



## Male Hypogonadism Diagnosed During Treatment for Infertility: A Case Report

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### ABSTRACT

Hypogonadism is a common condition, among older men, but extremely rare in young males, often goes undiagnosed and untreated. It can be associated with a number of signs and symptoms that affect quality of life, including feelings of low energy, decreased sex drive, decreased muscle mass and increased abdominal fat, a risk factor for metabolic syndrome and type 2 diabetes mellitus. We here present a case of 37 years male who was diagnosed as hypogonadism during assessment for infertility and later on treated for low testosterone levels after 2 years. If Testosterone Replacement Therapy is initiated, a patient's response and adverse events should be assessed at regular intervals and therapy adjusted accordingly.

**Keywords:** RP-HPLC, UV detection, Lamivudine, Tenofovir, validation, ICH guideline

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### 1. INTRODUCTION:

Male hypogonadism, which is a disorder caused by the inability of the testes to produce physiologic levels of testosterone and the normal number of spermatozoa as a result of a disruption of the hypothalamic-pituitary-gonadal axis.<sup>1</sup> There is two types of male hypogonadism, regardless of age of onset. Primary involves testicular failure that results in low testosterone levels, impairment of spermatogenesis, and elevated gonadotropin levels. Secondary results from central defects of the hypothalamus or pituitary and is associated with low-to-normal gonadotropin levels (luteinizing hormone [LH] and follicle-stimulating hormone [FSH]) and low testosterone levels. Appropriate hormonal stimulation restores fertility in secondary but not primary hypogonadism.<sup>1</sup> Low testosterone is associated with a broad range of physical, psychological and sexual symptoms including decreased energy and mood, fatigue, loss of muscle mass, decreased libido and erectile dysfunction. In addition, low testosterone is associated with other serious medical conditions including diabetes, cardiovascular disease and metabolic syndrome. The indication of testosterone-

replacement therapy (TRT) treatment requires the presence of low testosterone level, and symptoms and signs of hypogonadism. Clinical studies indicate that TRT may produce a wide range of benefits for men with hypogonadism that include improvement in libido and sexual function, bone density, muscle mass, body composition, mood, erythropoiesis, cognition, quality of life and cardiovascular disease. The most controversial issue is the risk of prostate cancer by testosterone, even though no evidence to support this risk exists.<sup>2</sup>

### 2. CASE REPORT:

A couple (37 years old male and 34 years female) presented with infertility after eight years of marriage. In Female, blood investigations showed hypothyroidism and normal levels of gonadal hormones. Ultrasound showed presence of fibroid in myometrium of uterus, which later treated for hypothyroidism and was concluded that it is not the cause of infertility. The male semen analysis showed sperm count 1million/ml, normal sperm 60%, abnormal head 27%, abnormal tail and mid piece 13%, motility 56%, viable sperms 61% and dead sperms

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39%.USG scan pelvis and scrotum reveals testes were small. The right testis measured 36×15×23 mm across and 6.71 ml in volume. The left testes measured 31×17×24 mm across and 6.90 ml in volume. The echo pattern of testes was normal. The prostate was normal and measured 48×19×28 mm across and 13-53 ml in volume. There was bilateral refluxing varicocele.

The hormone analysis of male showed FSH 7.20 mIU/ml, LH 8.49 mIU/ml, testosterone 156ng/ml, free testosterone 6.06pg/ml, Prolactin 0.49ng/ml, progesterone 0.32 ng/ml, T3 1.19 ng/ml, T4 8.26ug/dl and TSH 3.28uIU/ml. the fasting blood sugar was 136 mg/dl. He was taking Telmisartan H (80mg+12.5mg) for hypertension from last 3 months. Patient has normal puberty, the external genitalia, body and facial hairs, coitus and erections were normal as per age. All the blood investigations like Haemogram, Haematocrit, Urine routine and microscopy, Liver Function Tests, Kidney Function Tests and lipid profile were within normal limits. He underwent surgery for B/L varicoceles; varicocelectomy under mini laparoscopy was done. The seminal fluid culture was positive for citrobacter freundii for which appropriate antibiotics were given as per sensitivity. After 3 months of operation, he was prescribed inj Human chorionic gonadotropin 5000IU/ week for 12 weeks to increase the sperm count and proceed for IVF.

After 2 years, he again presented with symptoms of low mood, lack of enthusiasm, decreased muscle mass, obesity, decreased libido, erectile dysfunction and depression. The total testosterone levels were 138 ng/ml and free testosterone 5.06 pg/ml, He was diagnosed as case of primary hypogandism and keeping in view of the features of metabolic syndrome as having truncal obesity, Diabetes, hypertension and depression, it was decided to go for hormone replacement therapy after getting all the investigations done.

