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A multi-center double-blind randomized trial on the use of G5 or HTF medium for human preimplantation embryo culture in IVF/ICSI

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Abstract

Study question: Should G5 or HTF be used for culturing embryos in IVF/ICSI?

Summary answer: A higher, but non-significantly different ongoing pregnancy rate was obtained in the G5 group compared to the HTF group. Other outcomes such as clinical pregnancy, number of utilizable embryos, number of embryos implanted after a fresh transfer and the number of cryopreserved embryos available for transfer at a later date at the end of the study all significantly favored G5.

What is known already: A wide variety of culture media for human preimplantation embryos in IVF/ICSI treatments currently exists. It is unknown which medium is best in terms of clinical outcomes.

Study design, size, duration: Between September 2010 and May 2012, 836 couples (419 in the HTF group and 417 in the G5 group) were included in this multi-center, double-blind randomized controlled trial. Allocation was performed centrally by an online computer program. Each couple was treated until a live birth was obtained within a maximum timeframe of one year of IVF/ICSI treatment. The allocated medium was used in all treatment cycles, including transfers with frozen/thawed embryos.

Participants/materials, setting, methods: Couples, who started IVF/ICSI treatment at one of the six participating centers and their affiliated clinics for a first cycle, or first cycle after a successful pregnancy.

Main results and the role of chance: A higher, but non-significantly different ongoing pregnancy rate was obtained in the G5 group compared to the HTF group [45% (189/417) vs. 39% (163/419); RR: 1.2; 95% CI: (0.99-1.38); P=0.07]. Clinical pregnancy [48% (199/417) vs. 40% (168/419); RR: 1.2; 95% CI: (1.02-1.39); P=0.03] favored G5. Number of utilizable embryos, number of embryos implanted after a fresh transfer and the number of cryopreserved embryos per woman left for transfer at a later date at the end of the study were all significantly in favor of G5.

Limitations, reasons for caution: This study was powered to detect a 10% difference in live births while a smaller difference could still be clinically relevant.

Study funding/competing interest(s): This study was funded by the NutsOhra foundation.

Trial registration number: NTR1979
Introduction

Subfertility is of major clinical and social concern. The most frequently used interventions to treat subfertility are in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). Despite their common use, IVF and ICSI are far from optimal treatments: the two largest data collections report a delivery rate per started cycle of only 20% and 22% respectively [1, 2].

A well-known factor that contributes to IVF/ICSI success is the medium that is used for oocyte and embryo culture. Several studies have shown the importance of the choice of embryo culture medium in this respect as it seems to impact embryo quality, pregnancy outcomes, and even the birthweight of newborns [3-10].

Despite the importance of culture media, a recent systematic review showed that randomized studies that compare clinical outcomes of different culture media are very limited in number and of low methodological quality [7]. Evidence-based selection of the best culture media from the wide range of available brands is currently not possible.

The aim of this multi-center, double-blind, randomized, controlled trial was to compare the clinical outcomes of two widely used embryo culture media, HTF medium and G5 medium.

Materials and methods

Study Design

We conducted a multi-center, double-blind, randomized, controlled trial in six hospital-based IVF centers (Academic Medical Center in Amsterdam (AMC), Catharina Hospital in Eindhoven, St. Elisabeth Hospital in Tilburg, Maastricht University Medical Center in Maastricht (MUMC), University Medical Center Groningen in Groningen (UMCG) and Radboud University Medical Center Nijmegen in Nijmegen (UMCN)) and five of their affiliated clinics (the Onze Lieve Vrouwe Gasthuis in Amsterdam, the Gemini Hospital in Den Helder, the Scheper Hospital in Emmen and the Maxima Medical Center in Veldhoven) in the Netherlands. The study protocol was approved by the institutional review boards of all participating centers and by the Central Committee on Research Involving Human Subjects (CCMO) in the Netherlands.

Allocation between two embryo culture media, G5 series (Vitrolife, Göteborg, Sweden) and HTF (Lonza, Verviers, Belgium), was performed centrally, one day before oocyte retrieval of the first cycle, by an online computer program with a 1:1 allocation using random block sizes of two and four couples. Stratification was performed for maternal age (<38 years of age and ≥ 38 years of age) and fertilization technique (IVF or ICSI) for each individual center. The allocated medium was used for all treatment cycles, including transfers with
cryopreserved embryos, which the couple received during one year of treatment in the specific center.

