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Male Accessory Glands and Sperm Function

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Abstract

With the advent of the techniques of reproduction, the functions of this fluid on the sperm function became a topic of lesser interest to the embryologist, urologist and andrologist. The interaction of spermatozoa with seminal plasma often goes unnoticed, but it is very likely that many substances produced by male accessory glands have impact on the sperm physiology. Seminal fluid contains several components besides spermatozoa; many of them are produced by a specific tissue and can be useful markers of secretion of the glands. The information in the 5th Manual of World Health Organization is very limited with respect to the interpretation in several characteristics abnormally high in semen. Male accessory glands secrete several factors such as alpha-glucosidase, fructose, prostaglandins, bicarbonate and citric acid among others, which are crucial for sperm physiology. This chapter deals with the interpretation of markers of accessory glands and their relation to some pathologies such as varicocele, infections, obstructions of the seminiferous pathways and some hormonal alterations.

Keywords: male accessory glands, seminal plasma, semen hyperviscosity, male infertility, citric acid

1. Introduction

The study of seminal fluid had great importance some decades ago, but with the advent of fertilization *in vitro*, intracytoplasmatic sperm injection and other techniques of reproduction, the functions of this fluid on the sperm function became a topic of lesser interest to the embryologist, urologist and andrologist. The interaction of spermatozoa with seminal plasma often goes unnoticed, but it is very likely that these substances have impact in DNA integrity, in the membranes and organelles on sperm and embryo.

2. Components of the seminal plasma

Seminal plasma has a wide variety of elements, which are formed by the testicle, the seminiferous ducts and the glands. Some proteins of seminal plasma produced by type of tissues are considered markers. The increase or decrease in the levels of these markers may be indicative of a pathological process in a specific tissue [1].

Spermiogram is the most important test in the study of infertile man. In the semen sample, the spermatozoa and the products of secretion of the seminiferous ways and accessory glands are evaluated. The fifth version of the seminal analysis of the Manual of the World Health Organization showed some lower reference index (LRI) established to the seminal characteristics in 95% of a fertile population [2]. However, the information in this manual is very limited in interpretation if some characteristics are abnormally high such as density sperm (polyzoospermia), pH (alkalinity), seminal volume (hyperspermia) and markers of male accessory glands fructose, zinc and neutral alpha glucosidase.

The ejaculated contains sperm, immature germ cells, cell debris, other cells and secretions that come mostly from the accessory glands. After centrifugation of semen, a pellet composed of spermatozoa, cells and cell debris is obtained in approximately 5% of the volume. Seminal plasma is the supernatant remaining after centrifugation and removal of cells and cell debris from seminal liquid forms almost the whole 95%. The accessory glands are prostate and seminal vesicle, whereas the epididymis is an organ located on the posterior border of the testes where the sperm mature and are stored. The epididymis has secretory capacity and is often referred to as an accessory gland. Therefore, seminal vesicles, prostate and epididymis secrete most of the semen around 70, 20 and 10%, respectively [3, 4], **Figure 1**.
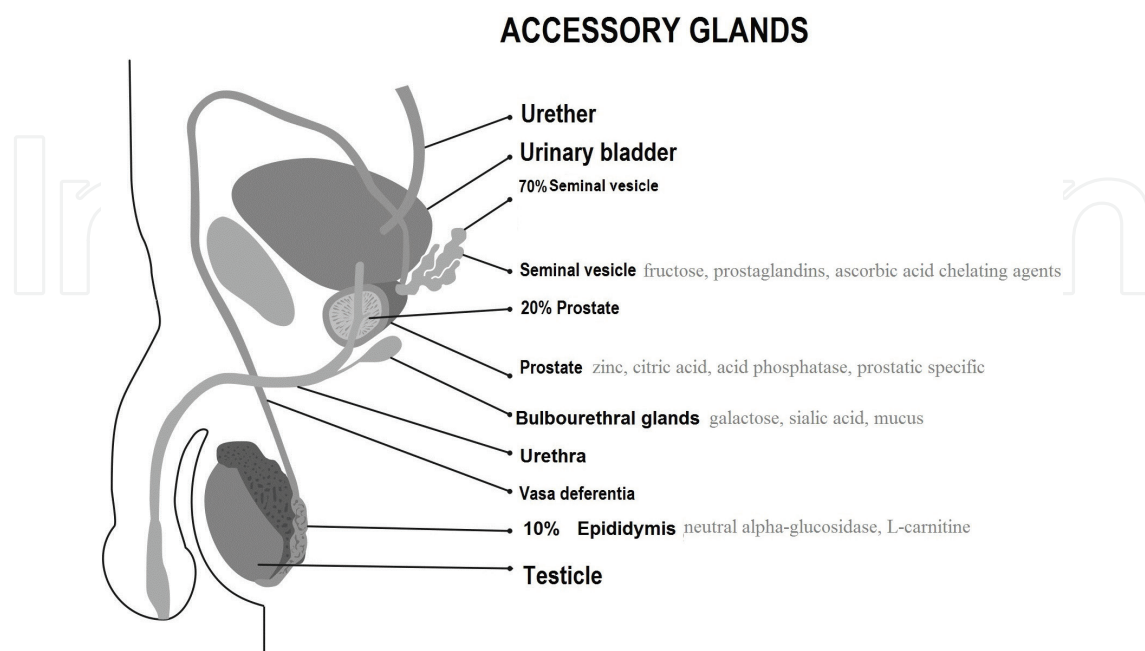
ACCESSORY GLANDS

