

Prostacyclin analogue (Iloprost) is safe for human embryo culture

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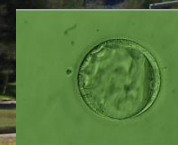
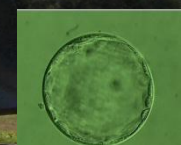
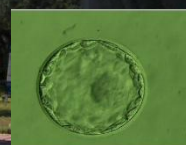
Introduction: Prostacyclin (PGI₂) has been found produced in the fallopian tube after ovulation in human and mouse models (1,2). PGI₂ stable analogue Iloprost (Ilomedin, Bayer Schering Pharma) is a FDA approved medication for pulmonary hypertension. In previous mouse embryo study, Iloprost significantly increased the complete hatching, implantation and delivery rates but did not increase the blastocyst formation rate (3). Although Iloprost showed no reproductive toxicology in previous mouse embryo studies (4), its effects on the *in vitro* development of human embryos have not been verified. Before universal applying Iloprost in human embryo culture, it is necessary to examine any toxic effect. This study examines the safety of Iloprost in the culture media. The blastocyst formation rate and quality of blastocyst are used as toxicity indicators.

Materials and Methods: The study has been approved by the Institutional Review Board and register in clinicaltrials.gov. The inclusion criteria are age less than 40, no TESE or embryo biopsy and with signed consent form. Totally 24 IVF cycles with 274 zygotes included in this study. Within each case, half numbers of zygotes were assigned to control group while the other half numbers of zygotes assigned to Iloprost group. The embryos in control group cultured with Medicult BlastAssist media with saline (vehicle). The experimental group cultured with Medicult BlastAssist media with 1uM of Iloprost. The examined outcomes are number of day 5 blastocyst, total number blastocysts (day 5 and day 6), and number of quality of blastocyst. A quality blastocyst was defined at least at 3BB stage (by Gardner's criteria, 5). If one digit below the cutline, it is considered not quality blastocyst.

Analysis: McNemar's test is used for statistical analysis.

Results

	Total # Zygotes	Day 5 blastocysts	Total Blastocysts	Quality Blastocysts
Control	138	60 (43%)	78 (57%)	30 (22%)
Iloprost	136	61 (45%)	90 (66%)	43 (32%)
Analysis	-	n.s.	P<0.005	P<0.001



Conclusions: If any toxic effect of Iloprost, the results should show lower number of blastocyst formation and lower number of quality blastocysts. The evidence does not support any toxic effect. The significant increase of total number and quality of blastocysts suggests Iloprost gives beneficial instead of toxic effect. The data support to continue into efficacy study.

Reference:

1. JC Huang et al. J Clin. Endocrinol. Meta. 87:4361-4368, 2002.
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3. JC Huang et al. Hum. Reprod. 19:1856-1860, 2004.
4. R. Battenfeld et al C. Toxicol Lett. 78: 223-34, 1995.
5. DK Garder et al. Fertil. Steril. 73:1155-1158, 2000.