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In vitro coculture system of autologous endometrial cells and human early embryo development: randomized study update

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INTRODUCTION

In vitro culture conditions, including culture medium, affect early embryo quality. Autologous endometrial coculture using the patient's own endometrial cells (EC) has been reported to mimic the microenvironment of early embryo development under IVF conditions.

STUDY DESIGN

This interventional, monocentric, randomized, double-blind controlled trial was conducted at **clinique ovo** from April 2013 to March 2015. Eighty-five IVF couples were enrolled into the study: 48 patients had their embryos grown in conventional culture medium (control group) and 37 patients had them grown using an autologous coculture system of EC: Endocell (coculture group).

METHODS

For each patient, an endometrial biopsy was performed during the lutheal phase of the cycle prior to ongoing IVF. For the coculture group, EC were isolated from biopsies and cultured from the day after ovulation triggering. At day 2, embryos were placed either on EC or in conventional culture medium according to patient randomization.

STATISTICS

Homogeneity of the control and study groups have been verified for demographic data as well as IVF protocols and efficiency. Statistical analysis have been performed using non parametric tests considering the small sample size.

RESULTS

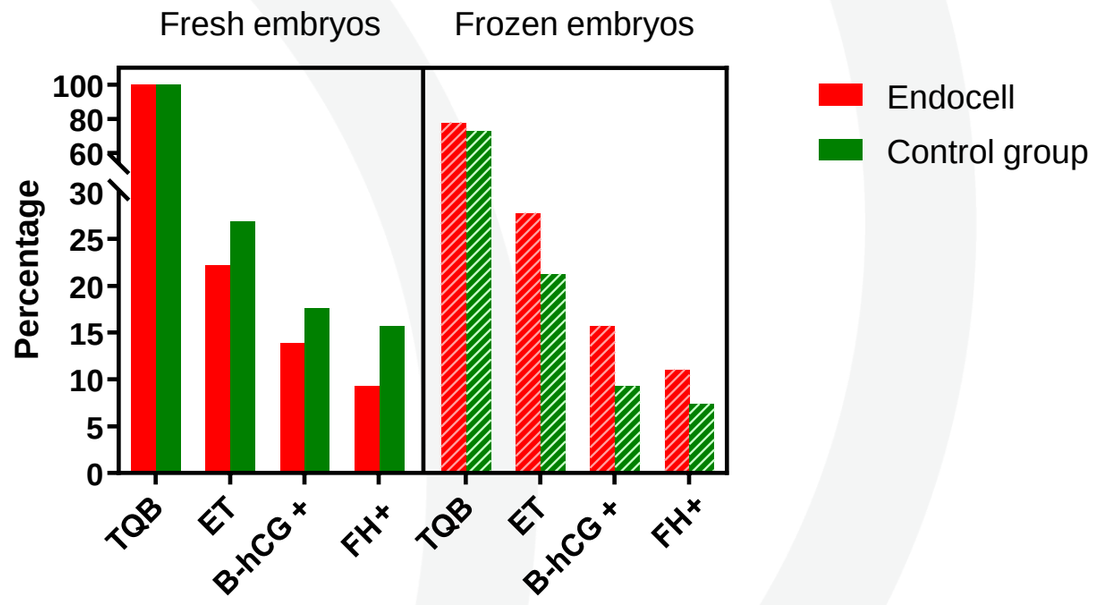
Following IVF, embryos were put respectively either in autologous coculture or in conventional culture medium. The blastulation rates were 63,8% (139/218) versus 64,3% (171/266) respectively. Considering blastocysts quality, the proportion of top quality blastocysts (TQB), suitable for fresh replacement or cryopreservation, versus total blastocysts in the coculture group was higher (77,7%) compare to the control group (63,2%), but not significantly. However, in terms of efficiency, the number of women obtaining 2 TQB or more for fresh transfer or cryopreservation was significantly higher in the coculture group (82 %) versus the control group (60%).