He was given testosterone gel 1% w/v 5gm per day. After 2 days of treatment there was marked improvement in mood, energy levels and libido. After two weeks of treatment, his total testosterone level was 350 ng/ml and free testosterone 14.76 pg/ml. The compliance was poor and even after the improvement, it was difficult for him to apply the gel daily and risk of exposure to baby and partner. He was shifted on Injection Testosterone esters 100mg/ml every two weekly. The fasting blood sugar level was 102 mg/dl. The effects were good after the injection but before the next dose, the results were disagreeable. The dose was increased to 250mg/ml every 2 weekly, the free testosterone 327 ng/ml and free testosterone 12.25 pg/ml after 3 months of treatment in between the injection dose. As the changes in mood were up and down, patient was not happy with the treatment. Finally it

was decided to put him on long term testosterone therapy in the form of testosterone undecionate, as he did not have any comorbidities. Injection Testosterone undecionate 1gm/4ml was given as two injections two ml was injected in each side intramuscularly. Second dose was given after 6 weeks and then every 10 weeks. After one year of treatment, compliance is good and patient's experience with the treatment was good. With each 10 weekly dose, the total testosterone levels were 424 ng/ml and free testosterone 14.00 pg/ml. Serum prostate specific antigen (PSA) rose from 0.56 to 0.676 ng/mL after 52 weeks, remained within normal limits. All other investigations like LFT, KFT and blood sugar were in normal range. The cognitive functions, erections, libido, energy levels and muscle mass increased. The overall wellbeing was improved.

### 3. DISCUSSION:

The cause of Hypogonadism in this case is most probably B/L varicocele leading to damage of testes and decrease in serum testosterone levels and sperm counts.

The literature analyses and results suggest that conditions such as germ cell apoptosis and DNA damage are common features in hypoxia, varicocele and testicular torsion. Normally, the testicles are kept in the scrotum 2 to 7°C below body core temperature. The spermatogenic process is fairly independent of changes in other vascular beds in the body. Pathologies such as varicocele or testicular torsion and environmental exposure to low oxygen (hypoxia) can result in changes in blood flow, nutrients, and oxygen supply along with an increased local temperature to the testicles that damage the testes and induce adverse effects on Leydig cell function and spermatogenesis.<sup>3</sup>

The Hypogonadism in Males study estimated the prevalence of hypogonadism [total testosterone (TT) < 300 ng/dl] in men aged >45 years visiting primary care practices in the United States. Among men not receiving testosterone, 756 (36.3%) were hypogonadal; odds ratios for having hypogonadism were significantly higher in men with hypertension (1.84), hyperlipidaemia (1.47), diabetes (2.09), obesity (2.38), prostate disease (1.29) and asthma or chronic obstructive pulmonary disease (1.40) than in men without these conditions. The prevalence of hypogonadism was 38.7% in men aged > 45 years presenting to primary care centers.<sup>4</sup>

Testosterone compounds are available from almost 70 years, but the pharmaceutical formulations are still less than ideal. Testosterone esters have been used for treatment as 2- to 3-weekly injection interval but they generate supranormal testosterone levels shortly after the injection and then testosterone levels decline, becoming subnormal in the days before the next injection. The rapid

fluctuations in plasma testosterone are subjectively experienced as unpleasant. Testosterone undecanoate is a new injectable testosterone preparation with better pharmacokinetic profile. After 2 initial injections with a 6-week interval, the following intervals between two injections are almost 12-weeks, amounting eventually to a total of 4 injections per year. Plasma testosterone levels and its metabolic products estradiol and dihydrotestosterone are within the normal range during treatment. The "roller coaster" effects of testosterone ester injections are not observed with testosterone undecanoate. It reverses the effects of hypogonadism on bone and muscles, metabolic parameters and on sexual functions. No polycythemia has been observed and no adverse effects on lipid profiles. Prostate safety parameters are well within reference limits. Its safety profile is excellent due to the continuous normal levels of plasma testosterone.<sup>5</sup>

An International, multicenter, Surveillance Study on long-acting-intramuscular TU conducted at 155 centers in 23 countries in Europe, Asia, Latin America, and Australia. Patients received up to five Testosterone Undecanoate injections during 9-12 months. Results of the 1,493 hypogonadal men enrolled for study, 1,438 (aged 49.2 ± 13.9 years) having received 6,333 injections were analyzed. Scores of mental and psychosexual functions (libido, vigor, overall mood, and ability to concentrate) improved markedly, while mean waist circumference decreased from 100 to 96 cm. Blood pressure and lipid parameters were altered in a favorable and significant manner. After four TU injection intervals, the percentage of patients with "low" or "very low" levels of sexual desire/libido decreased from 64% at baseline to 10%; moderate, severe, or extremely severe erectile dysfunction decreased from 67% to 19%. At the last observation, 89% of patients were "satisfied" or "very satisfied" with TU therapy. The most common ADRs were increase in hematocrit, increase in PSA, and injection site pain (all <1%). No case of prostate cancer was observed.<sup>6</sup>

It is clear now that Testosterone Undecanoate is effective and safe as the standard injectable formulation in young males and requires only 4-5 injections per year in long-term treatment while maintaining serum Testosterone levels within the physiological range.

#### 4. CONCLUSION:

Testosterone replacement therapy is not for infertile men. Testosterone replacement in hypogonadal men decreases fertility by decreasing gonadotropin production by negative feedback and lowering production of sperms by sertoli cell. Testosterone replacement therapy must be given to the right person at right time in right dose at right intervals with monitoring of total testosterone, free testosterone and PSA levels at regular intervals. TRT is

effective in normalizing serum testosterone levels, providing a beneficial cardiovascular effect, and improving sexual function and overall quality of life. Testosterone undecanoate is a valuable new contribution to the treatment options for male Hypogonadism.

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