Figure 1. Male accessory glands and their main products of secretions.

The production of the seminal fluid begins in the tubule recti, the rete testis and the epididymis inside the testicle. The testicle and the epididymis are found inside the scrotum. At the time of ejaculation, the sperm exit the scrotum and reach the vasa efferentia [1]. A part from providing the suitable environment for sperm nurturing, transport and maturation, during the transit in male reproductive tract functional and dynamic exchanges of molecules among spermatozoa and reproductive fluids occur. In the epididymis, the first organ in which post-testicular maturation takes place, a gradient of molecules, such as endocannabinoids provide the suitable environment for the acquisition of sperm motility [5] and defective spermatozoa are eliminated through the activity of molecular chaperones/cochaperone and de/ubiquitinating systems [6]. Prior to ejaculation, sexual arousal stimulates Cowper's glands located in the urethra, which produce a mucous and alkaline fluid that helps protect sperm from the remains of acid urine present in the urethra and in the urethral orifice. The secretion of Cowper's glands is known as pre-ejaculatory fluid. Occasionally, during long exciting phase, the secretion can reach up to 1 mL of the fluid, usually contained in one to three drops which appear at the opening of the glans of the penis [7]. The bulbourethral glands secrete galactose, sialic acid and mucus that lubricate semen, allowing more efficient sperm transfer. Despite being rich in components with potential diagnostic value, seminal plasma has been evaluated in the clinic rarely [1]. For these reasons to determine the causes of male infertility, tract genital fluid remains a field still unknown to many specialists in human reproduction.

2.1. Biomarkers of male accessory glands

2.1.1. Fructose

Fructose is the main sugar related to metabolism and sperm motility, it is an important marker of the performance of seminal vesicles. Al-Daghistani et al. proposed a reference range of fructose in fertile men: 367.5 ± 21.8 mg/l [8]; so that in a seemingly normal volume of 1.5 ml as outlined in the fifth WHO manual for seminal analysis concentration, the value of seminal fructose should be 20 μmol/ejaculate, over lower reference limit: 13 μmol/ejaculate [2]. The value of fructose expressed in "lower reference limit" discards if an extremely high value of fructose can be associated to an alteration in the metabolic pathway of sugars. Abnormally high values of fructose had been cited in individuals with diabetes, oligozoospermia and azoospermia [9–11]. The use of testosterone including in men with male accessory glands infection (MAGI) increases the seminal fructose [12]. Besides, lower values of fructose are detected in ejaculates with high sperm density with motile spermatozoa, so that the spermatic fructolysis decreases the concentration of fructose [13]. This controversy makes necessary to correct the fructose levels with the sperm concentration; hence, the value of corrected fructose (mg/ml) may be calculated by the logarithm (log10) of the concentration of spermatozoa/ml. It is necessary to remain in mind that the sperm motile activity and the fructose (mg/ml) must be multiplied by the log10 of the concentration/ml of "motile spermatozoa," to obtain an even more reliable parameter: true corrected fructose (FCV) [14]. Interestingly, the value of FCV has been related to condensation of sperm chromatin, zinc chelation and fertilization. The ejaculate of any fertile man may contain spermatozoa with different degrees of chromatin stability. After the introduction of sperm into the oocyte, an appropriate decondensation of the nuclear chromatin and the subsequent formation of the male pronucleus are essential for fertilization

