

Commentary





Commentary: physiological intracytoplasmic sperm injection (PICSI), an alternative to the standard ICSI procedure

Abstract

The rationale of this study is to uncover sperm selection by hyaluronic acid (HA) binding which could advance fertilization pace and embryo quality in Intracytoplasmic sperm injection (ICSI) cycles. HA a sperm binding nonsulfated glycosaminoglycan required as a part of normal fertilisation. Physiological Intracytoplasmic Sperm Injection employs sperm binding to Hyaluronic acid to opt for which sperm to use for Intracytoplasmic sperm injection. PICSI and their latent benefit are still in tranquil being explored. We expect more detailed facts in the coming few years in relation to for whom these modus operandi are most useful apart from cases discussed. Usually if the sperm binding is less than 65% the PICSI dish is used to select the sperm. The medley of sperm selection for ICSI is essential and directly authorise the male input to the embryo therefore visual evaluation alone should certainly not be the only aspect involved when selecting a sperm for ICSI failed cycle twice. But unfit sperm with DNA fragmentation and compromised maturity is able to appear normal and healthy, but if selected for injection/insemination can go ahead to deprived embryo quality and likely a pregnancy loss.

Keywords: picsi, hyaluronic acid, conceiving rate, DNA fragmentation

Volume I Issue 2 - 2015

Aamir Javed, Farnaz Mozafari, Ashwini LS, Debashree Ganguly³

¹Centre for R&D In Life Sciences Research Laboratory, Bangalore, India ²Rama's Test Tube Baby Center, Bangalore, India ³Jahar Infertility Research Institute, Kolkata, India

Correspondence: Aamir Javed, Embryologist And Biotechnologist, Centre For R&D In Life Sciences Research Laboratory, Bangalore, India, Tel +919916389255, +918042046206, Email aamir.javed0077@gmail.com

Received: August 3, 2015 | Published: September 9, 2015

Abbreviations: HA, hyaluronic acid; IVF, *in vitro* fertilization; RIF, recurrent implantation failure; ICSI, intracytoplasmic sperm injection

Introduction

There are various techniques and procedure that have rapidly been emerged over 3 decades in the field of assisted reproduction but the success rate remains alike.^{1,2} About a 20percent of patients are diagnosed infertile without specific causes.3 In totting up, petite ratios of couples not succeed to conceive despite multiple in vitro fertilization (IVF) or ICSI Intracytoplasmic sperm injection procedures. The reasons of recurrent implantation failure (RIF) are not mirrored yet. One of the apprehensive aetiologies of RIF is low implantation impending potential of embryo and this could be because of a bungling incompetent spermatozoa.4 Quite a few sperm assortment methods were established to advance the quality of embryo.^{5,6} Farhi et al.⁷ Yagci A et al.⁸ Morrell JM.⁹ stated that young juvenile patients with compound IVF crashes and failures illustrated relatively elevated incidences of male factor infertility exemplified by low fertilization rate with Intracytoplasmic sperm injection (ICSI). Amid the novel sperm selection techniques, ICSI using hyaluronic acid (HA) combining IVF media has been recommended to have advanced precise and reduces biological risk than other selection methods.¹⁰ Not present in the progression of in vitro sperm selection is the in vivo selection of the efficient most capable, proficient and competent sperm afforded by the zona pellucida, corona cells and cumulus cells surrounding and adjoining the oocyte. In the female reproductive tract, hyaluronan employ a vital role in the selection of functionally competent sperm during in vivo fertilization. The in vitro selection of sperm for ICSI is decisive and optical judgment unaided may consent to the isolation and selection of sperm carrying diverse altitudes of pathogenesis and deformities. The improved intensity of advance maturity and genetic integrity associated with hyaluronan binded (HB) sperm advocate that the application of HB sperm in ICSI may provide to perk up the paternal input to the embryo and thus clinical outcomes. The current commentary therefore sought to highlight the use of HB sperm to those sperm opted via conventional and optical means in the treatment of patients.

