



## More early pregnancy losses following short stimulation protocol treatment compared to long stimulation protocols in an IVF program

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**Objectives:** To investigate the effects of stimulation protocols on the pregnancy losses after  $\beta$ -HCG positive pregnancies

**Design:** Retrospective clinical data analysis

**Setting:** Private fertility center

### Materials and methods

The IVF data of  $\beta$ -HCG positive patients (age <40) following day 3 or day 5 embryo transfer in 2007 and 2008 is pooled and subjected to statistical analysis with Graphpad Prism 5. The patients were given various hormonal stimulation regimes. For the long protocol treatment, the patients were given a standard protocol of Lupron suppression beginning at cycle day 21 and gonadotropin stimulation beginning at cycle day 3. For the short protocol treatment, patients started gonadotropin injection on cycle day 3, when a follicle of 1.4 cm was observed; Cetrotide was given to patients for ovulation suppression until HCG administration. Retrievals were conducted 38 hours after HCG injection. Recovered eggs were fertilized with ICSI or insemination depending on the parameters of sperm analysis. The embryos were cultured with the sequential media in 5% O<sub>2</sub>, 6% CO<sub>2</sub> at 37 °C. Good quality of embryos at day 3 or day 5 were selected for intrauterine transfer under the ultrasonic guidance. The pregnancies were detected by the levels of HCG at the day 12 (day 3 ET) or day 10 (day 5 ET) following embryo transfers and further confirmed weeks later by fetal heart beats. The patients were grouped according to the stimulation protocols, various endpoints (listed in the table) were compared among the different groups. The difference of percentage data was examined by  $\chi^2$  test and means were analysed by students T test.

### Results

**Table 1. Short stimulation protocol negatively influences the pregnancy maintenance following initial embryonic implantation**

Stim. protocol	# Preg. patients	D3 FSH Value (IU/L)	E2 Levels (pmol/L)	Endom. Thickness (mm)	# embryos transferred	HCG Levels (IU/L)	Total # of HCG positive patients	Total # of HB positive patients (%)
Short	52	7.68±0.4*	8571±795*	10.6±0.3	2.3±0.1	299±65	52	<b>34 (65)*</b>
Long	158	4.9±0.2	12830±435	10.7±0.2	2.2±0.1	351±44	158	<b>129 (81)</b>
P value		<b>&lt;0.0001</b>	<b>&lt;0.0001</b>	<b>0.83</b>	<b>0.45</b>	<b>0.54</b>		<b>0.02</b>

Data with \* are statistically different (p<0.05)

## Conclusions

- We observed that the patients with short stimulation protocol coupled with higher FSH values of cycle day 3 and lower E2 levels had more pregnancy losses in first 5 to 7 weeks following establishment of pregnancies by  $\beta$ -HCG.
- In a separate investigation, no significant differences were revealed in term of the index of the transferred embryo quality among the short and long stimulation groups (data not shown).
- Early pregnancy losses are associated to many aspects of embryo implantational physiology, including endocrine associated angiogenesis, immunology, genetics etc.
- Further evidence is needed to elucidate which facet of implantational physiology is negatively influenced in a short stimulation protocol.

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