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HORMONAL DISORDERS ASSOCIATED WITH INFERTILITY IN MALE

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ABSTRACT: Various hormone levels in males with subnormal semen analysis were performed. This study evaluated the sera levels of Prolactin (PRL), Follicle Stimulating hormone (FSH), Luteinizing hormone (LH) and Testosterone level (TESTO) in males with Azoospermia, Oligospermia, Asthenospermia, and Normospermia, with decreased motility according to recent World Health Organization Standards.

The hormonal profile showed normal or low level of testosterone while FSH and LH level indicated inverse/negative correlation to sperm concentration whereas no significant change between serum Prolactin and semen density was detected between different groups.

KEY WORDS: Serum FSH, Serum LH, Serum Testosterone, Serum Prolactin, Infertility.

INTRODUCTION

In general infertility is defined as that failure to conceive after 1 year of regular un-protective intercourse with the same partner. However, the term "Infertility" implies a definitive inability to conceive. Therefore, couples who do not conceive in > 1 year should be regarded as Sub-fertile. According to these definitions, approximately 14% of the couples are sub-fertile (Martin, 1999). To be more exact the term sub-fertile means a male who failed to conceive after I year of regular unprotected intercourse with the same partner and who had a sperm count of less than 20 million/ml (Wong, 2000).

Hormones and their role, which affect the spermatogenesis are testosterone and is secreted by leydig cells located in the interstitial of the testis. Testosterone is essential for growth and division of germinal cells in forming spermatozoa. Leutinizing hormone is secreted by anterior pituitary gland. This hormone stimulates the leydig cells to secrete by anterior pituitary gland and stimulate sertoli cells, without this stimulation conversion of spermatids to spermatozoa is not possible (Martini, 2001).

Human prolactin (hPRL) is a single chain polypeptide of 199 amino acids. It is produced by the anterior pituitary gland and its secretion is regulated physiologically by inhibitory (Talwalker *et ai.,* 1963) and releasing factor (Bower *et ai.,* 1971) of hypothalamus. Hyperprolactinemia has been established as a common cause of infertility and gonadal disorders in man and women.

Human follicle stimulating hormone (FSH, follitorpin) is a glycoprotein, consists of two non-covalently associated subunits designated a and ~. The a subunit of FSH contains 92 amino acids and the ~ subunit of FSH is unique and confers its immunological and functional specificity. FSH and LH control growth and reproductive activities of the gonadal tissues, FSH promotes follicular development in the ovary and gametogenesis in the testis (Catt and Piercer, 1978, Franchimant, 1973).

Human luteinizing hormone (LH Lutropin) is a glycoprotein hormone with two dissimilar subunits a and ~, the a subunit of LH contains 92 amino acid residues and the ~ subunit contains 112 amino acid residues and considerably different from that of FSH and TSH (Pierce and Persons 1981,) However, the ~ subunit of LH and hCG are similar, the structural similarities between LH and hCG are responsible for the observed similarity in biological properties (Bishop *et ai.1976).* The primary role of LH in male is to stimulate the production of testosterone by the ley ding cells, LH through the production of testosterone together with FSH regulates spermatogenesis in the sertoli cells of the seminiferous tubules of the testis. Testosterone exerts a negative feedback on the release of LH (Griffin and Wilson, 1985).

The hormonal regulation of testis begins in the hypothalamus which synthesizes and releases in a pulsatile manner, a decapeptide gonadotropin releasing hormone (GnRH), this hormone regulates the secretion of pituitary hormone which in turn through a complex feed back mechanism between the various hormones, regulate testicular hormone secretion.

Table
Mean (:!: SEM) hormonal level of Azoospermic, Oligospermic, Astbenospermic and Normospermic Patients.

No. of Patients	Condition	FSH mlU/ml	LH mlU/ml	Prolactin nmol/ml	Testosterone nmol/ml
50	Azoospennic	22.9:!:6.3**	12.2:!:5.4**	254:!:20 NS	8.85:!:2.2 NS
50	Oligospermic	16.6+2.8**	10.6:!:0.8**	242:!:25 NS	8.3:!:2.7 NS
50	Asthenospermic	3. 19:!:0.9 NS	4.2:!:0.9 NS	239:!:19 NS	11.05:!:3.0 NS
50	Normospermic	5.5:!:1.0 NS	5.6:!:0.5 NS	258:!:34 NS	22.5:!:3.5NS

NS= Non-Significant (P>0.05), *Significant (P<O.05), **= Highly significant (P<O.Ol)
Number patients for each observation = 50.

Two pituitary gonadotropic hormones are present in male Luteinizing hormone (LH) and follical stimulating hormone (FSH). LH stimulates the leyding cells to convert cholesterol to testosterone. FSH induces the sertoli cells to form androgen-binding protein, which may assist testosterone movement toward the seminifreous tubular leu men and the epididymius. FSH also induces the sertoli cells to convert testosterone to 5-dihydrotrstosterone-17~estradiol. The 5a-DHTT is more active than testosterone. Testosterone is responsible for the maintenance of spermatogenesis, where as FSH is needed to initiate spermatogenesis at the onset of puberty.