Mechanism of sperm binding

Hyaluronan is a naturally occurring biopolymer (polysaccharide) found in all human cells and is a foremost constituent of the *cumulus oophorus* layer that enfolds the human oocyte. The head of a mature sperm holds a hyaluronan-specific ligand receptor that facilitates mature sperm to unite to hyaluronan. Comparatively, immature sperm do not unite. Competent, mature, biochemically active sperm unite to the hyaluronan where they can be selected by the embryologist and used for ICSI procedure. This modus operandi mimics a focal step in the innate fertilization course of action, the binding of mature sperm to the oocyte complex. As a consequence, the opted spermatozoa are indispensable alike as one that would be successful and doing well in the natural reproductive progression. Nevertheless, this advancement does not imitate the genomic integrity of the spermatozoa and its aptitude to deliver the best paternal contribution to the zygote.

Why PICSI is important?

The modus operandi of fertilisation is intended to rule out incompetent sperm and select the best sperm with the ideal genetic composition to the oocyte and fertilises it. The mature sperm cells are more competent to bind to hyaluronic acid, implication that it is enhanced and ensemble to fertilising the oocyte. ¹¹ PICSI toils on the root that the better sperm are in this reverence, the better they are in all high opinions, including motility their ability to penetrate and inserts to an oocyte.





A sperm's ability to bind to HA draw a parallel to:

- a. Normal head morphology better fertilizing potential¹²
- b. Reduced amount of DNA fragmentation
- c. Reduced chromosomal Aneuploidy
- d. Amplified chromatin integrity
- e. Principle Cellular maturity

PICSI recommendation in cases which:

Sperm defect is inferred, sperm immaturity, chromosomal anomaly, an elevated number of sperm with defected integrity of DNA.¹²

- i. Deprived embryo quality has been found on Day 2 to 5 (Blastocyst conversion rate).
- ii. Border line sperm count with low fertilisation with ICSI.
- Repeated embryo transfers without implantation have occurred.
- Repeated miscarriages and early pregnancy loss have occurred.
- v. Reduced sperm morphology and motility.
- vi. The woman is over 38 years old.
- vii. Low quality cryopreserved sperm.
- viii. Sperm sample aspirated by PESA.

NOTE: Patient undergoing TESA procedure where sperms are immotile limits to use PICSI and patients with occasional spermia where sperm counts limits to ≤ 1 million/ml.

What are the advantages to PICSI?

Basically PICSI is a more filtered way of selecting the best competent sperm for fertilisation process. Despite the fact that conventionally sperm are selected for ICSI based on their morphology and motility quotient, PICSI consents to for this choice to be complete based on the sperm's capability to fertilise and perform the role job. Additionally the PICSI dishes are fairly easy to use. The technique of selecting sperm based on their facade and appearance is also flawed because chromosomal imperfections can still be found within healthy glance sperm.

What are the disadvantages to PICSI?

At present there are no specific drawbacks to PICSI be fully instituted. Except in TESA sample where sperms are immotile PICSI cannot be employed and patients with occasional spermia where sperm counts limits to $\leq 1 \, \text{million/ml}$.

Discussion and conclusion

Consent to our anticipation, selection of HA-bound sperms has advantages in terms of fertilization and following embryo cleavage in ICSI cycles.¹³ Preceding researches have shown consistent descriptions concerning the effect of HA-binding selection method on IVF/ICSI upshots. Majority of studies using HA-containing medium in ICSI/IVF cycles highlights similar or advanced fertilization and cleavage rate.^{14,15} Castillo-Baso et al.¹⁶ Studies takes an account of patients with abnormal sperm parameters, it is hypothesized that the sperm selection using HA-binding might be advantageous.¹⁶ Have stated that zygotes formed with HA-bound spermatozoa illustrated

