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SEMEN BIOCHEMISTRY

THE BIOCHEMICAL ANALYSIS OF SEMINAL PLASMA IS AN
EXTREMELY VALUABLE TOOL IN THE FIELD OF MALE
INFERTILITY

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Abstract

Seminal biochemistry is a complement to the semen analysis in the investigation of male infertility. It informs the clinician about the functional status of the epididymis, the prostate and the seminal vesicles. The biochemical exploration of human semen is based on the assay of certain compounds of the ejaculate, these being secreted by the accessory glands (prostate and seminal vesicles) and by the epididymis. The volume and the composition of seminal plasma are altered in various disorders, and particularly in inflammatory processes of the genital tract. The biochemical analysis of several seminal plasma compounds, a second-line investigation, is an extremely valuable tool in the field of infertility exploration.

Introduction

The exploration of male infertility is a constant issue in reproductive health. While semen analysis remains the first-line investigation, important complementary tests such as semen biochemistry provide substantial added value for the aetiological understanding and the management of sperm abnormalities.

Indeed, the post-testicular maturation of spermatozoa results from a constant interaction between the male gametes and the specific environment of the secretions of the epididymis and of the accessory genital glands. Epididymal fluid is composed mainly of proteins synthesised and secreted in a highly regionalised manner by the epididymal epithelium. Spermatozoa thus undergo spectacular transformations, becoming motile under the combined action of a rise in intracellular cyclic AMP, of the ionic environment and of a specific protein (Forward Mobility Protein: F.M.P.). Prostatic secretion is a colourless, acidic fluid representing 20 to 30% of semen and containing a number of enzymes, acid phosphatase, citric acid, ions (Zn^{2+} and Mg^{2+}), spermine, etc. Vesicular secretion, for its part, is voluminous (two thirds of the semen volume) and contains fructose (a reducing sugar),

prostaglandins and potassium. Seminal biochemistry (or semen biochemistry) therefore makes it possible to explore abnormalities of the male excretory ducts. It relies on the assay of specific markers of the epididymis (alpha-1,4-glucosidase, carnitine), of the seminal vesicles (fructose) and of the prostate (citrate and zinc), which make up the seminal plasma. The assay of the biochemical markers of semen thus constitutes a complement to semen analysis in the investigation of male infertility, since it informs the clinician about the functional status of the epididymis, the prostate and the seminal vesicles.

1. The constituents of seminal plasma

The various constituents of seminal plasma are produced by one or another of the accessory glands and therefore constitute topographic markers. For the epididymis, the usual markers are:

- L-carnitine,
- Alpha-glucosidase, in its neutral form (the acid form also originating from the prostate),
- Glycerophosphocholine.

For the seminal vesicles (whose secretions optimise sperm motility), the following are essentially retained:

- Reducing substances (which prevent agglutination and degeneration of the sperm membrane), with fructose and ascorbic acid,
- Prostaglandins,
- Bicarbonates,
- Semenogelin (related to fibronectin), which is a structural protein involved in the coagulation and the liquefaction of semen; its subunits could be involved in the regulation of motility,
- Lactoferrin: a bacteriostatic and immunomodulating factor.

The specific secretions of the prostate protect spermatozoa against various types of aggression (germs, free radicals, antibodies);

They also regulate the expression of their main functions: motility, capacitation, chromatin decondensation. These include:

- Citric acid, which modulates the osmotic balance as well as
- The movements and the morphology of spermatozoa,
- Zinc, which acts as a protector of the motility and the vitality of spermatozoa when they are placed in contact with germs and polymorphonuclear cells,
- Prostatic acid phosphatase,
- Gamma-glutamyl transpeptidase (GGT),
- Muramidase,
- Prostate-specific antigen (PSA), which is involved in the liquefaction of semen,
- EGF: Epidermal Growth Factor.
- The secretions of the Cowper's glands produce factors that allow a lubrication of the urethra (facilitating the flow of semen) and coagulation factors.

From certain data resulting from the study of seminal fluid — volume, pH, assay of some of its constituents — it is therefore possible to draw certain conclusions as to the diagnosis and the topography of obstructions located on the excretory ducts; these data also make it possible to assess the functional value of the accessory glands in the context of infections or inflammation of the semen.

