

## In vitro culture of human embryos with micro-vibration increases take-baby-home rates: data of 4303 patients during four years.

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What is known already: It is shown that mechanical stimulation of ciliated epithelial cells in culture induces a wave of increasing Ca<sup>2+</sup> that spreads from the stimulated cells to neighboring ones. In the absence of extracellular Ca<sup>2+</sup> these mechanically stimulated cells showed no change or a decrease in Ca<sup>2+</sup>, whereas Ca<sup>2+</sup> increase in neighboring cells. The in-vitro culture of human embryos in a medium subjected to regular short intervals of mechanical agitation leads to increased development rates. This type of treatment tries to mimic conditions in nature whereby oviductal fluid is mechanically agitated by the epithelial cilia. This phenomenon can be explained by the fact that an embryo developing in vivo is naturally exposed to constant vibrations of around 6 Hz with the periodically repeating increase to 20 Hz.



**Materials methods:** This work was performed from August 2010 to December 2014. Written informed consent was obtained from all the participating couples for the culture of pronuclear oocytes and embryos. Patients were distributed on four age-groups: <29 years, 30-34 years, 35-39 years and  $\geq$ 40 years. Patients with unexplained infertility were stimulated in the IVF- or ICSI-cycles. Informed consent was obtained from 4303 patients (median age 34±4.6) for the culture of pronuclear oocytes (two per patient) under two different conditions: with mechanical agitation (20 Hz delivered over 5 seconds once every hour) (2152 patients, n = 4304) as well as without mechanical agitation of the culture medium (2151 patients, n = 4302). Embryo transfer (two embryos per patient) was performed on Day 3 or Day 5 after oocyte retrieval. Take-baby-home rates were analyzed by ANOVA for categorical variables using the CATMOD Procedure of SAS (SAS Institute Inc., 2011). The terms included in the model were: type of culture (vibration vs. static), age of patient donor and their interaction. Comparisons between age-groups were performed by pairwise contrasts and Bonferroni-Holm adjustment for multiple comparisons using the MULTTEST procedure of SAS.

**Results:** The following take-baby-home rate was detected for Groups  $\leq 29$  years, 30-34 years, 35-39 years and  $\geq 40$  years, respectively (static vs. vibration): 29.3% vs. 32.9% (P>0.1, increasing on the level of tendency), 27.1% vs. 38.7% (P<0.05), 23.8% vs. 28.9% (P<0.05), 9.1% vs. 14.5% (P<0.05)





**Conclusion.** In vitro culture of embryos under micro-vibration conditions significantly increases take-baby-home rate for patients of 30 years and older.