Decisions to include a couple and written informed consent of the couples were obtained via their gynecologists that were unaware of the allocation sequence. Participating couples, attending gynecologists and outcome assessors were fully blinded as to the allocated treatment. The allocation sequence was revealed to the primary investigators only at the end of the study. The allocation of the couples to one of the two groups was performed by the embryologists based on the outcome of the online allocation. Blinding of the embryologists was not possible since they performed the procedures in the laboratory.

*Study population and sample size calculation*

All couples that were scheduled for an IVF/ICSI treatment at one of the participating centers or their affiliated clinics for their first, or first after a successful pregnancy, cycle were eligible to participate in this study. Couples undergoing preimplantation genetic diagnosis (PGD), couples for whom IVF was used to prevent the transmission of HIV and couples undergoing a modified natural cycle [11] were excluded.

Based on a cumulative live birth rate of 40% after one year of IVF/ICSI treatment (2 - 3 cycles) in the participating centers in the years preceding this study, we calculated that a sample size of at least 784 couples would be needed to detect an increase of 10% (from 40% to 50%) in live birth rate after one year of treatment with a power of 80% at a significance level of 0.05.

*Study procedures*

All procedures that the included women underwent, such as ovarian hyperstimulation, follicular aspiration and oocyte fertilization were the routine IVF/ICSI procedures that these women would receive when not participating in the study in the particular center where they received treatment.

The G5 series are sequential media that include G-IVF medium for fertilization, G1 medium for culturing embryos from day one to day three and G2 medium for culturing embryos from day three to day six. HTF is a medium for continuous uninterrupted culture of oocytes and embryos from fertilization up to day three of culture. To keep the same methodology as when using G5 media, the embryos were moved to a new culture dish containing HTF on day three for further culture. HTF was supplemented with 10% pasteurized plasma solution (Central Laboratory of Blood Transfusion, Amsterdam, the Netherlands).

In case of IVF, the oocytes were incubated in dishes containing G-IVF (Vitrolife, Göteborg, Sweden) or HTF, according to the culture medium allocated to every woman, with 10,000 - 100,000 progressively motile spermatozoa per ml for fertilization. The next morning, the
cumulus cells were removed and all fertilized and unfertilized oocytes were transferred to a clean dish containing the allocated medium, G1 or HTF. On day three of culture the embryos were transferred to a new dish containing G2 or HTF.

In case of ICSI, the oocytes were denuded using cumulase (Origio, Malov, Denmark), injected with a single immobilized spermatozoon and directly thereafter cultured in dishes containing G1 or HTF according to treatment allocation. On day three of culture the embryos were transferred to a new dish containing G2 or HTF. Transfer of the embryos was performed in G5 or HTF accordingly. Transfer of one, two or three embryos was performed according to the local policies of each participating center.

Embryo culture in each of the culture media was performed following the instructions of the manufacturers, i.e. at 37°C and 6% CO₂ for G5 and 37°C and 5% CO₂ for HTF. Three centers cultured oocytes and embryos in 20% O₂ (University Medical Center Groningen, Catharina Hospital and University Medical Center Nijmegen) while the other three cultured oocytes and embryos in 5% O₂ (Academic Medical Center, St. Elisabeth Hospital and Maastricht University Medical Center). Embryo morphology was assessed daily and the number of cells as well as the percentage of fragmentation were scored based on a structured scoring sheet available in all centers [12]. All embryologists in all centers participated in a national external online embryo scoring quality control scheme (www.embryoonline.eu). Embryos of sufficient quality were transferred to the uterine cavity of the women on day 2 or 3 after culture. Cryopreservation of supernumerary good quality embryos was performed one or two days after embryo transfer.

In case of multiple cycles per woman, the allocated medium was used for all treatment cycles that the woman received during a one year time frame after allocation. In case of a transfer with cryopreserved embryos, the allocated medium was used for culture and transfer of these embryos as well.

