BIOCHEMICAL EFFECT OF OBESITY ON MALE INFERTILITY

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Abstract

Obesity is considered a global health issue affecting more than a third of the population and it may lead to various complications such as diabetes mellitus (type 2), cardiovascular diseases, prostatic carcinoma, osteoarthritis, accelerated ageing, neurodegeneration and infertility/subfertility in both male and female. Obesity of male can affect negatively on the quality of important seminal parameters such as sperm count, motility and morphology. This review study was launched to find out the biochemical mechanism of the effect of obesity on seminal parameters hence the male infertility. Based on the review result, it is proved that obesity has a negative effect on the quality of seminal parameters mainly on sperm count and motility. Due to the fact that these two parameters play an important role in male fertility, obesity has a negative impact on male fertility. Furthermore, the outcome of the review study could be considered as a platform for launching further researches on the topic and to consider the weight management more and more in the treatment regime of male infertility. Moreover, weight management may prevent certain other pathological conditions as well. This could be an additional advantage for the infertile/sub fertile patients.

Keywords: male obesity, biochemical mechanism, insulin, leptin, seminal parameters

Introduction

As a major health problem, obesity has reached epidemic extents worldwide. According to the WHO reports, nearly 650 million people were obese and more than 1.9 billion were overweight in 2016 worldwide [1]. Obesity is associated with the deposition of an excess amount of fat in the body. Adipose tissue which is located under the skin and intra-abdominal, is the layer which contains body fat. Quetelet index (BMI), and measurements of waist circumference can be used to detect the body fat [2] and body fat topography [3] respectively. People with a BMI of ≥30 kg/m^2 are considered as obese [2]. However, waist circumference is currently suggested as a more accurate marker of obesity

It has been found in certain research studies that obesity has been associated with several health risk conditions such as hypertension, high low density cholesterol level (LDL) and/or triglyceride level (TG), type 2 diabetes, coronary heart disease, stroke, gallbladder disease and also with infertility. Regarding human infertility, human beings are affected equally by obesity regardless of their sex. According to statistics, the prevalence of male infertility is 7% [4] and this is on the rise and continues to be an issue for many. Thus, paying attention on this is mandatory. Basically, male infertility depends on the alteration of the quality of semen.

Semen is a semisolid liquid produced by the organs of the male reproductive system. It is white, opalescent, slightly alkaline viscous fluid (pH between 7.35 to 7.50). The semen comprised of cells (spermatozoa) and the fluid (seminal plasma). The spermatozoa are synthesized by the testis of the male reproductive system and the seminal plasma is made up of various tubules and glands of the reproductive system such as prostate, seminal vesicles, bulbourethral glands. As the function of the seminal plasma, it helps keep the sperm alive. Further, the seminal fluid represents the largest portion of semen and its around 95%, the cellular composition represent the rest [5].

As it was mentioned, spermatozoa or sperm originates in the testes from the germ cells of the seminiferous epithelium. The process is called as spermatogenesis. The human male is able to ejaculates 200 to 300 million sperms during a coitus [5]. The sperm which is microscopic in nature composed of a head, a middle piece and a tail. The whole body of the sperm is covered by a plasma membrane. The head of the sperm contains an elongated haploid nucleus and anterior portion of it is covered by a cap like structure called the acrosome which contains the lysosomal enzymes needed for the fertilization of the ovum. Middle piece contains numerous mitochondria (power houses), which supply energy (ATP) for the cell. Sperm tail is thin and elongated and making 80% of the entire length of the sperm which helps in motility [5]. Thus, the cellular portion forms about 2-5% of the semen composition.

The Seminal plasma or the fluid portion of the semen is a complex liquid and made up of the secretions of the seminal tract and seminal glands. As the main function, seminal plasma serves as the vehicle for transporting already ejaculated spermatozoa. Moreover, it provides protection and nutrition to the spermatozoa during their onward movement in the female reproductive tract (vagina and uterus).

