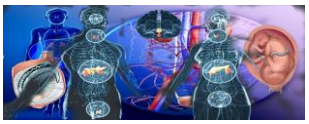
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Hypogonadism: A Testosterone Therapy in Men

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Abstract
Male hypogonadism is a condition in which the body does not produce enough of the testosterone hormone; the hormone that plays a key role in masculine growth and development during puberty. There is a clear need to increase the awareness of hypogonadism throughout the medical profession, especially in primary care physicians who are usually the first port of call for the patient. Hypogonadism can significantly reduce the quality of life and has resulted in the loss of livelihood and separation of couples, leading to divorce. It is also important for doctors to recognize that testosterone is not just a sex hormone.

Keywords: chronological age; puberty; low sperm count; erectile dysfunction

Introduction

Acute pancreatitis is an acute response to injury of the pancreas. Chronic Male hypogonadism is a clinical syndrome that results from failure to produce physiological concentrations of testosterone, normal amounts of sperm, or both. Hypogonadism may arise from testicular disease (primary hypogonadism) or dysfunction of the hypothalamic-pituitary unit (secondary hypogonadism). Clinical presentations vary dependent on the time of onset of androgen deficiency, whether the defect is in testosterone production or spermatogenesis, associated genetic factors, or history of androgen therapy.

The hypothalamic–pituitary–gonadal axis is of relevance in many processes related to the development, maturation and ageing of the male. Through this axis, a cascade of coordinated activities is carried out leading to sustained testicular endocrine function, with gonadal testosterone production, as well as exocrine function, with spermatogenesis. Conditions impairing the hypothalamic–pituitary–gonadal axis during paediatric or pubertal life may result in delayed puberty. Late-onset hypogonadism is a clinical condition in the ageing male combining low concentrations of circulating testosterone and specific symptoms associated with impaired hormone production. Testosterone therapy for congenital forms of hypogonadism must be lifelong, whereas testosterone treatment of late-onset hypogonadism remains a matter of debate because of unclear indications for replacement, uncertain efficacy and potential risks.

Complex Genetic Syndromes.

Primary hypogonadism resulting in androgen deficiency and impaired sperm production or in isolated impairment in sperm production or function may occur as a manifestation of complex genetic syndromes, usually in association with a number of congenital anomalies or defects and distinct morphologic developmental manifestations. Examples include the Alström, ataxia telangiectasia, Marinesco-Sjögren, Robinow, Rothmund-Thomson, Sohval-Soffer, Weinstein, Werner, and Wolfram syndromes.

The Testis and Male Sexual Function

Hypogonadism refers to low circulating levels of testosterone. Most androgen-deficient men are infertile. Primary hypogonadism indicates that the abnormality originates in the testis; secondary hypogonadism indicates a defect at the hypothalamus or pituitary, resulting in decreased gonadotropins (LH, FSH, or both). Combined primary and secondary hypogonadism occurs in aging and in a number of systemic diseases, such as alcoholism, liver disease, diabetes mellitus, human immunodeficiency virus (HIV) infection, hemochromatosis, and sickle cell disease. Obesity leads to low total and free testosterone levels.

Classification Of Male Hypogonadism

There are two basic types of hypogonadism that exist:

Primary: This type of hypogonadism – also known as primary testicular failure – originates from a problem in the testicles.

Secondary: This type of hypogonadism indicates a problem in the hypothalamus or the pituitary gland – parts of the brain that signal the testicles to produce testosterone. The hypothalamus produces the gonadotropin releasing hormone, which signals the pituitary gland to make the follicle-stimulating hormone (FSH) and luteinizing hormone. The luteinizing hormone then signals the testes to produce testosterone. Either type of hypogonadism may be caused by an inherited (congenital) trait or something that happens later in life (acquired), such as an injury or an infection.

Primary Hypogonadism

Common causes of primary hypogonadism include:

Klinefelter's Syndrome: This condition results from a congenital abnormality of the sex chromosomes, X and Y. A male normally has one X and one Y chromosome. In Klinefelter's syndrome, two or more X chromosomes are present in addition to one Y chromosome.

Role of Testosterone

Throughout the male lifespan, testosterone plays a critical role in sexual, cognitive, and body development. During fetal development, testosterone aids in the determination of sex. The most visible effects of rising testosterone levels begin in the prepubertal stage. During this time, body odor develops, oiliness of the skin and hair increase, acne develops, accelerated growth spurts occur, and pubic, early facial, and axillary hair grows.

Pathophysiology of Testosterone and Hypogonadism

The cerebral cortex – the layer of the brain often referred to as the gray matter – is the most highly developed portion of the human brain. This portion of the brain, encompassing about two-thirds of the brain mass, is responsible for the information processing in the brain. It is within this portion of the brain that testosterone production begins. The cerebral cortex signals the hypothalamus to

stimulate production of testosterone. To do this, the hypothalamus releases the gonadotropin-releasing hormone in a pulsatile fashion, which stimulates the pituitary gland – the portion of the brain responsible for hormones involved in the regulation of growth, thyroid function, blood pressure, and other essential body functions. Once stimulated by the gonadotropin-releasing hormone, the pituitary gland produces the follicle-stimulating hormone and the luteinizing hormone. Once released into the bloodstream, the luteinizing hormone triggers activity in the Leydig cells in the testes. In the Leydig cells, cholesterol is converted to testosterone. When the testosterone levels are sufficient, the pituitary gland slows the release of the luteinizing hormone via a negative feedback mechanism, thereby, slowing testosterone production. With such a complex process, many potential problems can lead to low testosterone levels.

Transdermal Patch

Transdermal testosterone patches are available in India under the brand name Androderm. Transdermal patches deliver continuous levels of testosterone over a 24-hour period. Application site reactions account for the majority of adverse effects associated with transdermal patches, with elderly men proving particularly prone to skin irritation. Local reactions include pruritus, blistering under the patch, erythema, vesicle formation, indurations, and allergic contact dermatitis. Approximately 10% of the patients discontinue patch therapy due to skin reactions. In one study, 60% of the subjects discontinued the patch between weeks four and eight due to skin irritation.

Intramuscular Injections

Intramuscular formulations are also available, sold as Depo-Testosterone (testosterone cypionate) and Delatestryl (testosterone enanthate). The testosterone is suspended in oil to prolong absorption. Peak levels occur within 72 hours of administration, but intramuscular administration is associated with the most variable pharmacokinetics of all the formulations. In the first few days after administration, supraphysiological testosterone levels are achieved, followed by subphysiological levels near the end of the dosing interval. Such fluctuations, are often associated with wide variations in mood, energy, and sexual function, and prove distressing to many patients. To reduce fluctuations, lower doses and shorter dosing intervals (two weeks) are often used. Injection site reactions are also common, but are rarely the reason for discontinuation of therapy.

Conclusion

Hypogonadism affects men of all ages, either through congenital or acquired causes. For patients who have clinical symptoms associated with their low testosterone levels, treatment is essential for the prevention of sexual, cognitive, and bodily changes. A variety of treatment options are available, utilizing different dosage formulations, and providing patients with choices that best meet their needs. Therefore, there is a clear need to increase the awareness of hypogonadism throughout the medical profession, especially in primary care physicians who are usually the first port of call for the patient.

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