Outcome measures

The primary outcome of the study was live birth rate. Live birth was defined as a pregnancy that resulted in the birth of at least one baby born alive, independent of gestational age. Since at the time of writing of this thesis data on live births were not yet complete, we focus here on the results of the secondary outcome measures, with ongoing pregnancy as the main outcome. Data analysis of live births is expected to be complete in the beginning of 2014.

Other secondary outcomes included clinical pregnancy, biochemical pregnancy, multiple pregnancies, miscarriages, implantation, embryo quality and fertilization. Ongoing pregnancy was defined as a viable intrauterine pregnancy after 12 weeks of gestation. Clinical pregnancy was determined by the presence of a gestational sac confirmed by transvaginal ultrasound examination at 6 - 8 weeks of gestation. Biochemical pregnancy
was defined as a serum β human chorionic gonadotropin level of at least 50 IU per liter 2 weeks after embryo transfer. Multiple pregnancies were defined by the presence of two or more fetal sacs at 12 weeks of gestation. Miscarriages were defined by fetal loss till 12 weeks of pregnancy. Implantation was determined by the number of fetal sacs as identified by transvaginal ultrasound examination at 6 - 8 weeks of gestation. The end of study participation for a particular couple was the achievement of a live birth, the passing of one year after allocation or withdrawal of consent by the couple. Only pregnancies achieved via IVF/ICSI at the participating center were included in the data analysis.

Statistical analysis

The rates of clinical and laboratory outcomes were calculated in each group with 95% confidence intervals. We used 2-sided chi-square statistics to test for significance of categorical variables and a one-way ANOVA for continuous variables. Data were analyzed according to an intention-to-treat principle and involved analysis of all women who were randomized according to their original group allocation.

One interim analysis of efficacy was planned to be performed one year after the initiation of the study by an independent data and safety monitoring committee. Primary outcome of this interim analysis was ongoing pregnancy for first, second, and third cycles, including transfers with cryopreserved embryos, that had been performed at that time. The data and safety monitoring committee had to use these proxy outcomes as otherwise an interim analysis would not have been possible before the completion of the inclusion of the study. Live birth data were only available at the end of the study, due to the design and inclusion rate of the study. For the same reason no formal stopping rules or adjusted statistics were applied. A blinded overview, which was available only to the data and safety monitoring committee, was used for the interim analysis.

Results

Between September 2010 and May 2012, a total of 836 couples were randomly allocated to undergo IVF/ICSI using either G5 (n=417) or HTF (n=419) medium for embryo culture (Figure 1). There were 412 couples in the G5 group and 395 couples in the HTF group that underwent the allocated intervention in all their cycles. Five couples in the G5 and twenty-four couples in the HTF group did not receive the allocated treatment in one of the performed cycles because of human error in identifying the couple as participating in the study. Only one couple (in the G5 group) withdrew informed consent prior to finishing the year of treatment, after two cycles. This woman was not pregnant and was analyzed as such. Nineteen couples were allocated in either of the two culture media without fulfilling the inclusion criteria; the primary reason being that they had underwent one or more previous unsuccessful IVF/ICSI treatments. Since our analysis is based on an intention-to-treat protocol, these couples were included in the analysis.
A multi-center double-blind randomized trial on the use of G5 or HTF medium

Figure 1: Flow chart of allocation, follow-up and analysis of the included couples.

The couples remained enrolled in the study for one year after allocation and in the case of pregnancy they were followed until delivery. No couples were lost-to-follow-up. The baseline characteristics of the couples are presented in Table 1. Four couples (three in the G5 group and one in the HTF group) received oocyte donation and twenty-two couples (eight in the G5 group and fourteen in the HTF group) had treatment with sperm from a donor. In these cases, the age of the donor was used for the calculation of the mean maternal and paternal age.

The number of women with an ongoing pregnancy in the G5 group was higher than the number of women achieving an ongoing pregnancy in the HTF group, but the difference was not statistically significant [45% (189 of 417) vs. 39% (163 of 419); RR: 1.2; 95% CI: (0.99-1.37); P=0.07]. Compared to women in the HTF group, significantly more women in the G5 group had a clinical pregnancy [48% (199 of 417) vs. 40% (168 of 419); RR: 1.2; 95% CI: (1.02-1.39); P=0.03]. The number of women with biochemical pregnancy was higher, but not significantly, in the G5 group compared to women in the HTF group [57% (236 of 417) vs. 50% (210 of 419); RR: 1.1; 95% CI: (0.99-1.28); P=0.06]. The number of miscarriages did not differ significantly between the groups (Table 2).