and normal embryonic development. Higher incidence of intact spermatozoa in unfertilized oocytes suggests that sperm has high chromatin stability. In infertile men, the condensation of the sperm chromatin may be elevated. The prostatic zinc condenses the spermatic chromatin, this metal binds to the metallothionein coming from the seminal vesicle and gives greater stability of the chromatin; however, this step is regulated by secretions of seminal vesicles that have a chelating action on zinc to allow decondensation of sperm chromatin during fertilization. For these reasons, insufficiency of seminal vesicles or excessive production of zinc by a prostatic inflammatory process may be associated with infertility due to failure in chromatin stability. The reference value found for FCV is ≥2.5 mg/million sperm/ml [11, 14].

2.1.2. Citric acid and zinc

The prostate produces a variety of substances such as zinc (Zn), citric acid (citrate), acid phosphatase and gamma-glutamyltransferase into others. These four have been considered reliable markers of the prostate gland [15, 16]. Zinc has a tendency to bind with other elements of semen; it can sometimes be bound to the surface of the sperm cells [17]. Zn is an essential trace element for the maintenance of germ cells, the progression of spermatogenesis, and the regulation of sperm motility. In addition, zinc exerts antioxidant functions; it competes with iron and copper for binding to cell membranes and some proteins; it displaces the redox-active metals making it more available to bind to ferritin and metallothionein, respectively; and finally, it binds to the sulfhydryl groups of proteins, protecting them from oxidation. On the other hand, heat-induced oxidative stress causes apoptosis of germ cells [18]. Animals undergoing scrotal heating exhibit a significant reduction in sperm motility and concentration, but the adverse effects of hyperthermia on the seminal parameters of patients with varicocele can be prevented if these are treated with Zn, although this proposal must be supported by larger experimental studies [19]. The LRI established for zinc is ≥2.4 μmol/ejaculate [2].

Citrate is probably the major ligand of zinc. Citric acid levels are regulated by testosterone, and like fructose can be observed elevated in oligozoospermic and azoospermic subjects without a convincing clinical explanation [20]. Citrate is one of the most important anions, although it has an affinity for calcium, magnesium and zinc, and much of the seminal citrate is strongly charged anion [21]. A relationship between seminal citric acid and acrosomal integrity has been found in semen after cryopreservation. This is due to during cryopreservation, the spermatozoa become more permeable to ionic calcium, which is the main inducer of the reaction acrosome; if the sample has high levels of citric acid, it increases the capture of the ionic calcium and reduces the induction of the acrosomal reaction [22]. Conversely, citric acid is lower in semen hyperviscosity and suggests that the hyperviscous samples are inadequate for intrauterine insemination or fertilization in vitro. Citric acid is an important anion with high affinity for ionic calcium, magnesium and zinc; hence, lower concentrations of citrate may to induce premature acrosomal reaction [23]. Citric acid may be found in low concentrations in semen of men with abnormal prostate growth, in hyperviscous samples and with high adiposity. Seminal volume and spermatozoa/ejaculate are reduced in men with morbid obesity, so the hypospermia is more associated with decreased secretion of the prostate than seminal vesicles; an inverse relationship between citric acid and chronic oxidative stress has

been observed. Citric acid has antioxidant and anti-inflammatory functions in tissues damaged by environmental factors; also it favors the synthesis of glycosaminoglycans in various tissues. In obese men, abnormal growth of the prostate is associated with low production of prostatic citric acid in addition to other hormonal disorders that compromise testosterone, estrogen, insulin, insulin growth factor (IGF-1) and leptin. In semen of morbid obese men, there is an increase of fructose and lower levels of citric acid [24].