better quality only when sperm morphology ≤4%; the benefit was not sustained when the morphology was $\geq 4\%$. This finding advocates that HA-binding technique would be beneficial and helpful only in male factor infertility. In natural process of fertilization hyaluronic acid (HA), is engaged in the mechanism of sperm selection medley because only mature competent spermatozoa which have their specific and exact receptors to bind to HA are able to arrive at the oocyte and fertilize it. As a physiological selector HA bounded sperm in in-vitro have revealed that their plasma membrane modelling and cytoplasmic and nuclear maturity is ideal.^{17,18} Moreover, HA-bound spermatozoa have a improved morphology^{19,20} and claims to trim down risk of being aneuploid²¹ DNA fragmentation. As because of this, selection of spermatozoa by HA prior to ICSI helps to optimize the outcome of the treatment and also have a number of erstwhile benefits. In practical HA-bound spermatozoa can be easily recovered using an injecting Pipette²² and having no appalling effects on post injection to embryos and because of its natural origin it can be metabolized by the oocytes.^{23,24} Moreover, HA-ICSI may speed up the time-consuming IMSI. On the other hand, PICSI HA-bound spermatozoa can be easily distinguished even by non-trained embryologists. At very least, HA clears a more natural substitute for handling spermatozoa prior to ICSI than the synthetic plastic polyvinylpyrrolidone (PVP), which is routinely used to diminish sperm motility during ICSI modus operandi in the majority of assisted reproduction centres and has been hypothesized to have lethal effects on oocytes.25 The largest study published to date as full article (428 patients) evaluated physiologic HA-ICSI to conventional PVP-ICSI disclosed that injection of HAbound spermatozoa concludes a statistically significant improvement in embryo quality and implantation. A positive drift in fertilization and pregnancy rates when injecting HA-bound spermatozoa has been reported.²⁶ Nasr et al.¹⁰ have also published a study reporting a higher fertilization rate when injecting oocytes with HA selected spermatozoa. It has been demonstrated that the injection of HA-bound spermatozoa improves embryo quality and development by favouring selection of spermatozoa with normal nucleus and intact DNA in fact; top-quality embryo rate is higher in HA-ICSI than in conventional PVP-ICSI and embryo development rate has also been found to be significantly increased.²⁷ HA should be considered the first choice for "physiologic" sperm selection prior to ICSI because of its capacity to reduce genetic complications and for its total lack of toxicity.

Acknowledgements

None.

Conflict of interest

Author declares that there is no conflict of interest.

References

- Worrilow KC, Huynh HT, Bower J, et al. The clinical impact associated with the use of PICSI-derived embryos. *Fertil Steril*. 2006;86(Suppl 3):S62.
- Wright VC, Chang J, Jeng G, et al. Assisted reproductive technology surveillance--United States, 2005. MMWR Surveill Summ. 2008;57(5):1–23.
- Kovacs P, Kovats T, Sajgo A, et al. The role of hyaluronic acid binding assay in choosing the fertilization method for patients undergoing IVF for unexplained infertility. J Assist Reprod Genet. 2010;28(1):49–54.
- Sharif KW, Ghunaim S. Management of 273 cases of recurrent implantation failure: results of a combined evidence-based protocol. *Reprod Biomed Online*. 2010;21(3):373–380.