Clinical characteristics according to treatment cycle are shown in Table 3. A total of 1,496 cycles [714 (mean of 1.7) for the G5 and 782 (mean of 1.9) for the HTF group] were performed (P=0.57).
Although not significant, the cumulative percentage of ongoing pregnancies was higher in the G5 group compared to the HTF group at all time points in treatment window of one year (Figure 2A). Women in both groups underwent a similar number of transfers, when using fresh embryos (714 vs. 783; \(P=0.57\)). The number of transfers using cryopreserved embryos was higher in the G5 group compared to the HTF group but the difference was not statistically significant (276 vs. 204; \(P=0.08\)) (Table 3 and Figure 2B). At the end of the study period, significantly more cryopreserved embryos per woman were remaining in the freezer in the G5 group compared to the number of embryos in the HTF group (1.3 vs. 0.8; \(P<0.001\)) (Figure 2C).

The embryo characteristics of all treatments are shown in Table 4. The number of fertilized oocytes in the HTF group was significantly higher compared to the G5 group [69\% (4,346 of 6,279) vs. 63\% (3,667 of 5,822); \(P<0.001\)] (Figure 3). The number of embryos that were transferred or cryopreserved, i.e. the number of utilizable embryos, and the number of embryos that implanted after a fresh transfer were significantly higher in the G5 group compared to the HTF group [1,974 vs. 1,778; \(P<0.001\) and 20\% (196 of 967) vs. 15\% (170 of 1,116); \(P<0.001\), respectively].

**Discussion**

In this randomized controlled trial we evaluated the effect of two commonly used culture media on embryo characteristics and pregnancy outcomes. A higher but not statistical significantly different ongoing pregnancy rate was obtained in the G5 group compared to the HTF group. Clinical pregnancy and embryo outcomes were significantly in favor of G5.
We now found a 6% difference in ongoing pregnancies. Despite the absence of a statistical difference [borderline significance (RR 1.2 (0.99-1.37))] this difference could be of clinical relevance, especially if we take into account that the study was powered to detect a 10% difference in live birth rates. Designing the study to be able to find a smaller difference between the media was not considered feasible at the time of study design due to the higher number of couples needed. This argues strongly in favor of broadening cooperation in large multi-center trials, as this is necessary to be able to establish smaller differences, which are still clinically relevant.

Based on the effect size for ongoing pregnancy rate and the fact that other secondary outcomes such as clinical pregnancy rate, implantation rate, and embryo utilization rate, all favor G5 we feel it is justified to conclude that G5 provides better treatment success than HTF. Complementary, the number of transfers using cryopreserved embryos was higher in the G5 group compared to the HTF group (276 vs. 204; \( P = 0.08 \)), and women in the G5 group had more cryopreserved embryos available in the freezer at the end of the study for transfer at a later date compared to the women in the HTF group (1.3 vs. 0.8; \( P < 0.001 \)), which further adds to the beneficial effect of G5. We will collect data from cycles transferring these cryopreserved embryos that are still in the freezer, and conduct a secondary analysis to compare the cumulative live birth rates over time.

To explain the differences between the outcomes of the two media we looked at the composition of the media. Even though a complete list with their components and concentrations used is not available because of patent issues, one of the differences is that the G5 medium has certain amino acids that the HTF medium lacks. Studies in human