2.1.3. α-1,4 Neutral alpha glucosidase

With respect to the epididymis secretion, an important marker has been mentioned in the last few years, the α-1,4 neutral alpha glucosidase (NAG), there are two forms, an acid of prostatic origin another neutral of epididymal origin. The neutral isoform is secreted primarily in the body of the epididymis and plays a role in the maturation of spermatozoa [25]. L-carnitine and glycerophosphorylcholine had been used as biomarkers of epididymal function, but in the last few years, NAG has been considered the most sensitive and specific epididymal marker [26]. In this face, an infectious/inflammatory process in the epididymis can cause total or partial obstruction of the spermatic transport, causing azoospermia or oligozoospermia respectively. The obstruction generates pressure in the epithelial duct or the efferent ducts, the hemato-testicular barrier is overcome and the production of antisperm antibodies can be triggered [27, 28]. The decrease of NAG in semen is associated with obstruction between epididymis and ejaculatory duct, hypoandrogenism, infection or inflammation of the epididymis [2]. But the importance of NAG as an indicator of obstructive azoospermia is partial; nonetheless, the presence of cysteine-rich secretory protein 1 (CRISP1) in seminal plasma may be considered better marker to distinguish obstructive azoospermia and nonobstructive azoospermia. Seminal plasma samples from nonobstructive azoospermic men have the presence of CRISP1, whereas CRISP1 has been observed absent or very low in samples from patients with obstructive azoospermia [29].

The recommended reference for NAG value is ≥20 mU/ejaculate [2]. In the presence of *Chlamydia trachomatis*, *Mycoplasma hominis* and *Ureaplasma urealyticum* fructose and NAG are lower than samples of men without infection, suggesting low glandular function in epididymis and seminal vesicles associated lesions in the glandular tissue and at the presence of bacteria [30]. In men with varicocele, there are not alterations in levels of fructose, citric acid, pH nor acid phosphatase activity, but there is an important decrease of NAG associated to epididymal dysfunction in varicoceles grade II-III, possibly associated with a detrimental in sperm quality. The epididymis is located inside the scrotum and posterior to the testis and its function is possibly affected by the scrotal temperature [31]. The epididymis has a reduced function during varicocele, which is associated with decreased NAG activity and lower-quality sperm membrane and nucleus. The epididymis is an important organ involved in sperm maturation. The production of antioxidants by the epididymis is essential to counteract the damaging events resulting from excessive reactive oxygen species (ROS) production originated locally and along the transit through the epididymis from the testis. Reduced NAG activity in human semen of men with varicocele has been shown related to increase in DNA fragmentation, low integrity of sperm membrane and reduction of binding to hyaluronic acid.

Therefore, varicocele may compromise not only the testis but also the epididymis, causing a reduction of seminal quality and impaired quality of the sperm membrane and nucleus [32].

2.1.4. Seminal pH

The seminal pH is close to neutral, in the vaginal acid medium provides the spermatozoa the conditions to reach and penetrate the cervical mucus. The ideal pH of human semen has been a matter of debate [33], there is a considerable variation in pH measurements reported by different researchers. The LRI of seminal pH established by WHO is ≥7.2 [2], unlike most references that had been expressed in ranges 7.2–8.0. The value ≥LRI does not give a clear idea to what extent the semen alkalinity is favorable for sperm physiology. Lower values are associated with low seminal vesicle function and the absence of ejaculatory ducts that affect sperm quality and fertility [2, 32]. In this way, it is important to note that the pH > 7.2 interpreted literally as normal, subtracts the previous information when the pH value was ≥7.8 for infections or seminal inflammations [2, 10, 34]. The alkaline environment of semen is maintained by basic polyamines, such as spermine, spermidine and putrescine [35]. The pH value may depend on the time elapsed since ejaculation and tends to increase immediately after ejaculation as a result of CO_2 loss. High values of pH would not be physiologically favorable for sperm physiology, elevated values are also associated with prolonged collection time associated with fructolysis and lactic acid production alter their value [36, 37].

