

# Oocytes from women of advanced reproductive age do not appear to have an increased risk of zona pellucida hardening

J.H. Check, D.S. Chase, D. Horwath, W. Yuan, M.C. Garberi-Levito, M. Press

Cooper Medical School of Rowan University, Department of Obstetrics and Gynecology  
Division of Reproductive Endocrinology & Infertility, Camden, NJ (USA)

## Summary

**Purpose:** To test the hypothesis that very advanced reproductive age leads to an increased risk of zona pellucida hardening by comparing fertilization rates and rates of failed fertilization with conventional oocyte insemination vs intracytoplasmic sperm injection (ICSI). **Methods:** Women aged  $\geq 45$  were given the option of ICSI vs conventional oocyte insemination in circumstances where there was no male factor present. They were advised of the theoretical benefit of ICSI overcoming zona hardening but also advised that ICSI might lower pregnancy rates and is more costly. **Results:** There were 364 cycles evaluated and 74% chose ICSI. The failed fertilization rates were similar – 28.4% (66/232) for ICSI vs 26.5% (35/132) for conventional insemination. The fertilization rates were similar 56.0% with ICSI vs 50.9% with conventional oocyte insemination. **Conclusion:** Based on similar fertilization and failed fertilization rates in women aged  $\geq 45$  undergoing IVF-ET, zona hardening does not appear to be a consequence of reproductive aging.

**Key words:** Reproductive aging; Zona pellucida hardening; Intracytoplasmic sperm injection; In vitro fertilization-embryo transfer; Pregnancy rates.

## Introduction

Some researchers suggest that oocytes obtained from women of very advanced reproductive age may also have increased zona pellucida hardening. Intracytoplasmic sperm injection (ICSI) may overcome zona hardening in these patients. The objective of this study was to determine if the oocytes obtained from women of advanced reproductive age ( $\geq$  age 45) have a tendency toward zona hardening. The assumption was made that if zona hardening was present, the use of ICSI would increase the fertilization rate and decrease the frequency of failed fertilization when compared with conventional insemination.

## Materials and Methods

Women aged  $\geq 45$  undergoing in vitro fertilization (IVF-ET) with husbands with normal semen parameters ( $\geq 8 \times 10^6$  million motile sperm per ml, morphology by strict criteria  $\geq 4\%$  normal, absence of antisperm antibodies, hypoosmotic swelling test  $\geq 50\%$ ) were given the option of inseminating their oocytes conventionally or by ICSI. They were advised of the possible benefit of ICSI for zona pellucida hardening, though there was little proof. Furthermore, they were advised that there are some data suggesting higher pregnancy rates with conventional oocyte insemination, which is a much less costly option [1-4].

## Results

The fertilization rates of those women having IVF cycles with no fertilization and poor fertilization were

compared according to method of fertilization. The results are shown in Table 1.

There were no significant differences between fertilization rates whether conventional insemination or ICSI was performed (chi-square). Similarly, choosing conventional oocyte insemination did not lead to higher rates of failed fertilization.

## Discussion

The data clearly show that there is no evidence to support the concept of zona pellucida hardening with advanced reproductive age. A comparison of fertilization rates following conventional oocyte insemination vs ICSI in women  $\geq$  age 45 were similar, as was the rate of completely failed fertilization.

One would argue as to how one can be sure that ICSI can overcome zona hardening. The evidence for this is provided by the marked improvement of fertilization rates of cryopreserved oocytes (which are well known to have zona hardening) by ICSI [5].

## References

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Table 1. — Fertilization rates of women 45 and older using their own eggs according to method of fertilization.

	Total eggs		1 egg retrieved		2 or more eggs retrieved	
	ICSI	Conventional	ICSI	Conventional	ICSI	Conventional
# cycles	232	132	117	63	115	69
# eggs retrieved	727	414	117	63	610	351
# metaphase II retrieved	586	399	117	63	469	308
# inseminated	586	399	117	63	469	336
# fertilized	328	203	65	39	263	164
% fertilized (zero excluded)	56.0	50.9	55.6	61.9	56.1	48.8
# cycles w/0% fert.	66	35	52	24	14	11
% cycles w/0% fert.	28.4	26.5	44.4	38.1	12.2	15.9

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Address reprint requests to:  
 J.H. CHECK, M.D., Ph.D.  
 7447 Old York Road  
 Melrose Park, PA 19027 (USA)  
 e-mail: laurie@ccivf.com