

## Conference Paper

# The Association Between Testosterone Levels and Relationship Quality in Reproductive Aged Couples

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## Abstract

Couple relationship is often interfered by disorder in sexual activities. Most of the problems are in women than men. One of the main factor tha contributed to sexual function are sex hormones. Sex hormones selectively responsive to sexual incentives inducing a neurochemical state that favourable to sexual response. Androgens play an important role in sexual desire, arousal, orgasm and satisfaction by interacting with receptors in the hypothalamus, together with the dopaminergic, serotonergic and opiatergic path, and the receptor genitals. Testosterone, molecular weight of 288.41 Dalton, is one of sex steroid hormones. It is the main androgenic hormone produced by the interstitial cells (Leydig). However, testosterone is an important precursor for the production of estradiol in the target tissue. Both testosterone and estrogen may affect sexual arousal. Decrease of testosterone in men is also related to declines in sexual desire, which can be restored with testosterone administration. Therefore, adding testosterone to estrogen in sexual disorder may be benefited. However, this practice was not widely use. Furhter sutdy is needed to assess its long term side effect.

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## 1. Introduction

Couple relationship is often interfered by disorder in sexual activities. Most of the problems are in women than men. Women who experience a decrease in sexual interest with or without interruption of sexual response should be assessed for psychological health, physical, and social in general. Stress, fatigue, relationship problems, depression, and common side effects of treatment contribute to a reduced sexual interest. Medical conditions that can cause fatigue and low welfare, such as iron deficiency and hypothyroidism, should be removed. While the presence of factors and conditions should not exclude women from testosterone treatment, they must be managed simultaneously [1].

Sex hormones exert both organizational and activational effects, which are relevant to sexual function, and their actions are mediated by non-genomic as well as direct and indirect genomic pathways. Research data suggest that sex hormones (estrogen, androgens and even progesterone) selectively responsive to sexual incentives inducing a neurochemical state that favourable to sexual response. When an imbalance occurs between the dopaminergic system, which increases sexual desire

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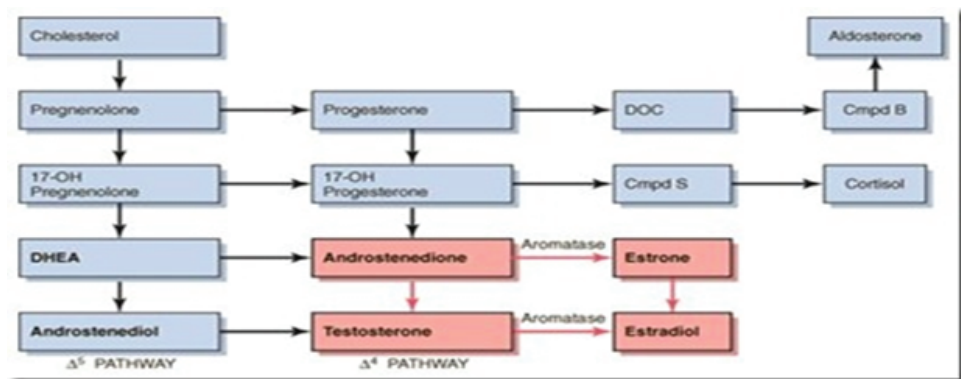


Figure 1: Synthesis of Testosterone.

and excitement, women may feel unable to begin the sexual response cycle. In addition, an overactive serotonergic system can decrease desire and delay orgasm. Stress and fatigue, and/or pharmacological compounds (i.e., selective serotonin reuptake inhibitors [SSRIs]) may activate endogenous inhibitory mechanisms. Alternatively, some metabolic and/or hormonal conditions (i.e. menopause) may endogenously blunt sexual excitatory mechanisms. The net balance between stimulatory and inhibitory factors brings about the ability to experience sexual desire. Other mediators have been postulated to play a critical role in women's sexuality, including oxytocin, melanocortins, opioid and endocannabinoid systems [2].

