

Does the culture medium used during IVF treatment affect twin birth weight discordance?



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Perinatal outcome of singletons after IVF or ICSI

Systematic review (17 studies; 14 matched controls)
Comparison of natural and assisted conceptions

- Preterm delivery (37 wk) RR 2.0 (1.8-2.3)
- Low birth weight (< 2.5 kg) RR 1.7 (1.5-1.9)
- Very low birth weight (< 1.5 kg) RR 3.0 (2.0-4.4)
- SGA (birth weight <10th centile for gestation) RR 1.5 (1.4-1.7)
- Perinatal mortality RR 1.7 (1.1-2.6)

Helmerhorst *et al.*, BMJ 2004

Possible causes for the worse perinatal outcome after IVF/ICSI

- Specific feature of the subfertile population
- Influence of hormonal stimulation
- Influence of in-vitro culture

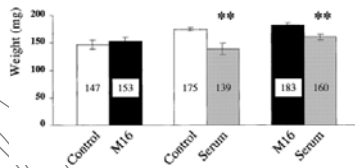
In vitro-culture

- Large offspring syndrome is seen after exposure of bovine and ovine embryos to a variety of unusual environments prior to the blastocyst stage
- Main characteristic is increased fetal growth; newborns frequently have a 2-fold or more increase in weight
- Most culture systems with which the LOS has been associated, involved the use of serum

Young *et al.*, Rev Reprod 1998

Effect of serum on fetal weight

- Culture of preimplantation mouse embryos in a chemically defined medium (M16) with or without calf serum
- Comparison between fetuses of the two different groups dissected from both uterine horns from the same recipient female at E14

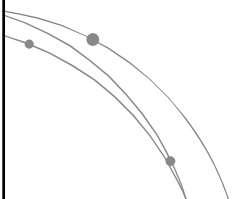


Khosla *et al.*, Biology of Reproduction 2001

Aim of present study

Effects of in vitro culture on human birth weight

- Singleton pregnancies
- Twin pregnancies





Twin discordance

- In the present study, we examine the effect of the culture medium used during IVF treatment on twin birth weight discordance
- Birth weight discordance in twins is associated with adverse perinatal outcome
(Amaru et al., Obstet Gynecol 2004; Branum et al., Obstet Gynecol 2003; Demissie et al., Obstet Gynecol 2002)
- Defined as $\geq 25\%$ difference in birth weight of the 2 children

In-vitro culture

- For our internal quality control program our IVF lab uses 2 distinct culture media systems for the IVF/ICSI procedure
- Therefore, we are able to compare the influence of different culture media on the perinatal outcome of pregnancies



M&M

- Alternate use of two commercially available sequential media systems in the period July 2003 – December 2006
- Culture media used:
 - Vitrolife (Göteborg, Sweden): IVF-50 and G1 version 3
 - Cook (Brisbane, Australia): K-SIFM and K-SICM
- Assignment:
 - Strictly alternating
 - Day before OPU
 - By lab technicians, unaware of patient characteristics or treatment cycles

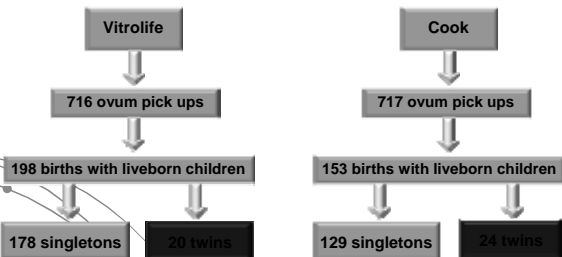


M&M

- Exactly the same ovarian stimulation, fertilization, culture and embryo transfer procedures were used in both groups
- Dichorionic twin pregnancies with live-born children after fresh embryo transfer following IVF/ICSI