4. Reminder! Mineral and bone disorders related to chronic kidney disease (CKD-MBD):

Seminal biochemistry may constitute a complement to semen analysis in the investigation of male infertility. It informs the clinician about the functional status of the epididymis, the prostate and the seminal vesicles. The biochemical exploration of human semen is based on the assay of certain compounds of the ejaculate, these being secreted by the accessory glands (prostate and seminal vesicles) and by the epididymis. The volume and the composition of seminal plasma are altered in various disorders, and particularly in the inflammatory process of the genital tract. The biochemical analysis of several seminal plasma compounds, a second-line investigation, would be an extremely valuable tool in the field of infertility.

As regards practical applications in the clinic, it should be borne in mind that:

- In cases of hypoandrogenism, all the markers are lowered.

- In cases of obstruction, biochemistry makes it possible to determine the level and the extent of the obstructive phenomena. A fall in L-carnitine and in alpha-glucosidase leads one to consider an epididymal obstruction. In cases of diffuse excretory involvement (proximal and distal), not only is a fall in the epididymal markers observed, but also in fructose of vesicular origin; much more rarely, citrate may be lowered or, paradoxically, raised. Certain difficulties may be encountered as regards interpretation when the involvement is very proximal (at the level of the testiculo-epididymal junction) or when it is unilateral, or even in the case of inflammatory involvement associated with a unilateral congenital anomaly of the seminal excretory ducts.
- Vesiculo-deferential agenesis and/or obstruction of the ejaculatory ducts are characterised by a reduced semen volume, an acid pH and a fall in the fructose level.
- A raised citric acid level shows a predominant participation of the prostate.
- A low level of the prostatic marker generally indicates an infection and/or an inflammation of the prostate, which may impair sperm motility.
- The epididymal marker makes it possible to differentiate an excretory azoospermia (low marker level) from a secretory azoospermia (normal marker level). But in certain cases of secretory azoospermia related to an orchiepididymitis with mixed lesions (testiculo-epididymal), or to KLINEFELTER syndrome, a low level of this marker may be found.
- Lastly, the assay of the epididymal markers makes it possible to monitor the post-surgical course after epididymo-deferential anastomosis. In cases of infection or inflammation of the genital tract (the inflammation possibly being the sequela of a patent or silent infection), seminal biochemistry may be useful to confirm a clinical suspicion. It is estimated that 35% of men are affected, at one time or another in their lives, by prostatitis.

Disorders of the coagulation and of the liquefaction of semen may also justify explorations of the seminal fluid, since this coagulation is controlled by the secretions of the seminal vesicles, and the liquefaction by the prostatic secretions. The most frequent indications for a request for semen biochemistry are:

- A low ejaculate volume

- An azoospermia
- A necrozoospermia
- An asthenospermia
- A leucospermia

In conclusion, semen biochemistry remains a major tool in the exploration of male infertility.

Table: Attempted interpretation of the results of semen biochemistry in different clinical settings.

	Epididymal markers	Seminal vesicle marker	Prostatic markers
	Carnitine, alpha 1-4 glucosidase, (glycerophosphocholine)	Fructose	Citrate, zinc, acid phosphatases
Epididymal / deferential obstruction	lowered levels (except in the case of an obstruction at the level of the epididymal head)	normal levels	normal levels
bilateral obstruction of the vesiculo-deferential junction, bilateral absence of the vasa deferentia (cystic fibrosis)	lowered levels	collapsed levels	normal levels
Obstruction at the level of the ejaculatory ducts	lowered levels	normal levels	normal levels
vesiculitis (inflammatory/infectious)		lowered levels	
hypoandrogenism of Klinefelter syndrome, testicular lesions, ... primary hypogonadism	lowered levels	lowered levels	lowered levels
diabetes mellitus		raised levels (depending on the assay technique)	
Prostatitis			lowered levels

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Seminal plasma analysis is from now on available at Laboratoire Sion. We assay carnitine, fructose and citrate.