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A Sperm Function Assay Identifies Previously-Undiagnosable Male Factor in Assisted Reproductive Technology

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PURPOSE & OBJECTIVES

For fertilization to occur, ejaculated sperm must gain the functional capacity to fertilize. Previously, an assay to detect sperm function demonstrated that cycle failure at Day 5 could be predicted when functional sperm were not present for both IUI and in IVF procedures (1-3). Importantly, IVF cycle failure occurred post-fertilization of eggs by non-functional sperm, raising the possibility that ICSI might be impacted. Here, the assay was evaluated in ICSI to determine if absence of the sperm function detected via the assay would impact formation of good quality blastocysts (GQB).

MATERIAL & METHODS

This was a prospective double-blind study. A functional sperm assay (Kinetix Assay), which detects expression patterns of an Fc receptor (FcR) and other markers, was performed on semen samples used during routine ICSI procedures (n=58). Briefly, 5ul semen aliquots were analyzed at 30-min intervals to determine sperm expression patterns for FcR, among other markers. Expression patterns of FcR and other markers were analyzed. Semen samples were categorized as "functional" or "non-functional" based on expression patterns. ICSI was performed using standard protocols and the assay was not used to alter any aspect of the procedure. The fertilization rate and production of Day 5 good quality blastocysts per two pronuclei (GQB/2PN) with standard Gardner criteria ($\geq 3BB$) were evaluated. Cycle outcomes were compared to expression patterns indicating function to determine if correlations existed.

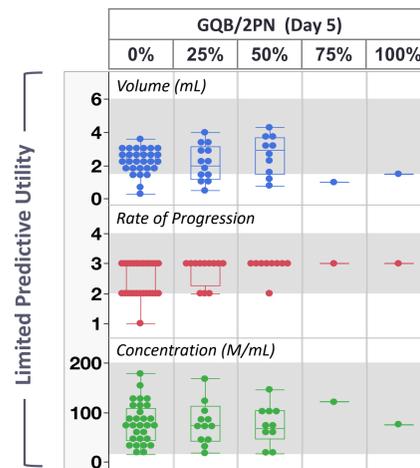
RESULTS

Non-functional sperm produced complete cycle failure--0% GQB/2PN in 14% (8/58) of all ICSI cycles evaluated. The risk difference in reproductive outcome among functional vs non-functional sperm was -0.72 (95% CI: -0.84, -0.60). The risk ratio was 0.28 (95% CI: 0.18, 0.44; p=0.0002; Fisher's exact test). Conversely, semen samples with functional sperm produced an average of 28% GQB/2PN in 86% (50/58) of the ICSI cycles studied. Non-functional specimens were indistinguishable from functional ones by standard semen analysis (WHO criteria).

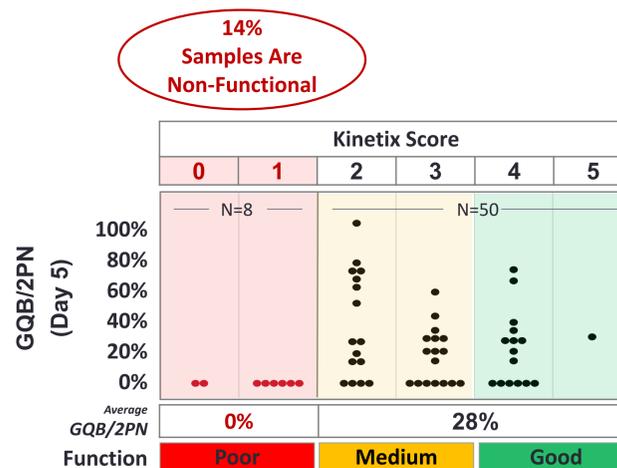
The **Kinetix Assay** measures sperm function in ejaculated specimens by detecting expression patterns of sperm markers, including an Fc Receptor correlated to fertility by other investigators. These patterns correlate to fertility outcome and enable recognition of previously-undetected sperm fertility issues causative of cycle failure.

ICSI Study Results: Patient Cohort: N = 58 couples, N = 58 ICSI cycles

Standard Semen Parameters cannot identify the dysfunction



Kinetix Assay Identifies Sperm Dysfunction responsible for 14% of ICSI cycle failures



CONCLUSIONS

In this study, ICSI procedures conducted with non-functional sperm per Kinetix assay resulted in no Day 5 GQB. While a low percentage of these cases obtained good quality blastocysts on Day 6-7, many publications indicate such blasts have significantly more aneuploidy and lower clinical pregnancy rates (4,5). Our results suggest sperm dysfunction identifiable by assay may account for some delayed development. This assay has the ability to identify ejaculates with risk of cycle failure and low-quality blast production so another specimen can be utilized, reducing stress and facilitating patient satisfaction and retention.

CASE STUDY

Kinetix Assay Results Parallel ICSI Outcomes

Two case reports illustrate the assay's ability to identify phenotypic fertility function in clinical semen samples that impact ART outcome. The presence of "normal" semen parameters and adequate female-side retrieval values are not sufficient for good blast formation when sperm function is deficient per Arex Assay.

Kinetix Assay Report Case: A		Kinetix Assay Report Case: B	
Female Patient: Age: 37	Male Patient: Age: 37	Female Patient: Age: 40	Male Patient: Age: 36
7 Oocytes	Sample Vol. (mL): 2.3	11 Oocytes	Sample Vol. (mL): 2.3
7 Eggs Injected	Rate of Progression (1-4): 2	11 Eggs Injected	Rate of Progression (1-4): 3
6 Eggs Fert. Norm	Conc. (M/mL): 39	7 Eggs Fert. Norm	Conc. (M/mL): 17
2 Total Blasts	GQB/2PN 0%	5 Total Blasts	GQB/2PN 67%
0 Good Blasts		4 Good Blasts	

Kinetix Score	EJACULATE FUNCTION IS:	Assay Result:	Indication:
0 (Poor Function)	POOR	Sample exhibits non-cycling function.	Complete cycle failure is expected.
3 (Medium Function)	GOOD	Sample exhibits robust sperm function.	Good quality blastocysts expected within fertility injection window.

Summary

- Standard semen analysis fails to identify ~14% of non-functional sperm samples that will cause cycle failure in ICSI, IVF and IUI.
- Cycle failure can be predicted and prevented by the Kinetix Assay.
- The assay provides additional guidance for patients with multiple cycle failures.

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