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**Table 2: Clinical outcomes in women per culture medium used.**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>G5 (n=417)</th>
<th>HTF (n=419)</th>
<th>Risk Ratio (95% CI)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women with ( \geq 1 ) ongoing pregnancy</td>
<td>189 (45)</td>
<td>163 (39)</td>
<td>1.2 [0.99-1.37]</td>
<td>0.07</td>
</tr>
<tr>
<td>Total no. of ongoing pregnancies</td>
<td>191</td>
<td>164</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women with ( \geq 1 ) clinical pregnancy</td>
<td>199 (48)</td>
<td>168 (40)</td>
<td>1.2 [1.02-1.39]</td>
<td>0.03</td>
</tr>
<tr>
<td>Total no. of clinical pregnancies</td>
<td>206</td>
<td>170</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women with ( \geq 1 ) biochemical pregnancy</td>
<td>236 (57)</td>
<td>210 (50)</td>
<td>1.1 [0.99-1.28]</td>
<td>0.06</td>
</tr>
<tr>
<td>Total no. of biochemical pregnancies</td>
<td>256</td>
<td>221</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women with ( \geq 1 ) miscarriage( ^{\dagger} )</td>
<td>61 (15)</td>
<td>51 (12)</td>
<td>1.2 [0.85-1.70]</td>
<td>0.31</td>
</tr>
<tr>
<td>Total no. of miscarriages</td>
<td>65</td>
<td>57</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data presented as numbers (%)

* CI denotes confidence intervals

\( ^{\dagger} \) 18 women had a multiple pregnancy in the G5 group and 21 women had a multiple pregnancy in the HTF group

\( ^{\dagger} \) miscarriages calculated up to 12 weeks

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and animal embryos have shown that the addition of amino acids in the culture medium can indeed be beneficial for embryo development in vitro [13-18]. However, no studies in humans looked specifically at the effect of amino acids on pregnancy rates or live births.

As far as we know, there are no other randomized controlled trials comparing the efficacy of these two culture media for human IVF/ICSI treatment [7]. The reason why G5 and HTF culture media were used for this study is because HTF was the culture medium initially used by the majority of the Dutch IVF centers and that many centers considered switching to G5. Two previous studies compared the efficacy of HTF medium and G2 medium; G2 is an earlier version of G5 and is no longer on the market [19, 20]. The exact differences in components and their concentrations between these two culture media are not known. One study was a quasi-randomized trial with 294 couples which showed that culturing embryos using G2 media resulted in a significantly better embryo quality and reproductive performance (implantation and birth rate) compared to culturing embryos using HTF [19]. The other study in 558 frozen-thawed zygotes showed that G2 medium supported better the development of frozen-thawed human embryos in vitro and provided better embryo quality and higher pregnancy rates than HTF medium [20]. Both studies are indicative of a better efficacy in embryo development and clinical outcomes of G2 over HTF but they fall short in study design and number of included couples.

Although we conclude that G5 is superior to HTF, there are still many other media available. A trial comparing all available culture media simultaneously is simply not

<table>
<thead>
<tr>
<th>Table 3: Clinical characteristics according to treatment cycle.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>No. of fresh cycles started&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cycle 1</td>
</tr>
<tr>
<td>Cycle 2</td>
</tr>
<tr>
<td>Cycle 3</td>
</tr>
<tr>
<td>Cycle 4</td>
</tr>
<tr>
<td>Fertilization procedure</td>
</tr>
<tr>
<td>IVF</td>
</tr>
<tr>
<td>ICSI</td>
</tr>
<tr>
<td>No. of fresh embryo transfers&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>No. of fresh cycles with ongoing pregnancy</td>
</tr>
<tr>
<td>Cycle 1</td>
</tr>
<tr>
<td>Cycle 2</td>
</tr>
<tr>
<td>Cycle 3</td>
</tr>
<tr>
<td>Cycle 4</td>
</tr>
<tr>
<td>No. of transfers with cryopreserved embryos</td>
</tr>
<tr>
<td>As part of cycle 1</td>
</tr>
<tr>
<td>As part of cycle 2</td>
</tr>
<tr>
<td>As part of cycle 3</td>
</tr>
<tr>
<td>As part of cycle 4</td>
</tr>
<tr>
<td>No. of transfers with cryopreserved embryos leading to an ongoing pregnancy&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>As part of cycle 1</td>
</tr>
<tr>
<td>As part of cycle 2</td>
</tr>
<tr>
<td>As part of cycle 3</td>
</tr>
<tr>
<td>As part of cycle 4</td>
</tr>
</tbody>
</table>

Data presented as numbers (%), percentages calculated per number of fresh cycles started

<sup>a</sup> Percentages calculated per number of fresh cycles

<sup>b</sup> One woman in each group had two embryo transfers using fresh and vitrified oocytes