When it comes to the formation and maturation of spermatozoa, the seminiferous tubules of the male testis generate sperm cells and the epididymis helps to store them. Electrolytes such as sodium, potassium as well as energy sourcing glyceryl phosphorylcholine are added to the sperm in the epididymis. In epididymis sperm become mature and enter another storage area called the ampulla which is a part of vas or ductus deferens. The ampulla secretes a yellowish fluid which has ergothioneine, a substance which removes oxygen and also secretes fructose which nourishes the sperm. During the ejaculation secretions from the prostate gland and seminal vesicles are added. These secretions dilute the semen concentration and provide a suitable environment for sperm cells. The seminal vesicle secretes seminal fluid which has a contribution of 50-65% of the seminal volume [5]. This fluid contains amino acids, citric acids, fructose, potassium, phosphorus, and hormones such as prostaglandin.

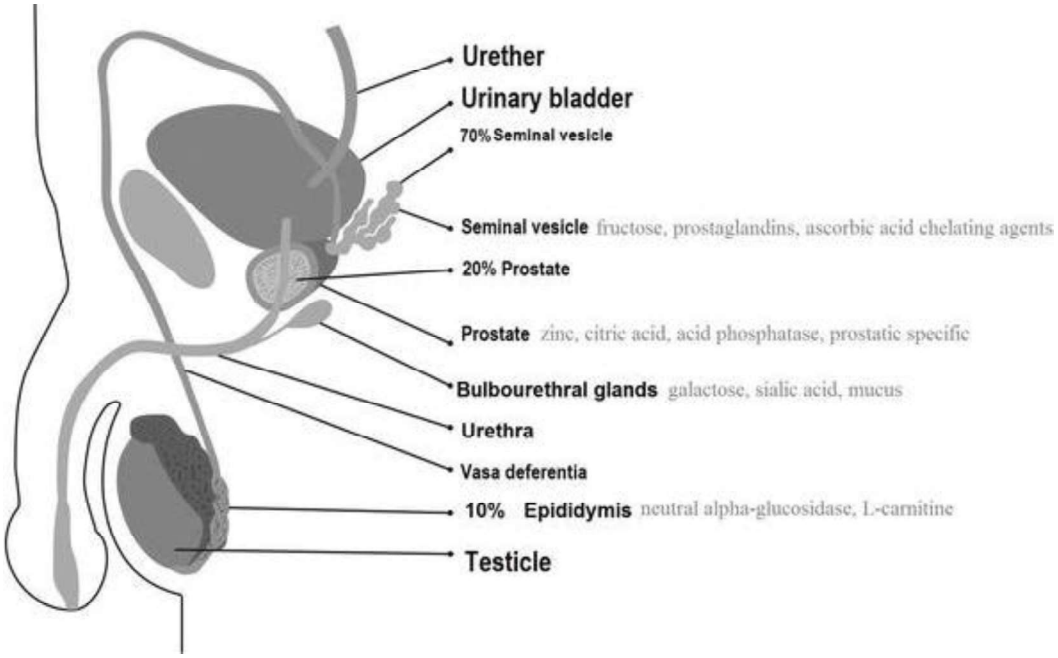

Figure 1: Accessory glands of the male reproductive [5]

The prostate gland contributes 20-30% of the semen volume and it adds acid phosphatase (an enzyme), calcium, zinc, sodium, potassium, proteolytic enzymes (serine proteases) and fibrolysin (an enzyme which reduces blood and tissue fibers). These enzymes and proteins assist in coagulation and subsequent liquefaction of semen. Coagulation helps semen to be as a semisolid mass in the vagina and liquefaction of it after around 30 minutes assist in sperm to move up along the vaginal wall easily. Most of the immunoglobulin (secretory Ig-IgA) present in the semen are produced by the prostate. The bulbourethral gland produces galactose, sialic acid and mucous which act as lubricant for semen. These components make up to 5% of the volume of the semen [5]. The seminal plasma along with the sperm finally forms the semen. Thus, in the ejaculation nearly 2-3 ml of semen is emerging which is white or opalescent in color.

