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An Update of Sperm Preparation : A Review of Supplementation Substances to Improve Sperm Quality

SILVIA W. LESTARI[1,4], SARAH H. LESTARI[2] and RIA MARGIANA[3,4]

[1]Department of Medical Biology, Faculty of Medicine Universitas Indonesia.
[2]Master Program in Biomedical Sciences, Faculty of Medicine Universitas Indonesia.
[3]Department of Anatomy, Faculty of Medicine Universitas Indonesia.
[4]The Indonesian Reproductive Medicine Research and Training Center (INA-REPROMED).
*Corresponding author E-mail: finallysilvia@gmail.com

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ABSTRACT

One etiology of the unsuccesful intra uterine insemination (IUI) is sperm preparation. There are some limitations of sperm preparation utilization which may decrease fertilization rates leading to IUI failure. Nevertheless, there are some substances which suggested could improve the outcome of sperm preparation. This review aimed to summarize the substances that could improve the sperm quality, thus increasing success rate of IUI, as an update of sperm preparation. Several researches which have developed agreed that the supplementation of antioxidant, hormone and drugs could improve the quality of sperm. The addition of dithiothreitol and superoxide dismutase during centrifugation could prevent some harmful effects such as membrane plasma disruption caused by lipid peroxidation process. The supplementation of myoinositol before and after capacitation increased total and progressive motile sperm significantly. Astaxanthin decreased the generation of ROS in sperm. Furthermore, LH could increased intracellular Ca^{2+} as a second messenger of signal transduction pathways during sperm capacitation, whereas prolactine prolonged human sperm motility and prevent caspase activation. In addition, the supplementation of pentoxifylline could enhance the motility of post-thaw sperm and its longevity in vitro.

Keywords: Sperm preparation, Substances supplementation, Sperm quality.

INTRODUCTION

It is have known that the success rate of Intrauterine Insemination (IUI) remains low, ranging about 10 to 20%.[1] Sperm preparation should be standardized in order to achieve an enormous success rate of a program. In sperm preparation, there are two methods that frequently performe, namely Swim-up (SU) and Density-gradient Centrifugation (DGC).[2] Nevertheless, there are some controversies related to the deterioration of the SU and the DGC methods such as non-optimal progressive motile sperm which may decrease of fertilization rates leading to IUI failure. Recent studies demonstrated one of which from both of sperm preparation methods could select for better sperm quality by evaluate sperm morphology and chromatin condensation after sperm preparation.[3-5]

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The most important part of the semen is the sperm, and the quality of semen involves either quantity or quality of sperm. Mostly, the decreased sperm quality play role more in causing male infertility, compared to sperm quantity. There were many researches accomplished in order to increase the success rate of IUI through sperm preparation manipulation. This review aimed to summarize the substances that could increase the sperm quality in sperm preparation as an update to increase the success rate of IUI. These researches provided several substances such as antioxidant, hormones and drugs that could increase the sperm quality in sperm preparation could increase the sperm motility as demonstrated in table 1. (Table 1)[6, 7]

Substances Supplementation of Sperm Preparation in Improving Sperm Quality

Antioxidant Supplementation

During sperm preparation, sperm undergo a complex series of centrifugation affecting deleterious effects on sperm movement parameters, motility and acrosome reaction. The side effect induced by centrifugation could be prevented by addition of antioxidants prior to sperm preparation. DTT and SOD supplementation as potent antioxidant in the preparation medium improved both the level of hyperactivated sperm and velocity of the sperm significantly and maintained levels of induced acrosome reaction.[7, 8] Dithiothreitol (DTT) could prevent membrane plasma disruption caused by lipid peroxidation process which generated from reactive oxygen species (ROS).[7] In addition, DTT as an of potent antioxidant could induce chromatin destabilization and sperm nuclear stability.

The total and progressivity of sperm motility was increased significant after the addition of myoinositol before and after capacitation. Previously research in agreement observed that myoinositol have antioxidant properties and present in huge concentrations particularly in seminal liquid.[9] Myoinositol, sugar like molecule, could increase cytosolic Ca^{2+} and inner mitochondrial Ca^{2+} thus enhance sperm motility and increase the number of spermatozoa with high inner mitochondrial membrane potential (MMP). The molecular mechanism of myoinositol is suggested by having a role in the chemiotaxis and human sperm thermotaxis through phospholipase C activation, leading to the origination of inositol triphosphate and calcium channels initiating.[9]

Several researches developed in agreement said that myoinositol increase the number of spermatozoa with progressive motility in vary of semen analyses result.[9, 10] Palmier *et al*.,[11] studied in vitro myoinositol effect on sperm quality, findings showed that the reducing motility caused by the freezing-thawing process was diminishing the sperm quality and fertilization rate. By the treatment of myoinositol to the thawed samples were proved more efficacious and showed a significant difference in improvement of sperm progressive motility. Furthermore, the findings shown that myoinositol had not toxicity effect and proved to be well tolerated if added to the medium.[10-12]

Astaxanthin is recognized not only for having anti-cancer, anti-diabetic and anti-inflammatory properties but also antioxidant activity that could improve sperm quality. Astaxanthin acts by inhibiting intracellular radical generation thus induce low ROS production by improving tyrosine phosphorylation of sperm head and acrosome-reacted cells values. Findings showed that astaxanthin incubation during sperm preparation could generate the enormous number of spermatozoa undergo capacitation-like membrane which allow the phosphorylation of tyrosine on sperm head.[13]

