



Impact of Seminal components on seminal quality

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Abstract

Infertility is frequently a silent struggle for couples. Factors of both female and male are equally accountable, thus it has become a global concern. Male infertility is mainly due to the suboptimal quality and quantity of sperm. Seminal components play an important role in understanding male infertility. Plasma components of seminal “(SP)” play a vital role in metabolism of sperm, along with function of sperm, their survival, and transportation in the reproductive tract of female. “(SP)” is known to contain broad variety of macro- and microelements. The human seminal fluid is rich in elements like calcium, zinc, magnesium, iron, and other trace elements. With these attributes, a thorough examination of SP may serve as a good predictive marker to evaluate male fertility and reproductive disorders in addition to the physical characteristics of semen. This review paper focuses on the properties of biochemical with current understanding of human seminal plasma along with their relevance to ascertain male fertility.

Keywords: Infertility, seminal plasma, sperm function, biomarker

1. Introduction

In accordance with WHO, infertility refers to a disease related with pregnancy that affect the system of reproduction even after one year of unprotected sexual relation (1). It can be due to the male factor, the female factor, or a combination of both. Male infertility is becoming a growing global issue, with male sperm quality declining across the African, European, North American, and Asian continents. Male infertility is caused by deteriorating sperm quality and quantity (2). Understanding of additional cause of infertility among male is critical for better diagnosis and treatment of childless couples. Components of seminal plasma of human include the secretions from the epididymis, testis, and glands of male accessory such as prostate, seminal vesicles, and Cowper’s gland. SP acts as a carrier, protector, and nourishment medium for spermatozoa after ejaculation, as well as a functional

modulator of spermatozoa. Spermatozoids are dip into fluid proteins of constantly changing medium and chemicals. Plasma of seminal issues a safe environment for the spermatozoa that serves as a channel for ejaculated spermatozoa to reach the genital tract for female. Buffering abilities provides protection for the spermatozoa from the vaginal acidic environment (3).

Various ranges of microelements along with macro elements are found in mammalian seminal plasma and spermatozoa. Viability characteristics of spermatozoa is an effect of physiologically active components of inorganic has been explored both in animals and humans (4). Manufacture of ions of “*sp*” involve (*Zn+*, *Ca++*, *Cl₂+*, *Na+*, and *K+*), substrates of energy such as glycerylphosphocholine, fructose, and sorbitol, components that are organic such as peptides, amino acids, along with proteins of lower molecular weight and higher molecular-weight, cytokines, lipids, hormones and many more. Compounds that contain nitrogenous element such as urea, ammonia, creatinine, uric acid, and some are reducing substances including hypotaurine and also found in SP (5). Different organs such as tract of male reproduction refers to the components of “SP” has been controlled by the storage capacity, size along with the output of secretion in different organs of male reproduction system (6). This review attempts to summarize current knowledge about the roles of SP components in sperm quality and male fertility. We intend to evaluate the functions of the SP components, as well as their utility as diagnostic biomarkers and potential additives to male fertility and sperm quality. Present review briefs on some of these seminal plasma components that play important roles in male fertility and can be used in the future for better identification, assessment, along with infertile male’s treatment.