2.2. Other chemical components of semen

2.2.1. Calcium, magnesium and selenium

Zinc and magnesium concentrations in seminal plasma have been correlated with sperm quality [38]. The administration of selenium, magnesium, and calcium reduces the oxidative stress caused by intoxication. Calcium and magnesium have favorable effects on hematological and other biochemical parameters, but selenium is the most effective, it achieves the best protective effects against arsenic poisoning in humans [39]. Seminal calcium has been related to metabolism and sperm motility, acrosome reaction and fertilization [40]. Magnesium is bound to other molecules, which can sometimes bind to the surface of spermatozoa [41]. Selenium in semen has been correlated positively with concentration, motility and sperm morphology. Selenium has been related to the development of spermatogenesis, in the development of Sertoli cells; furthermore, it is a component of glutathione-peroxidase. Spermatozoa from selenium deficient mice have incomplete chromosome decondensation with increased incidence of DNA breaks. The increase of lipid peroxidation is observed in selenium deficiency but also observed when its intake is excessive. The concentration of selenium in seminal plasma of men with varicocele is lower than in normozoospermic men. Elevation of the scrotal temperature is considered to be one of the main factors that endanger spermatogenesis and steroidogenesis in the varicose testis. Selenium concentration is reduced in varicocele and has been associated with decreased sperm concentration, morphology and motility [19]. Oral selenium treatment may help restore seminal quality in many infertile men with varicocele.

2.2.2. Copper

This ion acts as a cofactor of different important enzymes and is associated with the sperm quality in rodents and humans [42]. Low doses of copper (Cu) may have favorable effects on sperm function [43], and elevated levels of Cu have been observed in the seminal plasma of men with varicocele compared with fertile men [15]. In older men, copper levels in seminal plasma have been positively associated with sperm DNA fragmentation [41]. In semen of infertile men with low seminal quality, copper levels were inversely related to sperm concentration. This relationship is not observed in normal samples of infertile men or in fertile men samples [44].

2.2.3. Proteins

In the human semen thousands of proteins have been reported, of which 7346 of them originate in the testicle. The prostate is the second source of proteins, which has aroused interest in their study because they produce high concentrations of proteomes in cases of prostate cancer. Seminal plasma proteins arise from secretions from seminal vesicles (~65% of semen volume), prostate (~25%), testis and epididymis (~10%) and bulbourethral and periurethral glands (~1%) [1]. Most seminal proteins are derived from the seminal vesicles, although the source of albumin is primarily of prostatic origin [45]. Albumin makes up about one-third of the semen protein content. The amino acid content of semen is much higher than that of plasma, and it increases rapidly (especially glutamic acid) within the first few hours after ejaculation [46].

Some of the proteins or their isoforms detected in the seminal plasma were zinc alpha-2-glycoprotein 1, clusterin, lactotransferrin, prostate specific antigen. Prostate is a very rich source of protein (35–55 g/l). The large variation in the number of proteins identified by any given technique depends mainly on the sample preparation and mass spectrometry technology available. Two proteins responsible for semen coagulation have been detected: the prolactin-induced protein (PIP) and Semenogelin (Sg), which are observed different between fertile and infertile men and could have an impact on sperm physiology. PIP is higher in semen samples of fertile men that in fertile men, while increased Sg concentrations are found in asthenozoospermic samples. Other proteins as epididymal secretory protein EI precursor, albumin preprotein, lactotransferrin, extracellular matrix protein E1 precursor, prosaposin isoform a preprotein and cathepsin D preprotein not play a significant role in sperm physiology [47]. Transferrin is one of the serum proteins, which has been characterized in the seminal plasma, but its role in male infertility is unclear [48]. However, a study found correlation of transferrin with sperm morphology. It demonstrated that seminal plasma transferrin concentration is correlated with sperm count and percent motile sperms. Thus, Sertoli cell-dependent secretion of transferrin has a positive influence over spermatogenesis and can be used as a marker of testicular function [49]. Many proteins have been differentially expressed in the seminal plasma of men with poor sperm quality. The overexpression or underexpression of some proteins suggests their role in male infertility.

3. Volume and seminal viscosity

Low reference index of seminal volume in fertile men is 1.5 ml. The term hyperpermia is not included in the last manual of seminal analysis. In a previous study of healthy men, the 95th percentile of the skewed data distribution was 6.3 ml and nearly 50% of them had low sperm concentrations. Seminal volume increase (hyperspermia) has been associated to male accessory gland in patients with bilateral prostate-vesiculo-epididymitis (PVE) more than those with monolateral PVE or prostatitis [50, 51].

The prevalence of hyperviscosity in subfertile men is around 26.2%, and it may be mild, moderate or severe. Treatment may be completely successful only in subjects with mild hyperviscosity with a positive semen culture. In these subjects, progressive motility percentage, straight line velocity and linearity of sperm increase. Pathogenesis was strictly related to infective/inflammatory factors in only 48.0% of cases; therefore, it is possible that biochemical, enzymatic or genetic factors have a role in this condition [52].

