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LETTER TO EDITOR

Overweight and obesity: The allies of prostate inflammation

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To the Editor,

World Health Organization (WHO) defines infertility as the inability of a sexually active partner to achieve a clinically confirmed pregnancy after at least one year of intercourse without contraceptive protection on fertile days (1). As women are primarily responsible for the conception, childbirth, and postpartum, fertility problems have been related to fertile female capacity. However, men play an essential role, being responsible for about 50% of alterations in fertility due to dysfunctions in the male reproductive tract, including varicocele, hypogonadism, poorly descended testicles, testicular tumors, and even anti-sperm autoantibodies (2-4). However, a high percentage of cases of male infertility is still of idiopathic cause. Male infertility has also been associated with aging and unhealthy lifestyles, such as cigarette smoking, recreational drug use, alcohol, sedentary lifestyle, psychological stress, as well as environmental factors such as pollution and heat exposure (5, 6). Additionally, there is a relationship between infertility and non-contagious diseases or chronic diseases, including cancer, chronic respiratory diseases, cardiovascular diseases, diabetes mellitus, obesity, and prostatitis (7-10) producing stress and general deterioration of health, including seminal parameters and fertile male capacity.

Prostatitis and obesity

Prostatitis is a common urogenital disease with a worldwide prevalence between 2.2 and 9.7% and an average of 8.2% (11), and has been directly related to seminal parameters alteration and male fertility (8). On the other hand, the increasing trend of obesity is associated to the decline of male fertility (20). In fact, it has been reported that men with a high BMI tend to be infertile more often than men with adequate body weight (12).

Several studies have been reported in which an alteration of seminal quality and male fertility is found, along with an increase in the incidence of obesity. Furthermore, in the United States, it has been found that sperm counts decrease by 1.5% annually, and obesity has been considered as a possible etiological agent of infertility and reduced fertility (13).

To the best of our knowledge, there is insufficient evidence to link obesity and prostatitis. Some studies have tried to relate these two pathologies, as *Wallner et al.* (14), who found that having a high BMI acts as a protective factor for prostatitis. Although this finding elucidates the relationship between prostatitis and obesity, future studies are necessary. While the relationship between prostatitis and obesity is still unknown, the latter has been involved with the risk of suffering from other prostate diseases, such as benign prostatic hyperplasia and prostate cancer (15, 16).

Inflammatory status and antioxidants: A threat to fertility with a therapeutic alternative

Obesity implies an increase in abdominal or visceral adipose tissue, which leads to rise in hormone levels in addition to a chronic inflammatory process (18), which is precisely due to abundant white adipose tissue in obese men, where increased aromatase activity has been found (13, 17).

Adipose white tissue is considered an endocrine organ, responsible for producing around 30 biologically active peptides, such as leptin and adiponectin, and can even secrete adipokines (as modulating agents) (13). Leptin, a hormone derived from adipose tissue, known as the regulator of food intake and body energy expenditure, is mediated by hypothalamus (18, 19) and is necessary for proper functioning of reproductive system (20). This hormone is generated in excess in obese people, contributing to a decrease in androgens and altering male fertility (20). It should be mentioned that obesity is positively associated with a hyperinsulinemic state, which suppresses the production of androgen transporting proteins, such as *sex hormone-binding globulin* (SHBG) and decreases circulating testosterone levels (21).

The main component of adipose tissue are adipocytes, specialized cells that can secrete various adipokines, such as tumor necrosis factor α (TNF-α), interleukin 6 (IL-6), and tissue factor (18). Some of these adipokines have been linked to infertility, testicular cancer, and chronic inflammatory conditions (22). Constant inflammation leads to a release of *reactive oxy-*

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gen species (ROS) and *reactive nitrogen species* (RNS) (23), which generate direct toxic effects (oxidative stress) on sperm, altering conventional seminal parameters such as concentration, motility, and morphology (24) and increases DNA damage to sperm and its membrane (25), composed mostly of polyunsaturated fatty acids, which give it fluidity, but also high susceptibility to oxidative stress, due to production of reactive aldehydes, which react with aminoacids, and can even alter mitochondrial function (26).
As therapy against oxidative stress, there are antioxidants, which normalize spermatozoa's functioning altered by ROS and RNS, becoming used as therapy in cases of chronic prostatitis and male infertility (27, 28). There is scientific evidence that supports the hypothesis that sperm are protected from oxidative stress thanks to antioxidants present in seminal plasma (29). Some examples of these therapeutic alternatives are superoxide dismutase, catalase, coenzyme Q10, carnitine/L-carnitine, vitamin E, isoflavones and green tea (30).

Analysis of our data

To analyze the relationship between prostatitis, obesity, and oxidative stress, a geometric representation of the information obtained from 40 volunteers with a BMI greater than 25 was made through *principal component analysis* (PCA) using Prism 9.0 statistical software (*GraphPad Software, San Diego, CA, USA*) (Figure 1). The group included fourteen men with chronic prostatitis symptoms and twenty-six men asymptomatic for urogenital infections. The variables were the ones related to oxidative stress, including sperm membrane lipid peroxidation, antioxidant capacity in serum and semen, production of reactive oxygen species and body mass index.

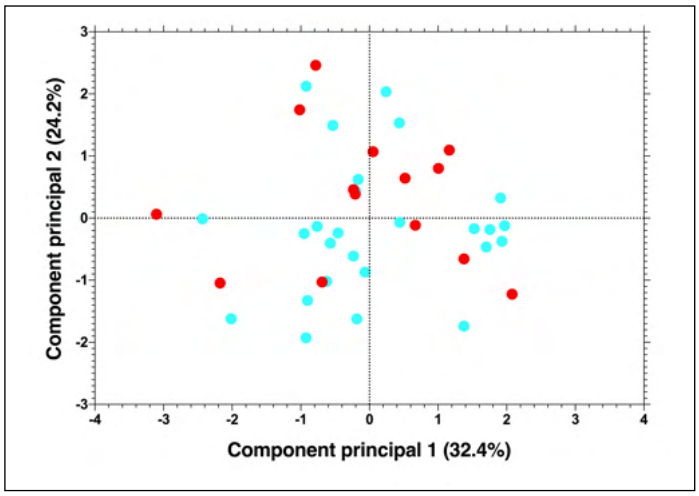

Figure 1.
Principal component analysis.
The principal component 1, X-axis in figure 1, is considered as the principal axis, because it presented the highest coefficient of variability within the system, with a value of 32.4%, while the principal component 2, collected 24.2% of the variability of the data.

Conclusions

This analysis showed that 73.1% of controls were located on the lower side, and 64.3% of the patients were located on the top of the graph. Indicating that subjects with chronic prostatitis symptoms present a particular distribution of semen parameters compared to asymptomatic controls, which supports the relationship of oxidative stress with prostatitis.
In conclusion, prostatitis and obesity are pathologies that are entirely related to male fertile state, and in cases of infertility they should be considered as etiological factors. Both coincide in the production of an inflammatory condition, altering sperm function. This damage can be lessened with antioxidant supplementation, an option that should not be ruled out as a therapeutic alternative. Finally, future studies that link prostatitis, obesity, and antioxidants may help developing strategies that could allow us to continue assessing importance of male sexual and reproductive health.

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