Table 1: Embryo quality

	Control	Coculture	p value
Embryos on coculture	218	266	
D3 useful embryos / Embryos on coculture	78,9 %	83,0 %	ns
Total Blastocysts (D5 and D6) / Embryos on coculture	64,3 %	63,8 %	ns
TQB / Embryos on coculture	40,6 %	49,5 %	ns
TQB / Total Blastocysts (D5 and D6)	63,2 %	77,7 %	< 0,05
Patients obtaining 2 or more TQB	60 %	82 %	< 0,05

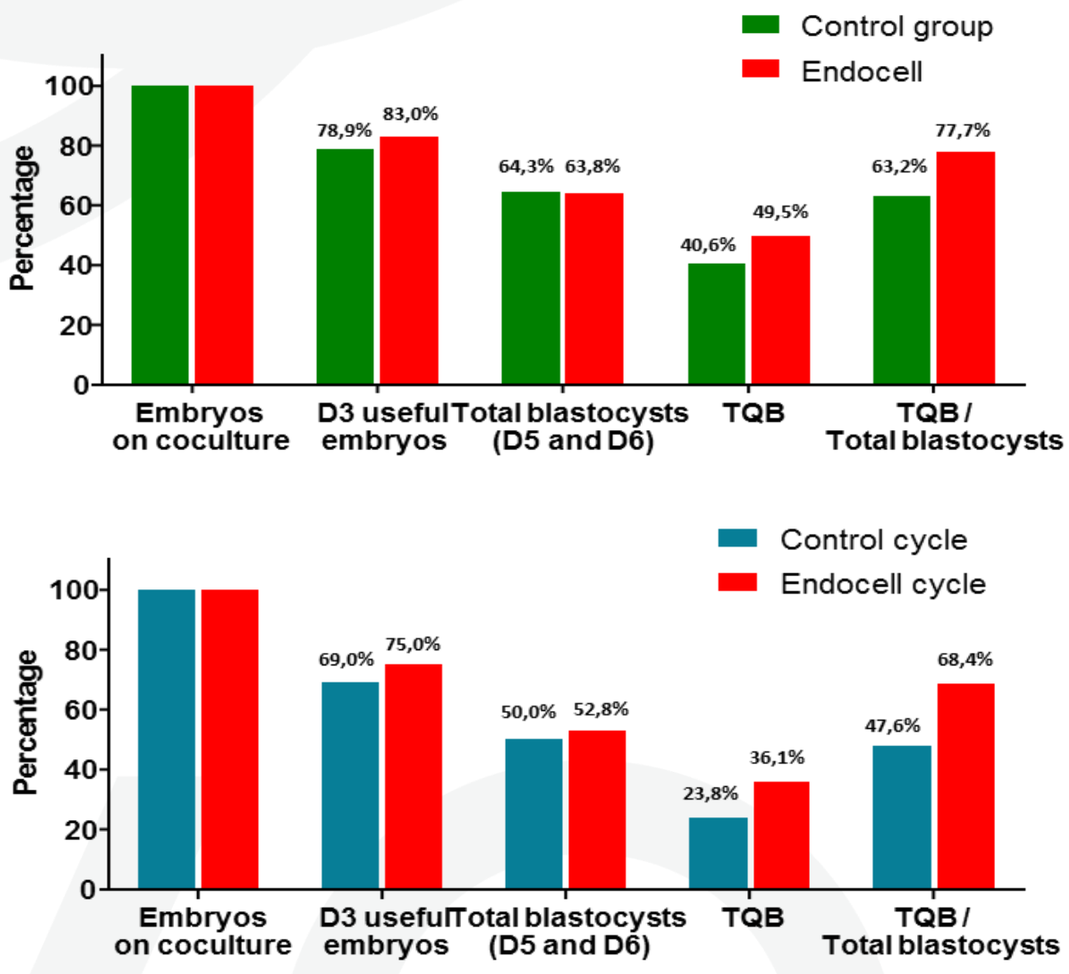
Pregnancy outcomes have been compared between groups and fresh versus frozen embryos. Since coculture didn't improve pregnancy rates with fresh embryos, but it did with frozen embryos, it suggests that growth on coculture provides higher quality embryos that are more resistant to cryopreservation and survival (Figure 1).

Figure 1: Pregnancy outcomes following fresh versus frozen embryo transfer



In single patient comparison (control group randomized patient coming back for coculture), the proportion of TQB versus total blastocysts in the coculture group was also higher with coculture (68,4%) compared to conventional culture medium (47,6%) (Figure 2).

Figure 2: Blastulation rates in Endocell vs control group (upper panel) and in single patient comparison (lower panel)



CONCLUSION

Based on these data, the use of a coculture system for embryo development increasing the number of available embryos per cycle could potentially lead to the need of less IVF cycles per patient. In addition, embryos obtained from coculture seem to survive better to embryo cryopreservation and their pregnancy outcome is better.

ACKNOWLEDGEMENT : Laboratoires Genevrier L'EXIGENCE DE VOTRE SANTÉ — OVO LABO