Hormone Supplementation

Luteinizing hormone (LH), a heterodimeric glycoprotein, secreted by the anterior pituitary has a crucial role in inducing ovulation. It is suggested that spermatozoa undergo capacitation through female reproductive tract may be exposed to LH promoting protein kinase A (PKA) activity in this cell. The molecular mechanism of LH in regulating sperm function one of which is by increasing the concentration of Ca^{2+}. Ca^{2+} is a second messenger that has a role in sperm signal transduction pathways including changes in sperm capacitation such as sperm motility and acrosomal reaction. LH binds to LH/hCG receptors located in sperm thus stimulate G-protein (Gs) and Gq proteins in activating adenylate cyclase thus leading to activation cascade of signal transduction which regulating sperm capacitation.[14]

Table 1: Substances and the role in increasing sperm quality

Agent	Examples	Mechanism of action	Role	Advantage or disadvantage	Reference
Antioxidant	Dithiothreitol (DTT) and Superoxide dismutase (SOD)	Induce chromatin destabilization and sperm nuclear stability.	Improved the rates of hyper activation and the acrosomal reaction of sperm motility.	Prevent membrane plasma disruption caused by lipid peroxidation process by ROS during sperm preparation	Griveau et al., 1994 [7]
	Myoinositol	Increasing cytosolic Ca^{2+} and inner mitochondrial Ca^{2+}	Enhances sperm motility and increases the percentage of spermatozoa with high inner mitochondrial membrane potential (MMP)	*Fertilization rate and embryo quality rate could be different according to MMP of spermatozoa •Myoinositol incubation enhance the percentage of spermatozoa with high MMP in OAT, but not in normozoospermic men •Further studies are required to clarify if the specific effect on sperm fertilization ability is indeed dose-dependent	Rubino et al., 2015 [12]
	Astaxanthin	Inhibit intracellular radical generation by improving sperm head Tyr-phosphorylation and acrosome-reacted cells values without affecting the ROS generation	Induces low ROS production and low percentages of acrosome-reacted cells	Astaxanthin incubation enhance the high number of spermatozoa undergo capacitation-like membrane alteration which allow Tyr-P of the head	Donà et al., 2013 [13]
Hormone	LH	•Stimulating calcium influx •Promoting protein tyrosine phosphorylation	Modulating sperm function variables related to capacitation	Activate specific pathways in sperm by stimulating calcium influx, protein tyrosine phosphorylation and changes in motility but had no effect on sperm AR	López-Tores et al., 2017 [14]
	Prolactin	•Stimulation of Akt phosphorylation	Prolonged human sperm motility and prevent	•Prolactin is a pro-survival factor for human sperm	Pujianto et al., 2010 [15]

Drug	Pentoxifylline	•Inhibit phosphatidylinositol -3-OH kinase •Inhibits cyclic adenosine monophosphate (cAMP) phosphodiesterase •Increasing intracellular cAMP concentration and tyrosine-phosphorylation	caspase activation •Enhance post thaw sperm fertilizing ability by decreasing acrosome loss during the freeze-thaw process and increases the post-thaw agonist -induced acrosome reaction rate •Improve sperm movement without any harmful effects on sperm DNA integrity	•Prevents the human sperm from intrinsic apoptotic pathway Pentoxifylline may be utilized as a supplement to the cryomedia but in higher concentrations may be detrimental to membrane integrity	Esteves et al., 2007 [16]; Ghasemzadeh et al, 2016 [17]

Prolactin receptor (PRLR) is identified in human sperm and located in the neck, midpiece, and principal piece of the sperm.[15] Thereby it is suggested that there was an essential function of prolactin hormone on human sperm. Findings said that prolactin is a pro-survival factor for human sperm that act through stimulation of Akt phosphorylation, and inhibit phosphatidylinositol-3-OH kinase. Prolactin avoids the human sperm from apoptosis through intrinsic pathway related to cell senescence.[15]

Drug Supplementation

Pentoxifylline is a phosphodiesterase inhibitor which could be utilized to encourage motility and fertilizing capacity of sperm.[16] Pentoxifylline performances by preventing the production of cyclic adenosine monophosphate (cAMP) phosphodiesterase, intensifying intracellular cAMP concentration and tyrosine-phosphorylation. Previously research showed that after 1-hour incubation with pentoxifylline improved the total motility of sperm after the freeze-thaw process. Pentoxifylline could improve post thaw sperm fertilizing ability by reducing acrosome loss during the freeze-thaw process and rises the post-thaw agonist-induced acrosome reaction rate. In addition, Pentoxifylline could improve sperm movement without any harmful effects on sperm DNA integrity.[16-18] The author assessed that pentoxifylline may be utilized as a supplement to the cryomedia but in higher concentrations may be detrimental to membrane integrity.

CONCLUSION

The findings in unison performed that the supplementation substances such as antioxidants, hormones, and drugs as explained above could be used in sperm preparation in order to increase sperm qualities. The mechanism of these substances in increasing sperm qualities were vary such as the lipid peroxidation that generated by ROS, regulating Ca^{2+} as a second messenger in sperm capacitation, and also maintaining the cAMP level in sperm motility. In conclusion, these supplementation substances could be use to increase the sperm quality which leading to the improvement of IUI success rate.

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