Androgens play an important role in sexual desire, arousal, orgasm and satisfaction by interacting with receptors in the hypothalamus, together with the dopaminergic, serotonergic and opiate path, and the receptor genitals. Combining androgen and estrogen appears to increase a woman's sexual function, evidence obtained from studies in patients with estrogen-only, when testosterone was added [3].

## 2. Testosterone

Testosterone, molecular weight of 288.41 Dalton, is one of sex steroid hormones. It is the main androgenic hormone produced by the interstitial cells (Leydig) in response to LH stimulation of the anterior pituitary gland. In women 50% of testosterone is produced by the ovaries and adrenal glands are directly released into blood [4].

The production of testosterone in women is derived from three sources: the ovaries, adrenal glands, and from changes in the peripheral circulation of androgen. Testosterone levels reduce in accordance aging. This decrease is related to a combination of factors: production of androgens from the adrenal glands progressively decrease as aging, although the production of testosterone from the ovary is usually intact after menopause, adrenal secretion against androstenedione decreased by approximately 50%. Lower androstenedione causes a significant decrease in testosterone in peripheral changes to the current menopause [24].

Biological data support an important physiological effects of testosterone in women. Testosterone act directly via androgen receptors throughout the body, including in the areas of the brain, particularly the hypothalamus and amygdala; and peripheral side

including bone, breast, skin, skeletal muscle, adipose, vascular, and genital tissues. The effects mediated by aromatization of testosterone to estrogen as hormone androgen is an essential precursor for the biosynthesis of estrogen on ekstragonad and ovarian tissue [5].

However, testosterone is an important precursor for the production of estradiol in the target tissue. Ovaries make estrogen by converting testosterone into estrogen. Testosterone is converted from dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS) and androstenedione from ovarium. After menopause, when the ovaries are not able to do its job, the fat tissue of women become the main source of estrogen that are made by converting adrenal androgens into estrogens in adipose tissue [4].

### 3. Testosteron and Sexual Activity

The role of testosteron androgen is already understood: it is important toward the sexual arousal, vibration and receiving sexual stimulant [6]. Imbalance biosynthesis or metabolism of androgens in women may have an unpleasant effect on the whole system. Testosterone, estrogen may affect sexual arousal, bone mineral density, muscle mass, adipose tissue distribution, Moog, energy, and ability to live physiology [7].

There are multiple ways in which androgens target the brain regions (hypothalamic, limbic and cortical) involved in sexual function and behaviour. Testoteron acts directly or throughout aromatization to E2 contributes to the initiation of sexual activity and permission for sexual behaviour in multiple areas of the brain. A further non-genomic action by testoteron metabolites on sexual receptivity has been described at the hypothalamic level. On the other hand, the brain is a steroidogenic organ itself and it is capable of producing from precursors and/or de novo its own neurosteroids relevant to sexual pathways. The concept of intracrinology has to be taken into account because this local production seems to be more critical to women's sexual desire and function than peripheral androgens. Finally, it is worth remembering that every woman possesses her own threshold of tissue responsiveness to hormonal variation depending on several factors, from genetic disposition and age to lifestyle and personal experiences, and a wide range of individual responses may be observed at physical and behavioural level in basal conditions and following hormonal manipulations [2].

Decrease of testoteron in men is also related to declines in sexual desire, which can be restored with testosteron administration. However, reproductive-aged males treated with supraphysiological doses of testosteron do not report enhanced sexual activity, with mixed results for increased libido. In line with these findings, research focusing on natural variation in testosteron among reproductive-aged men has not found that higher testosteron males engage in more frequent sexual intercourse compared to individuals with lower testosteron [8,9]. Hooper et al. (2011) assessed self-reported assessments of relationship commitment and satisfaction among 90 heterosexual men and women. They showed that increasing levels of commitment predicting lower testoteron but no significant difference was found women's T ( $P > 0.05$ ) [10].