Results





Results

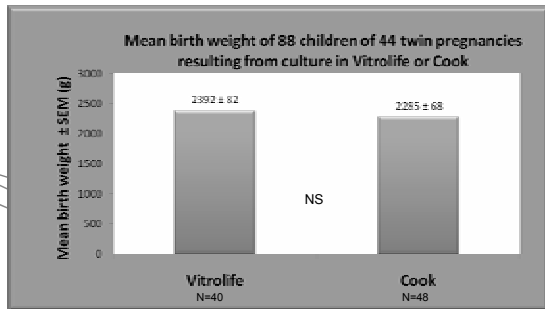
- 44 dichorionic twin pregnancies with live-born children after fresh embryo transfer following IVF/ICSI

	Vitrolife (n=20)	Cook (n=24)
Cycles with ICSI (% of total)	10 (50%)	16 (67%)
Maternal age in years (± SEM)	33.3 (± 0.9)	32.7 (± 1.0)
Gestational age in weeks (± SEM)	36.3 (± 0.6)	35.5 (± 0.5)

Maternal and paternal height, weight, BMI, age and smoking habits (≥10 sigarettes/day) were similar between the study groups

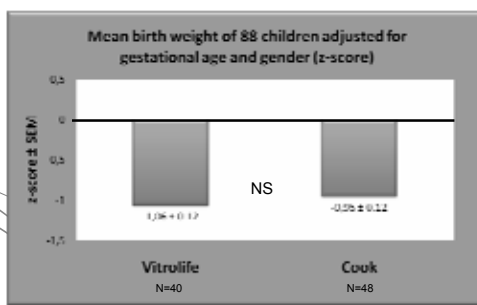


Results



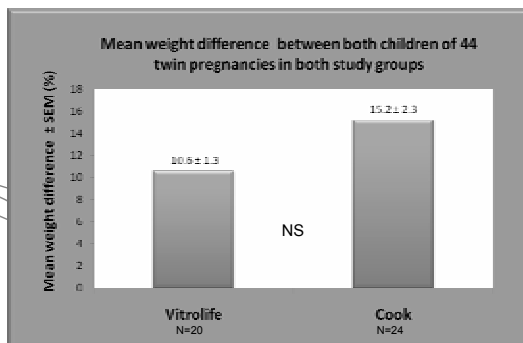


Results



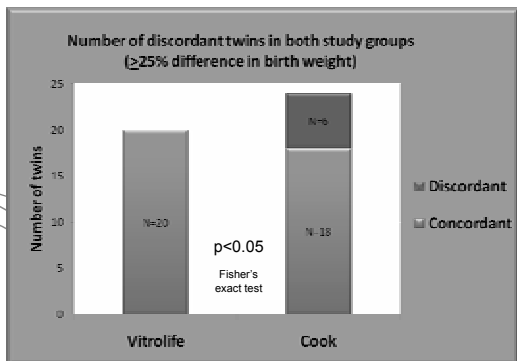


Results





Results





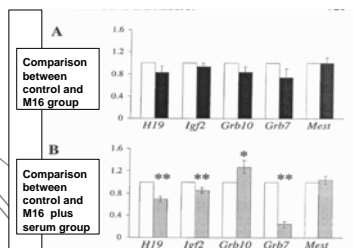
Discussion

- To our knowledge, this is the first study evaluating the influence of culture medium on growth discordance in twin pregnancies.
- Imprinted genes play key roles in the control of fetal growth. Altered imprinting can cause growth defects.
- Several animal studies have established a relationship between embryo culture and disrupted expression of imprinted genes



Discussion

- In vitro culture of preimplantation mouse embryos affects the expression of imprinted genes



Khosla *et al.*, *Biology of Reproduction* 2001



Discussion

- Considering increasing numbers of IVF/ICSI children worldwide (~ 46 000 in Europe in 2004*), research to optimize culture media for IVF procedures is very important.
- Larger studies are needed
- Our results indicate a significant relationship between the type of medium used to culture embryos during the first few days after fertilization and twin birth weight discordance.

* Nyboe Anderson *et al.*, Hum Reprod 2008



Cause

Disturbed epigenetic mechanisms?