<sup>c</sup> percentage calculated per number of embryo transfers with cryopreserved embryos

n.a. denotes not applicable
Figure 2: Clinical outcomes per medium used. (A) Cumulative ongoing pregnancy rate was higher throughout the study period for the G5 group compared to the HTF group. (B) Number of transfers performed using either fresh or cryopreserved embryos per group. The overall number of transfers is the same, but women that were allocated in the G5 group had more transfers with cryopreserved embryos compared to women that were allocated in the HTF group (P=0.08). (C) The number of cryopreserved embryos that are still available in the freezer is higher in the G5 group compared to the HTF group (P<0.001). That could lead to more transfers in the future and more ongoing pregnancies for women in the G5 group compared to women in the HTF group. * Indicates a significant difference.

Table 4: Embryo characteristics per culture medium used.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>G5</th>
<th>HTF</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulus-oocyte complexes - no. (mean no. per cycle ± SD)</td>
<td>6,477 (9.1 ± 5.3)</td>
<td>7,090 (9.1 ± 5.4)</td>
<td>0.95</td>
</tr>
<tr>
<td>Oocytes inseminated/injected - no. (mean no. per cycle ± SD)</td>
<td>5,822 (8.2 ± 5.0)</td>
<td>6,279 (8.0 ± 5.0)</td>
<td>0.61</td>
</tr>
<tr>
<td>Fertilized oocytes (embryos)* - no. (mean no. per cycle ± SD)</td>
<td>3,667 (5.1 ± 3.9)</td>
<td>4,346 (5.6 ± 4.0)</td>
<td>0.04</td>
</tr>
<tr>
<td>Fertilization rate - % per oocytes inseminated/injected</td>
<td>63</td>
<td>69</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Utilizable embryos^1 - no. (mean no. per cycle ± SD)</td>
<td>1,974 (2.8 ± 2.4)</td>
<td>1,778 (2.3 ± 1.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Embryos transferred from a fresh cycle - no. (mean no. per transfer ± SD)</td>
<td>967 (1.5 ± 0.6)</td>
<td>1,116 (1.5 ± 0.6)</td>
<td>0.19</td>
</tr>
<tr>
<td>Implanted embryos from a fresh cycle - no. (% of embryos transferred)</td>
<td>194 (20)</td>
<td>170 (15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Embryos cryopreserved - no. (mean no. per cycle ± SD)</td>
<td>1,007 (1.4 ± 2.4)</td>
<td>662 (0.9 ± 1.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cryopreserved embryos transferred - no. (mean no. per transfers with cryopreserved embryos ± SD)</td>
<td>324 (1.2 ± 0.6)</td>
<td>225 (1.1 ± 0.6)</td>
<td>0.22</td>
</tr>
<tr>
<td>Implanted cryopreserved embryos - no. (% of cryopreserved embryos transferred)</td>
<td>36 (11)</td>
<td>25 (11)</td>
<td>0.89</td>
</tr>
</tbody>
</table>

* ZFN zygotes and TPN/OPN zygotes that cleaved in 48 hours

^1 Number of embryos transferred or cryopreserved
devices for assisted reproductive technologies [21]. Companies should also report what studies have been performed to test these media and which endpoints were analyzed. The responsibility for proper introduction of culture media with new formulations lies with the manufacturers that should disclose the composition of the culture media and the rational behind it but also with the reproductive medicine professionals that should be more critical and compare success rates of new culture media to the older ones. As illustrated here by six participating centers, the randomized use of two culture media can be implemented easily in daily routine.

Since there is evidence that culture media can affect not only pregnancy rates but also neonatal health [5, 8], future studies should also include follow-up data on the children born. We are currently gathering these data form the children born in the current trial and will publish them at a later time.

In conclusion, we found a higher but not statistically significant difference in the number of women achieving an ongoing pregnancy after a year in the G5 group as compared to the HTF group. Given the fact that this difference reached borderline significance, the power calculation was based on finding a difference of 10%, the culture in G5 resulted in significantly better embryos and higher implantation and clinical pregnancy rates than HTF, we recommend the use of G5 for culture of human embryos during IVF/ICSI treatments over HTF.
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Conflict of interest

None

References