## 4. Laboratory Examination of Testosterone

There is few free testosterone in the blood circulation. As many as 60% of testosterone bound protein known as sex hormone binding globulin (SHBG) and 33% bound to the blood protein called albumin. Therefore only 1-2% of testosterone in the blood circulation in young women who are bound in blood or free in the blood [4].

Total testosterone was measured directly, radioimmunoassay method clinically useful in the study population of low testosterone in women. Free testosterone is calculated using equation Sodergard. Estimates of free testosterone has been shown to have a strong correlation with dialiasis equilibrium, which is generally accurate method of measurement of free testosterone. The results showed a decrease in total and free testosterone, dehydroepiandrosterone (DHEAS), and androstenedione by age, starting mid aged 30 years [5].

Although postoperative menopausal women may be the group most likely to benefit from testosterone therapy, women with natural menopause are equally likely to benefit. Women who experience premature ovarian failure, especially secondary chemotherapy or radiotherapy, also should be considered for therapy testosterone [1].

## 5. Testosterone Therapy

Doctors have given women testosterone for decades. Testosterone treated women experienced improvement in symptoms and improved the welfare of the common sexually if want to continue therapy. Randomized controlled trial have shown the efficacy of testosterone therapy compared with placebo for several parameters of sexual function. When considering starting testosterone treatment, women should be fully informed that although the combined findings from randomized trials of testosterone conducted to date have not shown an increased risk of breast cancer or cardiovascular disease, the evidence is not yet available on the safety of long term testosterone administration [1].

Methyltestosteron, synthetic testosterone, combined with estrogen ester and the FDA allowed using in women. This product is commercially known as Estraest (Abbot Laboraories) and Estratest HS (Abbott Laboratories), although only a generic version is available at this time. Bioidentical Testosterone is not allowed FDA for using in women.5,32 Decision use of testosterone, adding additional preparation is often conducted to choose methyltestosteron because it will increase the risk of hepatotoxicity and lipid effects are not pleasant [11].

The use of testosterone in women is most often considered in postmenopausal women, while women have symptoms such as reduced sense of comfort, low libido, unexplained fatigue, decreased muscle strength, and changes in cognition or memory, all sof this called "female androgen insufficiency". Several studies have shown that testosterone insufficiency resulted in low women sexual stimulation. Offer positive effect including improvement of sexual function, mood, pour density, and a skinny body. Although the data are limited, the addition of testosterone than estrogen in

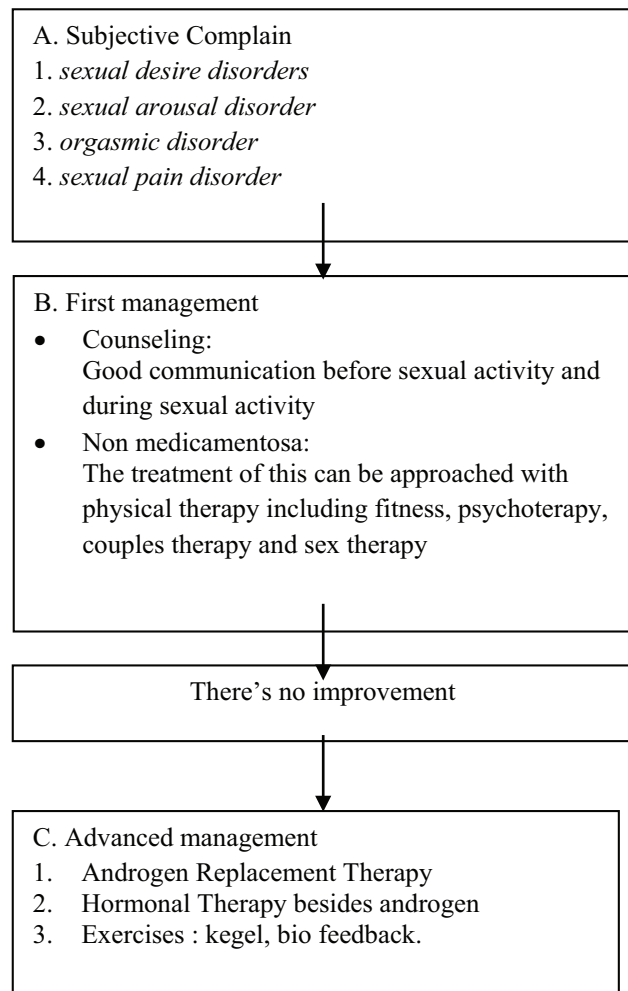
postmenopausal women resulted in a positive effect on sexual arousal. Data are inadequate to strengthen the use of testosterone to improve the symptoms of menopause, feeling comfortable, secure bone, or cognition [12].