The basic function of the semen is as follows;

- Containing of sperm/ spermatozoa which are used in fertility
- Survival of sperms with fructose and other enzymes
- Creation of alkaline buffered medium in the vagina
- Coagulation of the sperm cells
- Coating the sperm cells with capacitation inhibitors
- Facilitating sperm to move by proteolysis
- Activation and motility of the sperm cells
- Promote successful fertilization

There are several parameters which determine the quality of semen. Out of them four are considered as main parameters which determine the quality. Those main seminal parameters are the volume of semen, sperm count, sperm morphology and sperm motility. According to the WHO guidelines (2010) [6] the lower reference volume of semen is 1.5 ml. The normal reference sperm count is 15 million sperms per milliliter of semen. Basically, the sample which contains 4% [6] of normal morphological sperm cells would be considered as morphologically normal if the relevant male was able to make his partner pregnant within 1 year. Additionally, the value of sperm motility should be higher than 50% per milliliter of semen to be a quality semen.

According to certain studies, it is disclosed that the obese males are more prone to be infertile) [7]. More overly the scientists have pointed out the possible theories of affecting obesity on seminal parameters. In this review study, it is to point out the biochemical way of affecting of obesity on the quality of seminal parameters hence the male infertility. The outcome of the survey would be more important for the respective clinicians who are involved in the male fertility subjects to consider about weight management of the client in the fertility treatment regime.

Methods and Materials

This literature review study was made basically on the articles pertaining to obesity and male infertility. Thus, to gather the information on the topic; online journals, online magazines, relevant websites and published books (Library of the Faculty indigenous Medicine, University of Colombo) and book chapters were searched and screened during the period of December 2022 to March 2023. All the gathered information was reviewed and analyzed to find the biochemical association of obesity on male factor infertility hence, to determine the way of biochemical mechanisms.

Results and Discussion

The obesity of male affects the quality of seminal parameters negatively via various biochemical pathways. The gene of the DNA of spermatozoa contains the genetic information. The high level of insulin found in obese male can make fragmentation of DNA, which can decrease the fertile ability of sperm [8]. In addition, high level of blood insulin can also slow down the liver synthesis of testosterone transporting globulin, which ultimately can cause for inadequate availability of hormone in the testicular region. Testosterone is essential for synthesis and maturation of

spermatozoa in testis. Thus, according to the previous research studies, obesity can make poor quality semen via affecting sperm count (oligospermia) and morphology (teratospermia).

The level of oestrogen (a female hormone) in obese is rather higher than that of the normal males. The higher fat cell mass in white adipose tissues found in obese men secretes the enzyme called aromatase cytochrome P 45, which can convert androgen to oestrogen (aromatization of androgen). As elevated oestrogen levels prevent the synthesis of testosterone via negative feedback on the hypothalamus, the phenomenon may affect negatively on spermatogenesis [9]. This phenomenon of high estrogens in obese men has been mentioned by Daniel A. Potter, a Consultant Gynecologist in Huntington Reproductive Center in California and confirmed by a WHO study in 2009. This finding also proves that obesity makes poor sperm count (oligo spermia) via affecting male sex hormone testosterone.