2. Role of ZINC in seminal plasma

In order to control the physiological functions related to the body, reproductive systems along with synthesis of DNA Zinc is essential. Zinc is also need to control the cell division, enhance immune systems, healing of wound along with the expression of gene and the repair of cell. It has a vital role in the spermatogenesis in prostate, development of testicles normally, motility of sperm, vitality, synthesis of nucleic acid, along with stabilization of the membrane of sperm (7). Zinc regulates the function that is related with spermatozoa represents as a marker of the function of prostate, performs as a cofactor for various reactions of enzyme, along with assisting the preservation of motility in sperm (8). Zinc supplements are observed to increase the volume, motility of the spermandmaintain the appropriate morphology of sperm men with infertility. The quality of sperm among the men with infertility was notably increased after the supplementation of zinc (9). Zinc has a positive effect on spermatogenesis, capacitation, and the acrosome reaction during fertilization. It helps by modulating spermatogonial proliferation and differentiation. Testes have been protected by it from injury caused by toxic metals, higher temperatures, and fluoride. Deficiency of zinc plays an important threat for both poor quality and quantity of sperm in male infertility. Signs of prostatic inflammation were observed in men with less Zn content in chromatin. Lower zinc concentration was observed in the majority of the abnormal ejaculates like asthenozoospermia, and it can also negatively influence sperm motility, vitality, sperm membrane stabilization, nucleic acid synthesis, and protein metabolism. Though it does not show any direct correlation with fertilisation rates, it does affect pregnancy rates. Zhao *et al.*, discovered that content of zinc in men with infertility was notably in the lesser side in

compare to the men with fertility (9). Shortage of zinc in the testes is related with inappropriate minor sexual characteristics along with hypogonadism, and other reproductive matters (10). Higher zinc levels in seminal has deleterious impact on spermatozoa on acrosome response in males with normozoospermic (11).

According to the literature, there is a brief correlation between zinc and pregnancy, emphasizing the importance of assessing zinc in infertile males.

3. Role of calcium in SP

Calcium plays an important role in regulating various physiological activities, including sperm function. Inside some mammalian spermatozoa, the acrosome reaction is triggered by the calcium ion (Ca^{2+}). Ca^{2+} is well-known for the importance in motility in sperm cell also known as the second messenger universally helps in capacitation, reaction in acrosome, hyperactivation, chemotaxis, along with the processes of fertilization (12). Impairment of Ca^{2+} signalling in sperm is associated with male infertility (13). The estimation of calcium content in sperm might be of great importance because to its association with sperm motility, metabolism, the acrosome response, and fertilization (14). Sperm motility is correlated with changes in intracellular calcium ion concentration. The kinetics of changes in free calcium ion concentration in human spermatozoa are complex and crucial to sperm function. High seminal calcium can impact sperm functions and cause oxidative damage. High calcium levels may result in reduced testicular weight. Prien et al., observed that the serum of men with hypo motility had a significantly lower calcium level than that of men with normal motility (15). High calcium levels and male fertility are positively correlated, according to several research. (16). Another study discovered a significant decrease in the mean concentration of Ca in seminal plasma among the infertile men with of normozoospermic contrasted to men with fertility (17). Other studies have observed that reduced seminal Ca concentrations and intracellular Ca in sperm are correlated positively with reduced sperm motility in the epididymis of humans (18). Nishida *et al.*'s study showed enhancement of ability for fertilizing human sperm in a medium of low-calcium by applying preincubation. Moreover, a reduction level of plasma Ca in seminal indicates men infertility by these data.

Calcium causes an acrosome reaction in mammalian sperms. It plays a major role in motility. The outcome of male fertility was shown to be closely related to the sperm's calcium function level

4. Role of fructose in SP

Semen is unique among body fluids for its higher concentration of the monosaccharide fructose (average, 15 mM; normal range, 5 to 30 mM). Fructose is essential for the motility, viability, and functioning of the sperm. High concentrations of fructose are observed in the semen. (19). Mammalian spermatozoa require exogenous substrates for a variety of functions, including intracellular energy reserves, cell components, and, most importantly, motility support, which SP provides (20). The seminal plasma has excessive concentrations of fructose, which provides an anaerobic and aerobic source of energy for the sperm and has been obliquely associated with progressive sperm motility and viscosity (21). Seminal vesicle produces fructose, with some contribution from the ampulla of the ductus deferens. It is also a significant glycolysable substrate in seminal plasma and is commonly recognised as a

seminal vesicle function indicator. The fructose concentration in seminal plasma decreases and becomes undetectable, indicating that ejaculatory ducts are blocked. However, fructose level of seminal plasma determination is useful for auxiliary diagnosis of obstructive and non-obstructive azoospermia. (22). When evaluating the function of seminal vesicles and male factor infertility, seminal fructose is frequently evaluated as a marker. The content of fructose in fresh semen depends upon the secretion function of accessory glands, which is influenced directly by the activity of the male sex hormone (23). Poor spermatozoa quality, such as oligozoospermia and azoospermia, and hormonal dysfunction may be linked to low seminal fructose levels (24).