Preliminary research finds positive effects of testosterone implants on estrogen replacement therapy in postmenopausal women who have lost their libido. Studd et al showed 136 of 300 women (43.5%) came to the clinic complaining about loss of libido, one of the three major problems. Women are persistent loss of libido, even if it had been given oral estrogen (conjugated equine estrogens 1.25 mg/day), which is treated with hormone implan (50 mg estradiol and 100 mg of testosterone) for 3 months. Libido improvement occurred in 80% of women, with reports of sexual response is better or equal to the time before menopause [6].

Sherwin et al. showed that women who received the combination therapy of estrogen/testosterone experienced a greater increase in sexual arousal compared with those who received estrogen only. Sarrel et al. indicate that estrogen only is not enough to resolve with all aspects of sexual function. Methyltestosterone adding estrogen to produce a significant improvement in sensation, desire and frequency of sexual activity. Somboonporn et.al. is reviewing the available literature on this subject and assess trials involving 1,957 patients. Estimates collected from the study showed that the addition of testosterone to hormone treatment (HT) improves sexual function score for menopausal women. The author of this review concluded that there are benefits of combining androgen to estrogen in terms of sexual function. However, the study looks at the meta-analysis using different testosterone regimens, making it difficult to estimate the effect of testosterone on sexual function in association with HT [3].

A randomized, double-blind and controlled by Kocoskda showed no significant effect of testosterone or estrogen treatment for four weeks on verbal memory, verbal fluency, or spatial abilities in healthy natural postmenopausal women. HT, so that similar serum levels of sex hormones such as in this study, suggesting important clinical effects. Estrogen is the most effective treatment for the relief of menopausal symptoms such as flushing, sweating, and sleep disorders. Estrogen is also used for osteoporosis prevention and treatment of vaginal dryness and dyspareunia. Testosterone therapy has been proven improving psychosexual functioning and well-being in postmenopausal women who experience sexual desire disorder. However, they failed to find support sex hormones affect cognitive performance. In a study in women with hypopituitarism-androgen deficiency, they did not find the effect of testosterone in the treatment of cognitive function [13].

Cardozo et al. (Al-Azzawi, et.al 2009) describe the effects of hormone implants subcutaneously in pre and postmeopause 120 women who came to the clinic menopause. A total of 67 postmenopausal women receiving 286 implants (50 mg estradiol and testosterone 100 mg every 4-12 months) for 4 years. Kesembuhn loss of libido reported on 67 women who lost their libido just before the start of treatment. In another study, Dow and colleagues, evaluated the testosterone implants (100 mg) with estradiol implant therapy (50 mg) compared with single estradiol implants in postmenopausal



**Figure 2:** Management of testosterone insufficiency in menopausal women in Indonesia [15].

women who experience a decrease in sexual interest. There is no significant difference between the two group [6].

Burger et al. (Sood R, et al, 2011) compared the efficacy of a combination of 100 mg testosterone implants and 40 mg of estradiol compared with a single 40 mg estradiol in postmenopausal women (either spontaneously or due to surgery) that has decreased libido during the use of progesterone and estrogen. At 6 weeks, improved libido and sexual pleasure recorded in women who treated with testosterone, and the improvement lasted until 18 weeks [11,14].

In Indonesia, the management of testosterone insufficiency in menopausal women can be seen in this chart below, where they divide into first level of management, and if it failed, it has to be referred to second level of management which is usually performed by a gynaecologist.

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