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# EFFECT OF SLEEP ON SERUM TESTOSTERONE LEVELS IN YOUNG MALE PATIENTS WITH DEPRESSION

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***Background:*** In our previous study we have reported that the testosterone levels of the young male patients with depression are significantly less then the testosterone levels of controls. In this study we report the effect of sleep on the serum testosterone levels of the same subjects. Methods: A pre-sleep sample and a post-sleep sample of blood was taken on two consecutive nights. Strict criteria for assuring the quality of sleep were observed. Testosterone was measured by radio-immunoassay, and the results were compared for statistical significance. ***Results:*** There was a highly significant rise of serum testosterone levels in the post-sleep samples of controls. The same rise was negligible in the patients with depression. ***Conclusion:*** In young male patients with depression the normal response of serum testosterone to sleep is impaired. This may be related to the etiology or severity of depression.

## INTRODUCTION

Testosterone secretion affects neurobehavioral functions such as sexual arousal, aggression, emotional tone, and cognition in men. About 20% of men over age 60 have lower-than-normal levels. The psychiatric sequelae are poorly understood, yet there is evidence of an association with depressive symptoms[1].

The relationship between testosterone and depression has been reported to be inverse for men with below average testosterone and direct for those with above average testosterone[2].

The data suggest that a blunted testosterone and an elevated cortisol secretion are state markers of acute depression, which normalize independently from sleep structure. An interaction between the hypothalamic-pituitary-gonadal axis and the limbic-hypothalamic-pituitary-adrenocortical axis appears likely[3].

Medical research shows that testosterone has positive effects on mood, thereby reducing the chances of depression, and social science research finds testosterone to be related to the factors known to be positively related to depression[2].

Gonadal function may be disturbed in men with a depressive episode of moderate to high severity[4]. Testosterone replacement therapy has been reported to be an effective treatment of some depressive symptoms in hypogonadal men[5].

This study is a continuation of our previously reported study in which we reported that testosterone level is significantly decreased in young patients with major depression[6]. Here we report further study of the same subjects to observe effects of overnight sleep.

## MATERIALS AND METHODS

The study was conducted at Ayub Teaching Hospital, Abbottabad. 25 young patients admitted with major depression were included in the study. A group of matching healthy men from amongst the attendants of the subjects was used as controls. The age range of all these subjects was 25-35 years.

In both the experimental and control subjects it was ascertained that they were sexually normal. This was done mainly by history taking.

Two samples of venous blood were taken from each subject. A sample was taken at or about 12 in the midnight, this was called the 'Pre-sleep sample'. The second sample was taken at 6.00 am and this was called "Post-sleep sample". The same was repeated on the following night.

Strict monitoring of the sleep was done. Awakening during sleep for more than three times in a night, awakening for more than 10 minutes at a stretch and sleep for less than 6 hours in a night was taken as sleepless night. The pre-sleep samples drawn on nights with disturbed sleep were discarded. All of the subjects were on some sort of medications. Precautions were taken to exclude medications with effects on hypothalamic-pituitary-gonadal axis.

Serum was extracted from all the samples and was stored. All the samples were then collectively sent for serum testosterone evaluation by radio-immunoassay, using a Gamma-B Testosterone kit.

Means of the values for two nights for pre and post sleep samples were calculated along with standard error of mean. The results of pre-sleep and post-sleep samples were then statistically compared using SPSS.

## RESULTS

The results of the pre and post sleep samples in controls and patients groups are given in table-1. There was a highly significant post-sleep increase in testosterone level of the controls. There was a negligible (not significant) post sleep increase in testosterone level of the patients. There was a highly significant difference of testosterone levels in controls and subjects, in both pre-sleep and post-sleep samples.

**Table-1: Serum testosterone levels in the pre-sleep and post-sleep samples of Patients & controls**

| Time of Sampling | Serum Testosterone Level ( nmol/L) | |
|---|---|---|
| | **Controls** | **Patients** |
| **Pre-sleep** | 32.02 ± 0.53 | 28.07 ± 0.40 |
| **Post-sleep** | 36.39 ± 0.42 | 28.84 ± 0.33 |

*The following means were statistically compared*

- *Controls Pre-sleep vs Controls Post-sleep: p<..001*
- *Patients Pre-sleep vs Patients Post-sleep: Non significant*
- *Patients pre-sleep vs Control pre-sleep: p<..001*
- *Patients post-sleep vs Control post sleep: p<..001*

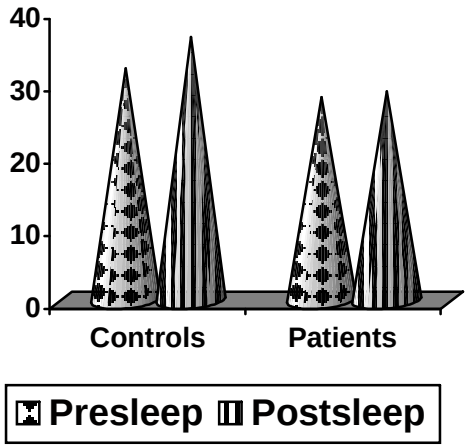


**Figure-1: Changes in testosterone levels in controls and subjects with overnight sleep**

## DISCUSSION

Our study clearly shows that the effect of sleep on serum testosterone level in depressed persons is different from that in the normal people. This may be related to quality of sleep or to the pattern of REM and NREM sleep. However, the reason for this needs further probing.

The relation between the rhythm of pituitary-gonadal hormones and sleep physiology in men is not fully elucidated[7].

A number of authors have reported variations in plasma testosterone during sleep[8-10]. Similarly some studies have reported about a circadian rhythm of testosterone and its relationship with sleep[11].

In a study by Judd *et al*[12]. mean testosterone levels during sleep were significantly higher than the wakeful levels. Similarly Schiavi *et al.*[13], observed abrupt elevations of plasma LH and testosterone during the night without a significant relationship to stages of sleep.

A sleep-wake rhythmicity in release of gonadotropins, particularly LH and thereby of testosterone, was seen to evolve transiently in twin boys across puberty[14].

In a recent study it was reported that in young adult men, testosterone levels begin to rise on falling asleep, peak at about the time of first REM, and remain at the same levels until awakening[7].

A study performed to determine the pattern of secretion of testosterone during the night in relation to the cyclically recurring periods of rapid eye movement (REM) and non-REM (NREM) sleep found no significant difference between the two[15].

Many studies of sex hormone concentrations in depression yielded inconsistent results. However, the activation of the hypothalamic-pituitary-adrenal system seen in depression may negatively affect gonadal function at every level of regulation[4].

Steiger *et al*[16]., suggested that a blunted testosterone and an elevated cortisol secretion are state markers of acute depression, which normalize independently from sleep structure. They suggested that an interaction between the hypothalamic-pituitary-gonadal axis and the limbic-hypothalamic-pituitary-adrenocortical axis appears likely.

In a study on patients with depression a significant fall in testosterone was reported after sleep deprivation[17] similarly sleep deprivation has been reported to cause a decrease in serum testosterone levels in normal persons.[18].

It is premature to say that abnormal response of testosterone to sleep may be a factor contributing to the degree of depression. However larger and better designed studies may reveal this relationship. Such studies may lead to a breakthrough in management of the male patients with depression.

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