- Nijs M, Creemers E, Cox A, et al. Relationship between hyaluronic acid binding assay and outcome in art: a pilot study. *Andrologia*. 2010;42(5):291–296.
- Ola B, Li TC. Implantation failure following in-vitro fertilization. Curr Opin Obstet Gynecol. 2006;18(4):440–445.
- Farhi J, Ben-Haroush A, Dresler H, et al. Male factor infertility, low fertilisation rate following ICSI and low number of high-quality embryos are associated with high order recurrent implantation failure in young IVF patients. Acta Obstet Gynecol Scand. 2008;87(1):76–80.
- Yagci A, Murk W, Stronk J, et al. Spermatozoa bound to solid state hyaluronic acid show chromatin structure with high DNA chain integrity: An acridine orange fluorescence study. *J Androl*. 2010;31(6):566–572.
- Morrell JM, Rodriguez-Martinez H. Practical applications of sperm selection techniques as a tool for improving reproductive efficiency. Vet Med Int. 2010;2011:894767.
- Nasr-Esfahani MH, Razavi S, Vahdati AA, et al. Evaluation of sperm selection procedure based on hyaluronic acid binding ability on ICSI outcome. J Assist Reprod Genet. 2008;25(5):197–203.
- Worrilow KC, Eid S, Woodhouse D, et al. Use of hyaluronan in the selection of sperm for intracytoplasmic sperm injection (ICSI): significant improvement in clinical outcomes-multicenter, double blinded and randomized trial. *Hum Reprod.* 2012;28(2):306–314.
- Ebner T, Filicori M, Tews G, et al. A plea for a more physiological ICSI. *Andrologia*. 2012;44(1):2–19.
- Parmegiani L, Cognigni GE, Bernardi S, et al. Physiologic ICSI: hyaluronic acid (HA) favors selection of spermatozoa without DNA fragmentation and with normal nucleus, resulting in improvement of embryo quality. Fertil Steril. 2010;93(2):598–604.
- Menezo Y, Junca AM, Dumont M, et al. Physiologic (hyaluronic acidcarried) ICSI results in the same embryo quality and pregnancy rates as with the use of potentially toxic polyvinylpyrrolidone (PVP). Fertil Steril. 2010;94(4):S232.
- Van Den Bergh MJ, Fahy-Deshe M, Hohl MK. Pronuclear zygote score following intracytoplasmic injection of hyaluronan-bound spermatozoa: a prospective randomized study. *Reprod Biomed Online*. 2009;19(6):796–801.
- Castillo-Baso J, Garcia-Villafaña G, Santos-Haliscak R, et al. Embryo quality and reproductive outcomes of spermatozoa selected by physiologic-icsi or conventional icsi in patients with kruger <4% and >4% normo-morphology. Fertil Steril. 2011;96(3):S159.

- Cayli S, Jakab A, Ovari L, et al. Biochemical markers of sperm function: male fertility and sperm selection for ICSI. *Reprod Biomed Online*. 2003;7(4):462–468.
- Huszar G, Ozenci CC, Cayli S, et al. Hyaluronic acid binding by human sperm indicates cellular maturity, viability, and unreacted acrosomal status. Fertil Steril. 2003;79(Suppl 3):1616–1624.
- Prinosilova P, Kruger T, Sati L, et al. Selectivity of hyaluronic acid binding for spermatozoa with normal Tygerberg strict morphology. *Reprod Biomed Online*. 2009;18(2):177–183.
- Parmegiani L, Cognigni GE, Bernardi S, et al. Physiologic ICSI: hyaluronic acid (HA) favors selection of spermatozoa without DNA fragmentation and with normal nucleus, resulting in improvement of embryo quality. Fertil Steril. 2010;93(2):598–604.
- Jakab A, Sakkas D, Delpiano E, et al. Intracytoplasmic sperm injection: a novel selection method for sperm with normal frequency of chromosomal aneuploidies. *Fertil Steril*. 2005;84(6):1665–1673.
- Balaban B, Lundin K, Morrell JM, et al. An alternative to PVP for slowing sperm prior to ICSI. Hum Reprod. 2003;18(9):1887–1889.
- Barak Y, Menezo Y, Veiga A, et al. A physiological replacement for polyvinylpyrrolidone (PVP) in assisted reproductive technology. *Hum Fert (Camb)*. 2001;4(2):99–103.
- 24. Aamir Javed, Ashwini LS. Oocyte Degeneration Subsequent Intracytoplasmic Sperm Injection (ICSI). *Medical Science*. 2014;13(49):9–15.
- Jean M, Barriere P, Mirallie S. Intracytoplasmic sperm injection without polyvinylpyrrolidone: an essential precaution? *Hum Reprod*. 1996;11(10):2332.
- Ergur AR, Dokras A, Giraldo JL, et al. Sperm maturity and treatment choice of in vitro fertilization (IVF) or intracytoplasmic sperm injection: diminished sperm HspA2 chaperone levels predict IVF failure. Fertil Steril. 2002;77(5):910–918.
- 27. Huszar G. Sperm testing and ICSI selection by hyaluronic acid binding: the hyaluronic acid-coated glass slide and petri dish in the andrology and IVF laboratories. In: Nagy ZP, Varghese AC, Agarwal A, editors. Practical Manual of In Vitro Fertilization: Advanced Methods and Novel Devices. New York, USA; 2012. p. 241–257.