5. Role of copper in SP

Copper plays an essential role in the production of male gametes by facilitating cell division. Copper plays a very important role in male infertility. At every step of somatic cells of testis along with gametogenesis and copper-dependent enzymes like ceruloplasmin, the somatic cells of the epididymis, superoxide dismutase SOD1 and SOD3, group of metallothionein, and cytochrome c oxidase are present. Copper can be toxic at elevated concentrations. Copper chelation can suppress the process of spermatogenesis (25). Higher copper level in sperm are known to be detrimental for maturation of sperm, level of fertility, and motility. (26). Considerable amounts of copper can also be found in liquids associated with sperm in the epididymis and prostate. Copper also affects the integral androgen distribution in terms of fertility on the axis hypothalamic-pituitary-testis. Changes in copper levels result in irregularities in sperm, male gonads, hormone production, and nutrient dispersal, which significantly reduce male fecundity.

Copper deficiency can impair ejaculation volume and concentration, as well as sperm motility and morphology (27). Both increase and decrease in the copper level is detrimental to the male fertility.

6. Role of Magnesium in SP

Magnesium acts as an intracellular calcium antagonist. Magnesium is involved in motility of sperm and also can be used as marker of seminal vesicle secretions (28). Nitric oxide production promotes penile erection. The adult human body contains about 1000 mmol, with about half of it in bone and the rest distributed evenly among muscles and other soft tissues. Only 11-17 mmol is found in the extra cellular fluid, the plasma concentration being 0.8-1.2 mmol/L (29). Seminal levels of Mg are often used as a marker to judge about premature ejaculation (PE) assessment. Magnesium levels were found higher in fertile men than the pre ejaculatory and infertile men (30,31). Reduced magnesium levels cause vasoconstriction due to increased thromboxane levels, increased endothelial cytoplasmic Ca^{2+} , and reduced nitric oxide. This could result in early discharge and ejaculation. (32). Mg deficiency may be induced by the presence of chelating substances in sperm as well as hypomagnesemia. (33). The consumption of higher amounts of magnesium leads to an increase in seminal levels of magnesium (34).

7. Role of citric acid in SP

Citric acid is an essential biochemical component of seminal plasma that not only improves prostate health but also aids in the coagulation and liquefaction of human sperm (35). Citric acid plays a vital role in balancing liquefaction, maintaining pH, Viscosity, sperm motility,

morphology, hyaluronidase activity and osmotic equilibrium of semen. The citric acid level was found to be lower in azoospermia and severe oligozoospermia(36). Citric acid concentrations have been reported to be lower in severe or chronic prostatitis (37).

8. Role of Non Protein Nitrogen compounds in SP

Protein catabolism along with nucleic acids helps in the formation of compounds of non-protein nitrogen or, (*NPNs*). Some *NPNs* are such as urea, ammonia, creatinine and uric acid. *NPNs* have been found in different biological fluids along with our body cells in our body that are in contact with it. Proteins, enzymes, different cations, Non Protein Nitrogen compounds, and other chemicals are found in seminal plasma. Some NPN chemicals and semen parameters have a relationship that has been demonstrated. Nitrogenous compounds that are found in semen are also passed through urine, with a lower concentrations than in urine.(38,39).

Uric acid is one among the antioxidative substances in the male reproductive system. Seminal UA levels have been positively correlated with the percentage of normal sperm morphology and viability. Seminal UA amounts were considerably lower in infertile males than in fertile ones. In studies, the UA level in seminal plasma has been shown to be comparable to that of the serum uric acid level. Therefore, determination of seminal UA levels may play an important role in the diagnosis of male infertility associated with the decrease of seminal antioxidation (40).