Hormonal integration of the hypothalamic pituitary-testicular axis is a basic requirement for normal spermatogenesis and any hormonal imbalance may result in the partial or complete compromise of fertility potential.

MA TERIALS AND **METHODS**

Subjects: A total of 200 subjects were included in the study. Subjects were categorized as normospermic, azoospermic, oligospermic and asthenospermic on the basis of their spermiogram.

Methods: Semen analysis is usually performed as part of the comprehensive investigation of an infertile couple, routine semen analysis was used to categorize the infertility as oligospermia, Azooseprmia etc.

Macroscopic and microscopic analysis was used. Macroscopic analysis includes determination of semen appearance, coagulation and liquefaction time, colour, odor, viscosity and volume. The microscopic analysis consists of determination of the presence of non-sperm cellular elements, sperm agglutination, sperm concentration, sperm motility and sperm morphology which are the standard parameters of routinely used to indicate the potential fertility "status of specimen".

Several ejaculates from the same subject used to be analyzed to obtained objective data, optimatory ejaculated should be analyzed every 2 to 3 weeks until four ejaculates have been studies to better assess the clinical diagnosis. Standard method for collection of semen was used. Semen was analyzed with in 30mm to 1 hour.

All the studies were conducted with the consultation of gynecologist at the Gyne Department of teaching Hosphital of Gomal Medical College D.I.Khan.

Blood samples of different category of infertile were collected, Blood serum was preserved and stored at O°C, measurements of Hormonal levels LH, FSH, Prolactin and Testeosterone levels were measured using double antibody RIAs using reagents supplied by National Institute of Health Islamabad. (FSH-RP-L, LHRP-I, were the standard used) All samples and standard were assayed in duplicate.

Hormonal Assessment: The hormonal profile was analyzed using Abbott Microparticle Enzyme Immunoassay (MEIA) technique for FSH, LH, Prolactin and Roche Cobos core system for Testosterone (Enzyme- immunological Test) and Boebringer Mannheim Immiunodiagnostics.

Statistical Analysis: Data were analyzed statistically, by application of Student's 't' test, as described by Steel and Tome (1960).

RESULTS

Male infertility can be assessed though spermiogram and hormonal profile (Guyton, 1981). Absence of spermatozoa in the semen ejaculate is called "azoospermia", count less than 20 million/ml "Oligospermia" and density of 20 million/mi but motility of less than 50% is called "asthenospermia' (Amelar, 1966).

Male infertility is associated with a reduction in the quantity of sperms (McElreavey *et aZ.,* 2002). Decrease in sperm density, eventually leading to azoospermia, has been found to be associated with raised FSH, LH and normal or low testosterone level (Merino and Carranza-Lira, 1995).

The results of the study are given in Table. The serum FSH levels of subjects in groups, Asthenospermic and Normospermic, were 3.19 :to.9 (Range 2.2-11) and 5.5:t1.0 (Range 2.1-12.7) respectively. Serum LH concentrations (mID/ml) in azoospermic subjects were higher than the values observed in all other groups, that is 12.20:t 5.4 (Range 0.1- 56.6) whereas the mean serum LH values varied between 4.2 to 10.6 mlU/ml in the other groups. There was no marked difference in the concentrations of serum prolactin levels nmol/L among the different groups of men.

DISSCUSSION

Present results show that in azoospermic and oligozoospermic men serum FSH levels were significantly elevated, which correlate with previous studies (Subhan *et aZ.,* 2000; Wong *et aZ.,* 2000). FSH profile in secretory azoospermic men has been found to be different from that found in men with excretory (obstructive) azoospermia (Garcia-Diez *et aZ.*, 1983). Of the 50 azoospermic men in our study, 18 subjects showed normal levels of serum FSH, indicating that they may be representing cases of excretory azoospermia. Increase in FSH levels, representing secretory azoospermia, may reflect decreased testicular activity resulting in an alteration of the normal feed back mechanism between the testes and the hypothalamic pituitary axis, though an impairment of the Sertoli cells, and decrease inhibit secretion (Subhan *et aZ.,* 2000). Tubular damage accompanied with a rise in serum FSH (Mann and Lutwak-Mann,
1981).

In addition to FSH, LH showed to be inversely correlated with sperm density (Garcia-Diez *et aZ.,* 1983; Stan well-Smith *et aZ.,* 1985). In the present study no significant differences were detected in the prolactin levels between different groups.

On the basis of present data, it is concluded that azoospermic and oligozoospermic subjects are accompanied by a significant rise in FSH levels, and decrease in serum testosterone level. Measurement of FSH in serum, therefore, may be used with advantage in the diagnosis of spermatogenic dysfunction and also to differentiate between secretory and excretory azoospermia (Subhan *et aZ.,* 1995 & 2000). Increased serum LH and decreased testosterone & levels indicate an abnormality in the steroidogenic tissue of the testis may not necessarily accompany the rise in FSH in men with depressed spermatogenesis. The need of measuring prolactin levels in the evaluation of male infertility, at present, appears unnecessary. However, for the evaluation of pituitary tumors, it is quite significant.

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