Epigenetic effect and IVF

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Why focus on epigenetics in vitro fertilization?
Since 2002, several cases of defects of genetic fingerprint have been reported in the literature with several abnormalities of the imprinting that occur more frequently for children conceived after medically assisted procreation children when compared to naturally conceived ones. In the vast majority of cases, it was children with Beckwith-Wiedemann syndrome, with a default center footprint. Therefore, many teams have tried to explain the mechanism of occurrence and different assumptions were made to determine the origin of this frequency increase, especially as these anomalies did not affect a specific locus but different loci. The hypothesis that a deregulation of the mechanisms of maintenance of epigenetic marks has been issued but which is the stage of the care that is at the origin of the appearance of these anomalies. But, is there only one?

Is ovarian stimulation? Is the embryo culture? Is impaired spermatogenesis? Is the in vitro fertilization technique itself? What is the impact of new techniques such as vitrification and in vitro maturation on epigenetic phenomena?

But what are these epigenetic abnormalities that were observed? When and how is implemented parental imprinting? How is it kept in short early development? Is that all the mechanisms of epigenetics, as methylation or histone modifications, are concerned, or only imprinted genes?

To try to answer these questions, a lot of works, more or less discordant have attempted to answer these questions.

First it was shown an impact of various factors such as stress, hormone levels or nutrition on the trans-generational transmission of epigenetic changes, and signing the fact that the environment has an impact on future generations. In humans, the model of DES (diethylstilbestrol) is an example of such an effect. In total, why IVF protocols would not have an impact on epigenetic marks.

Impact of ovulation induction: few studies have been conducted in humans, but the results seem to favor a disturbance of epigenetic profiles of imprinted genes. In mice, several studies were conducted which also suggest an effect of ovarian stimulation on the methylation and/or gene expression.

Impact of in vitro fertilization techniques: few studies have been conducted, and the results seem somewhat contradictory.

Impact of in vitro culture: If conflicting results were observed in humans, in mice, an effect of in vitro culture seems pretty obvious with deregulation of DNA methylation but also of gene expression.

Impact of impaired spermatogenesis: It now seems clear that there is a correlation between sperm counts and altered imprinted genes profile, possibly with transmission to offspring, since these changes were also observed in the placenta. Conversely, if the overall methylation profile of testicular tissue appears altered in patients with non-obstructive azoospermia, this does not seem the case in the semen of oligospermic patients.

In total, there is probably an impact of reproductive biology techniques on epigenetics. However, some diseases have been observed, the frequency is very low, even if frequency of the most frequent syndrom, the BWS one is increased by a factor of 4 to 10. But could it be only the tip of the iceberg?