Spermatozoa are sperm cells that, due to their dynamic movements, require a high energy supply (ie, CK enzymatic activity). Creatine Kinase (CK) is an enzyme that catalyses the regeneration of ATP from ADP, which is required for the production, transport, and utilization of energy within spermatozoa. Numerous isoforms of the enzyme have been identified, including mitochondrial and cytosolic isoenzymes (B, brain type; M, muscle type). Three cytosolic isoenzymes (MB, MM-CK, and BB) exist in heterodimeric or homomeric form, while two CKs in the mitochondria exist as octamers (Mib - and Mia -CK). Higher CK activity was linked to an increased incidence of morphologically abnormal spermatozoa in some studies: increased cytoplasmic retention resulted in sperm with larger head size and roundness, as well as a higher rate of amorphous sperm forms. The seminal malondialdehyde quantification along with plasma creatine kinase tend to obtained methods to differentiate samples of infertile from healthy in spite of the presence of obtained ranges of analysis of standard seminal. Smoking causes diminished activity of sperm CK and/or likely weaken energy of sperm homeostasis, thereby causing damage to sperm motility. Low counts of sperm in semen showed higher level of CK (41) Increased functional defects in sperm, such as diminished morphology and motility, may be indicated by elevated CK levels. Levels of Creatine Kinase refer as a biochemical marker in maturity of human sperm along with fertilizing potential.

9. Lipids in seminal plasma

Lipids are essential for sperm cell function, including viability, motility, maturity, capacitation, and fertilization. Phospholipids and cholesterol are required for human plasma membrane mechanisms. Changes in the lipid composition of spermatozoa been reported in infertile males. Hypertriglyceridemia reported, have deleterious effects on spermatogenesis. Lipids can also reduce sperm acrosome response kinetics, resulting in

negative effects on Leydig and Sertoli secretory capacity. Lipids can also reduce sperm acrosome response kinetics, resulting in negative effects on Leydig and Sertoli secretory capacity (42). Along with testosterone, steroid hormones also works under the precursor of cholesterol that is build in the Leydig cells, and plays an important role in ensuring normal spermatogenesis. The higher cholesterol levels will aid in the viability of the sperm even during cryopreservation and will protect against injury of sperm mediated by thawing. Cells of sertoli, cells of leydig, and developing cells of germ in the tubules of seminiferous contain enzymes involved in cholesterol metabolism, that put a strong point for spermatogenesis as the cholesterol may be crucial (43).Neergad *et al* has conducted an study with corporation between levels of cholesterol in plasma of seminal and quality of sperm among 403 men with age limit of 19 years from general population. Entire cholesterol amount between the seminal plasma was found to be firmly related to the concentration of sperm, motility of sperm, total count of sperm, along with morphology (44).Studies showed that the men with increased total cholesterol had correlations of positivity with motility of sperm, total sperm count, concentration of sperm and morphology (44,45). The quality of sperm perhaps indicates predictor of seminal with cholesterol amount inside plasma.

10. Conclusion

Infertility in men has become a significant contributor to infertility globally. Lower sperm count, motility, or morphology cannot account for all of men's diminished reproductive potential. Male fertility and reproduction processes demand tight and rigid guidelines. The composite secretion among the urogenital systems of male glands into seminal plasma contains a variety of components that can have an impact on the sperm's functionality. The differences in biochemical marker levels in seminal plasma may be related to the particular testis secretion, male accessory glands, and epididymis, as well as the prevalence of specific environmental factors that are vital for metabolism of sperm along with maintaining the functions. Seminal plasma components can be used as biomarkers for male infertility by providing information regarding sperm concentration, motility, and morphology. Analyzing the biochemical component concentration in the seminal fluid can also be a valuable method for assessing male fertility potential.

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