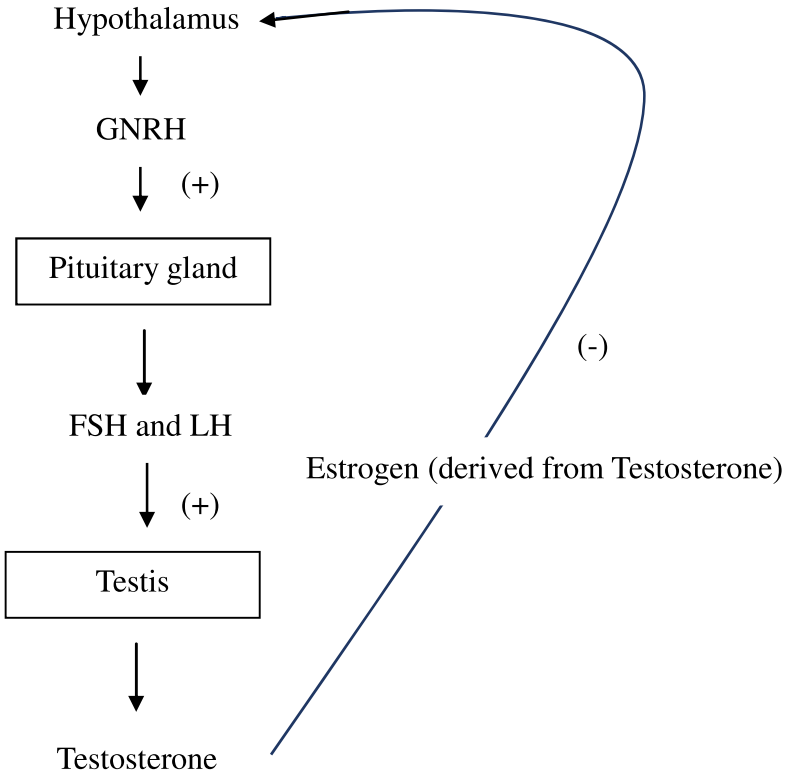

Figure 2: The negative effect of estrogen on the production of testosterone

Obese or overweight subjects may suffer from various social issues such as frustrations on a self-figure, sexual disturbances due to obesity, sleep disturbances (sleep apnea) due to respiratory issues, and certain other marital problems as well. These may cause to stress on them, which can again alter the level of testosterone, which is essential for spermatogenesis [9]. This finding describes another cause of less availability of male sex hormone in obese. Hence, this fact also may cause to oligospermia.

Further, obese males often tend to reduce physical activities which are necessary for synthesizing testosterone. Moreover, the sleep apnea result in obesity may lead to hypoxia, which could reduce the availability of oxygen to testis. For a successful spermatogenesis it requires a good oxygenation and a low temperature environment [9]. In the normal healthy individuals this is met by maintaining the scrotum out of the body. Anyway, the elevated scrotal temperature usually found in obese individuals, affect negatively on proper spermatogenesis [10] which ultimately could leave to oligospermia.

Leptin, which is a protein produced by white adipocytes [9] plays an important role in controlling food intake and energy expenditure, as well as the regulation of reproductive function. When the level of leptin elevates it affects on the brain to decrease the intake of food. Further, excess leptin also decreases the function of Leydig cell, hence the production of testosterone. Thus, the higher level of leptin, which found in obese male may affect badly on spermatogenesis. Leptin can damage the sperm cells also. Thus, high dose of Leptin found in obese may cause to oligospermia and teratospermia.

Excessive fat in the thigh and skin folds which covers the genital region are also a problem for the obese men in synthesizing sperms [11], as the scrotum and testis are overheated by the insulating effect of fat. [9]

Obesity is also associated with increased oxidative stress in the testicles [9]. High oxidative stress is consequence due to relatively high stress and high basal metabolic rate (BMR) seen in obesity. Though, the spermatogenesis process is not impaired, free radicals can damage sperm following production via attacking (crosslinking) DNA or peroxidation of membrane of sperm and their mitochondria. [12] Thus, the factor led to teratospermia and oligospermia.

There is a high ability to solubilize and get accumulated of lipid soluble environmental toxin in the adipose layer [13] of obsess individuals which also can be toxic on sperm production.[9]
The environmental toxin affects not only for male but also on the fertility of female.

Conclusion

According to the outcome of the review study, it is clear that variations in several biochemical and physical factors, such as high insulin, high leptin, high oxidative stress, high temperature, and high environmental toxins, which are fairly common in obese males, cause poor-quality semen via various biochemical mechanisms. Moreover, it's clear that obesity basically affects the sperm formation process negatively, hence the count of sperm in the semen. This is confirmed in other similar review studies, which also concluded that obese men are three times more likely to have oligospermia, a sperm count of fewer than 15 million/mL, compared to healthy men with a normal weight.

Thus, this finding could be a good platform for doing more research on the topic. Furthermore, it is better if clinicians who work on male fertility pay them much attention on male obesity as a causative factor of male infertility or subfertility. Finally, more researches should be carried out on the topic considering the present review study as a platform.

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