Human papillomavirus (HPV) has been detected in semen samples of infertile men, 10.5% of them showed only single type of virus, 5.7% corresponded to the high risk type and 6.1% were type low risk, in 6.1 were more than one type of HPV. Increase of semen viscosity was observed in the samples infected with the virus in single and multiple forms. Hypospermia, leukocytospermia and increased pH are found in infected samples with multiple types of HPV, probably the seminal changes are related to the negative effects of different forms of HPV in the prostate secretion and the fertility [53].

4. Male accessory glands and hormonal control

Male accessory sex glands display a consistent pattern of differential sensitivity to androgens and estrogens and that these hormones may exert their action on different cell types within the organ [25]. The development and differentiation of the male reproductive system in the fetus are directed by the fetal testis through the production of testosterone and anti-Müllerian hormone. In the fetal testes, Leydig cells produce testosterone, a steroidal hormone that promotes the growth and differentiation of Wolff's ducts such as epididymis and prostate. At the same time, the Sertoli testicular cells produce the Anti-müllerian hormone (HAM) that causes the regression of the Müllerian ducts. The development of the external sexual organs is generated from the differentiation of the genital tubercle, eminence (protuberance) located in front of the cloaca of the embryo. The secretion of the enzyme 5-α-reductase allows the transformation of testosterone to dihydrotestosterone (DHT), a hormone that differentiates the genital tubercle to the male external sex organs [54]. However, the possible impact of other glucocorticoid hormones has been proposed in experimental animals. Betamethasone has been used for inducing fetal lung maturation. Some studies reported that prenatal treatment with this drug reduced testosterone levels in the male fetus. In adulthood stage of these animals, lower values of FSH and sperm quality were observed; seminal vesicle weight was decreased while

testicular and ventral prostate weights were increased. The betamethasone exposure leads to long-term reproductive impairment in male rats. It is important to considerate the implications for humans, considering the use of this glucocorticoid in pregnant women [55].

Other drug that has negative impact on secretion of male accessory glands is atorvastatin because reduce acid phosphatases, NAG and L-carnitine in semen during the therapy, indicating an alteration of prostatic and epididymal functions with reduction of seminal parameters. The mechanism of the effect of atorvastatin on the function of accessory glands is not clear; possibly, the reduction in LDL-cholesterol levels affects the synthesis of testosterone by Leydig cells [56]. Dihydrotestosterone (DHT), estradiol, progesterone and prolactin receptors have been found in prostates of rats. It has been shown in these species that testosterone induces hyperplasia and also has an anti-inflammatory effect on that gland [57].

The effect of prolactin on the prostate was studied in hypophysectomized animals treated with LH and FSH without any supply of exogenous prolactin, the animals showed low weight in prostate and seminal vesicles [58]. Prolactin potentiates the effect of androgens on the prostate and seminal vesicles in rodents, possibly favoring the conversion of testosterone to dihydrotestosterone. Hyperprolactinemia in mice produces structural changes in the cells with the highest amount of androgen receptor in the epididymis and prostate [59]. Studies in castrated rats showed that prolactin stimulates the expression of epididymal and sialic acid alpha glucosidases, independent of androgens [60]. The reduction of glandular markers in the absence of infection could be related to unknown hormonal changes.

5. Markers of male accessory glands and infection

Infection of male accessory glands (MAGI) can occur as prostatitis, prostatic-vesiculitis and prostate-vesiculo-epididymitis. MAGI can have a negative impact on the secretory function of the glands and on fertility. MAGI is often acquired as a urethral infection, it has a chronic course and it spreads to one or more accessory glands, being able to cover one or both sides, rarely causing obstruction of the seminal routes. The seminal alterations are more evident when the infection reaches two or more glands. The inflammatory response has been associated with the alteration of the seminal parameters when affecting function of the epididymis, seminal vesicles and prostate, especially by diminishing the antioxidant properties of the seminal plasma [61].

