The advantage of using both Time-Lapse and PGS for embryo selection and evaluation

Abstract

The goal of every IVF lab is to select the most competent embryos for transfer for better clinical outcome. Both time-lapse enabled assessment and Preimplantation Genetic Screening (PGS) are methods well utilized by many IVF labs in order to select the most viable embryo. Each method has its own advantage and weakness. Performing both methods, will not only enhance your decision-making, but has also shown to improve clinical outcome in terms of implantation and pregnancy rate.

Introduction

Traditional procedures for embryo evaluation and selection are based on its morphological characteristics observed under the microscope at different time points. With the advent of time-lapse systems, embryo selection has moved from static observation to a dynamic process called as *morphokinetics*. However, information is still limited when it comes to the relationship between morphokinetic parameters, euploidy (or chromosomal compositions) and implantation potential.[1]

Preimplantation genetic screening (PGS) is now being used to help further improve embryo selection and assisted reproductive outcomes. Aneuploidy, which can be detected through PGS, plays a major role in implantation failure and early miscarriage, thereby, affecting Live Birth Rate outcome. Both Time-Lapse Monitoring and PGS have their strong and weak points, but if done in synergy, will bring about a positive outcome. This paper presents the advantages of doing time-lapse imaging in concomitant use of PGS in selecting the most viable embryo for transfer.

Non-Invasive Assessment thru Time-Lapse

Conventional incubation is limited only to the information gathered about the growth and changes in embryonic morphology at certain discrete time points. The introduction of time-lapse culture and monitoring offers the opportunity to observe changes in the morphology of the embryo during its entire development without any disturbances. Time-lapse incubation has the advantage of avoiding unnecessary environmental stressors, such as pH or temperature fluctuations, associated with the necessity to remove the embryos from the incubator for the routine static observation at discrete time points.[2]

As a result, time-lapse monitoring emerged as one of the most advanced non-invasive methods for evaluating the viability of the embryo to implant.[3] The group of Meseguer et al. was among the first

[1] (Yang, et al., 2014)
[2] (Swain, 2013)
[3] (Yang, et al., 2014)

to publish time-lapse data on morphokinetics and cleavage patterns, which were used to assess the chance of implantation and live birth.

Campbell et al. were also able to demonstrate a model that can be used to indicate the chance of an embryo to be chromosomally normal. Based on time-lapse data, they were able to create an ***Aneuploidy Risk Classification model*** which ranks embryos into high, medium or low risk with respect to chromosomal abnormalities.[4] However, this type of assessment needs to be optimized specifically for each clinic and may not be directly transferrable to another clinical setting as confounding factors may differ between different clinical setups.[5]

Aneuploidy risk assessment thru PGS

Several papers have been published which points that the main cause of embryo arrest, implantation failure, and pregnancy loss is on the presence of chromosomal aberrations or aneuploidy, which is common among *in vitro* fertilized embryos.[6] More than 50% of embryos obtained during IVF have chromosomal abnormalities. These aneuploid embryos are likely to fail to implant, be spontaneously aborted, or result in the birth of children with severe phenotypes.

Currently, preimplantation genetic screening (PGS) is one effective tool used by IVF clinics to detect and avoid the selection of aneuploid embryos for transfer. PGS is invasive and involves an embryo biopsy at day 3 or trophectoderm biopsy at day 5. However, embryo mosaicism is still prevalent, and the ploidy result may not be conclusive for the whole embryo. Mosaicism is quite high at both the cleavage and blastocyst stages of development, with its prevalence as high as 20%.[7]

Clinical results of Time-Lapse in synergy with PGS

The approach to using time-lapse together with PGS using array CGH for aneuploidy detection was first presented at ESHRE meeting in 2012.[8] A prospective study with sibling oocytes by Yang et al. (2014) on the selection of competent blastocysts reveals that by using time-Lapse monitoring in synergy with array CGH (Group A) yields a much higher clinical pregnancy outcome as compared to when using the conventional incubator and CGH (Group B). There were significant differences in clinical pregnancy rates between Group A and Group B (71.1% vs. 45.9%, respectively, p = 0.037). The observed implantation rate per embryo transfer significantly increased in Group A compared to Group B (66.2% vs. 42.4%, respectively, p = 0.011). Moreover, a significant increase in ongoing pregnancy rates was also observed in Group A compared to Group B (68.9% vs. 40.5%. respectively, p = 0.019). However, there was no significant difference in miscarriage rate between the time-lapse system and the conventional incubator (3.1% vs. 11.8%, respectively, p = 0.273).

[4] (Campbell, Fishel, & Laegdsmand, 2013)
[5] (Yalçınkaya, et al., 2014)
[6] (Yang, et al., 2014)
[7] (Scott & Galliano, 2016)
[8] (Chawla, Fakih, & Hellani, 2015)

Table 1. *Comparison of the clinical outcome between time time-lapse (Group A) and conventional incubator (Group B), as well as the mixed embryo transfer (Source: Yang et.al 2014)*

Parameters	Group A	Group B	Mixed	p value
Patient with SET	19	15	n/a	
Patient with DET	26	22	45	
Clinical pregnancies after SET	10	5	n/a	
Clinical pregnancies after DET	21	11	24	
Clinical pregnancy rate	71.1%	45.9%	53.3%	0.037[a]
Implantation Rate	66.2%	42.4%	47.8%	0.011[a]
Ongoing pregnancy rate	68.9%	40.5%	48.9%	0.019[a]
Pregnancy loss rate	3.1%	11.8%	8.3%	0.273[b]

[a] – Group A vs Group B, by Chi-square analysis
[b] – Group A vs Group B, by Fisher's exact test.

Conclusion

It has to be understood that PGS and time-lapse provides different answers. PGS is the tool that holds the information about the genetic composition of the sample obtained from the embryo, which will correlate whether the embryo is chromosomally normal or not. However, due to the prevalence of embryo mosaicism, PGS result may not be representative of the whole embryo. To better enhance your decision making, retrospective data from time-lapse can be used for further assessment of the embryo's development after biopsy.

If time-lapse assessment and PGS are done together, implantation and clinical pregnancy rates should improve as demonstrated by the study by Yang et al. It is also important to note that PGS is an invasive process and is relatively a costly method for embryo assessment. By using the risk model of Campbell et al. as an example, time-lapse can be used as an initial test to qualify which embryos are of at high risk for aneuploidy, which can then be sent for biopsy for confirmation. In such cases, PGS might be optional to those embryos that, according to time-lapse evaluation, may be risky for chromosomal abnormality. This approach may help reduce the total number of embryos to be biopsied and screened for aneuploidy, thereby reducing the cost of the procedure and enabling more couples to avoid this costly technique.

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