

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ABSTRACT

The role of elevated progesterone (P_4) levels on implantation success is controversial. Some studies have suggested that premature progesterone rise (PPR) (defined as peak P_4 levels >1.5 ng/ml) has a detrimental effect on IVF success, while others have been unable to demonstrate a negative effect. Recent data demonstrated that using ovarian stimulation with an LH/FSH ratio in the range of 0.3-0.6 yielded the lowest chance of PPR (20%) compared with ratios < 0.3 or > 0.6 (Werner 2014). However, the use of mono-HP-hMG (i.e a ratio of 1.0) has not been adequately evaluated.

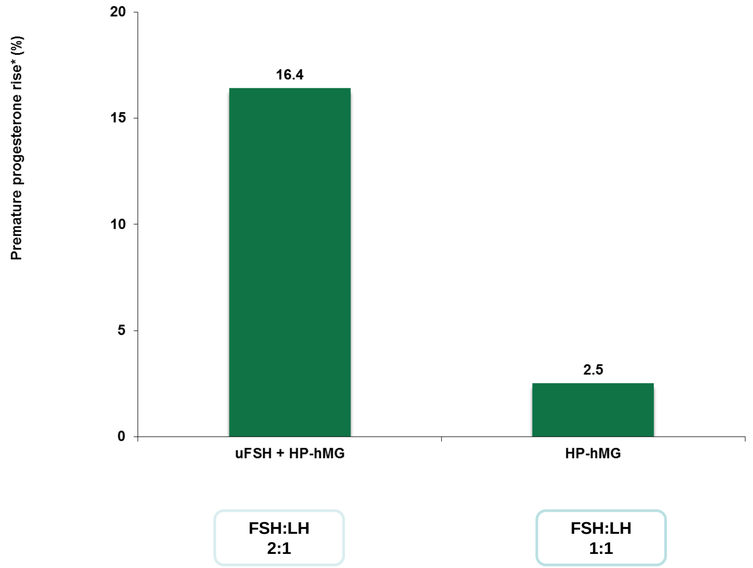
OBJECTIVES

We retrospectively compared the incidence of PPR in 157 cycles using HP-hMG (Menopur) and 249 cycles using a mixed uFSH-HP-hMG reported earlier (Sharara, ASRM 2015). We hypothesized that the higher hCG-derived LH content in HP-hMG would result in a lower PPR than the mixture of uFSH and HP-hMG at a 0.5 ratio. The higher hCG-derived LH activity at a 1:1 FSH:LH ratio allows a prompt conversion of progestins into androgens, and thus a lower circulating serum P_4 concentration.

METHODS

All patients received only HP-hMG (Menopur®) from day one of stimulation.

The incidence of PPR (defined as P_4 on day of hCG > 1.5 ng/ml) in the 157 cycles was compared to the incidence of PPR in 249 cycles using a mixed uFSH-HP-hMG in a 1:1 ratio initiated from day 1 of ovarian stimulation.



RESULTS

Characteristics of the mono-HP-hMG were as follows (mean ± SD): age = 35.3 years ± 3.7, BMI = 23.7 ± 4.1, AMH = 3.64 ± 3.52 ng/ml, FSH = 8.4 ± 5.5 IU/L, stimulation days = 9.5 ± 1.1, total HP-hMG dose (IU) = 3,359 ± 1,091, oocytes = 10.6 ± 5.1, MII = 7.8 ± 4.2, 2PN = 7.0 ± 3.8, peak E_2 = 1,578.5 ± 976.7 pg/ml, and peak P_4 = 0.81 ± 0.46 ng/ml. Cycles were divided into peak (day of hCG administration) P_4 ≤1.5 ng/ml compared to P_4 >1.5 ng/ml. The incidence of PPR was only 2.5% (4/157) in the mono-HP-hMG group, compared to 16.4% (41/249) in the mixed FSH-HP-hMG group (*P*= < 0.0001).

CONCLUSIONS

The 2.5% incidence of PPR with mono-HP-hMG is significantly lower than any reported PPR with FSH only (40%), or FSH/LH at 0.3-0.6 ratio (20% in the Werner study and 16.4% in our study). The use of mono-HP-hMG seems protective against the potential negative effect of elevated P_4 on implantation compared to mixed protocols. Whether there are differences between HP-hMG using HCG-derived LH activity and other hMGs where the LH activity is not hCG-driven remains to be studied.

Werner MD et al. *Fertil Steril*. 2014; 102(5):1312-7