Several protein components of seminal plasma are produced by certain types of tissues of the male urogenital tract; therefore, the difference in the concentration of these semen proteins could be indicators of a specific organ disease. This concept is best illustrated by the value of prostate-specific antigen (PSA) as a marker of prostate diseases. The PSA was originally discovered in semen and was isolated from it and is the most used marker to identify prostate cancer, being higher in semen than in blood serum [62]. PSA is a serine protease that cleaves semenogelin by hydrolysis and thus liquefies the semen coagulum and facilitates sperm motility and capacitation [63].

Soufir evaluated the markers fructose, acid phosphatase and citric acid as tools in the differential diagnosis of infectious processes and hypogonadism. The decrease of markers suggested that it is necessary to evaluate hormonal status and to rule out infection of accessory glands, which can affect sperm function and inability to achieve pregnancy naturally [64]. Glandular markers tend to be low in the presence of leukocytes and most likely in infection; nevertheless, these are significantly lower in hypogonadism. An infection could cause permanent damage of the secretory epithelium, so even after treatment may remain low [65]. This implies that in cases of seminal vesicle, infection levels of seminal fructose may be increased or decreased.

Male accessory glands infection may alter the elasticity in semen. Changes in levels of oxidative products in semen are related to seminal viscosity. Hyperviscosity has been associated with reactive oxygen species (ROS) generation, levels of cytokines TNF-α, IL-6 and IL-10 and seminal leucocyte concentration, and whether ROS production was related to the extent of infections/inflammations at one PR (prostatitis) or two PV (prostato-vesiculitis) male accessory glands. ROS production in PV was higher than in prostatitis. Seminal IL-10 levels in PV and PR patients were lower than those found in the controls. In PR men, the levels of hyperviscosity are positively related to TNF-α; the seminal hyperviscosity is associated with increased oxidative stress in infertile men and increased pro-inflammatory interleukins in patients with male accessory gland infection, more when the infection was extended to the seminal vesicles [66]. Seminal hyperviscosity is often associated with prostate infection, reduce citric acid and asthenozoospermia [52, 66]. These alterations have been reversed when properly treated with antibiotics, decreasing the concentration of leukocytes and proinflammatory cytokines. Around one-third of cases of seminal hyperviscosity does not respond to treatment with antibiotics because viscosity depends on other glandular factors that have not yet been clarified [52].

Many compounds secreted by the male reproductive tract may be important in the study of infertile man. It is advisable that before choosing any technique of assisted reproduction, the causes of infertility in man are more accurately evaluated, especially in cases of idiopathic infertility. Disorders of the male accessory glands are often associated with bacterial infections. These alterations must be carefully treated with the antibiotic therapy to which these bacteria show susceptibility [67]. The diagnosis and antibiogram would allow controlling resistance to antibiotics, but taking into account that when there is infection of the glands, antimicrobials have limited efficacy because they are anatomical compartments with barriers that can limit their reach, such as blood-prostatic barrier. Tissue lesions are greater as time progresses, for example prostatitis responds faster to treatment than prostate-vesiculitis and prostate-vesicle-epididymitis, that is, more glands are involved as time progresses [68]. In addition, it is possible to find the compartment of some microorganisms that tend to encapsulate or attach more strongly to the glycocalyx of the extracellular matrix of the gland or probably because of changes in local pH of seminal vesicles (alkaline) or prostate (acid), between others that limit antimicrobial efficacy [64]. Treatment of subclinical infections and secretory failure of male accessory glands can improve sperm physiology to achieve spontaneous pregnancies. It should be noted that the cost of assisted reproduction reflects a much lower percentage of live births than other less costly techniques for many infertile couples. Assisted reproduction already accounts for as many as 5% of live births in some European countries [69] so it is not negligible to investigate the factors that modulate the function of gametes.

6. Conclusions

The study of secretory products of male accessory glands in conjunction with correct seminal evaluation may help to exclude the high percentage of idiopathic infertility. Infectious or post-infectious processes in the epididymis, prostate and seminal vesicles can alter the seminal plasma quality and the physiology of spermatozoa.

The evaluation of compounds of the seminal plasma is useful to understand the process of natural fertilization and to achieve pregnancy naturally when the causes of infertility in man have been clearly established. These evidences suggest that the components of the seminal plasma participate in key events related to sperm function, fertilization and embryonic development in the female reproductive tract. However, the subject of sperm interaction and seminal plasma should continue to be studied to help explain the failure rates in assisted reproduction techniques.

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