

A CORRELATION OF SERUM INHIBIN WITH SPERM COUNT AND SPERM MOTILITY IN FERTILE AND INFERTILE MALES

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Inhibin is produced by Sertoli cells of the testis, provides negative feedback on FSH secretion, and may prove to be an important marker for the functioning of seminiferous tubules. The purpose of this study was to examine the relationship between the spermatogenic function of the tests of subfertile men and the plasma concentrations of inhibin. The study was carried out on twenty infertile (or subfertile) males and ten age-matched control subjects with proven fertility. Infertile subjects were subdivided into oligospermic, normospermic and azospermic on the basis of their sperm count. In infertile subjects mean serum inhibin concentration (30.4 ± 22.2 pg/ml) was higher as compared to fertile subjects (25.2 ± 8.5 pg/ml), although the difference was not statistically significant ($p > 0.05$). Among the subgroups of infertile subjects mean serum inhibin level in azospermics, who showed testicular atrophy on biopsy, was 8.2 ± 1.1 pg/ml, which was significantly lower ($p < 0.002$) than fertile subject. The mean sperm count of infertile subjects was significantly lower than fertile subjects ($p < 0.01$). The mean percentage of progressively active sperm was significantly lower in infertile than fertile subject ($p > 0.001$) while mean percentage of immotile sperms was significantly higher in infertile than fertile subjects ($p < 0.001$). Sluggishly motile sperms did not show a significant difference between two groups. No significant correlation of serum inhibin with either sperm count or sperm motility was observed in both, fertile as well as infertile subjects. These results indicate that serum inhibin concentration is decreased in case of damage to the seminiferous tubules, however absence of any correlation of serum inhibin with sperm count and sperm motility questions its validity in place of traditional parameters used for assessment of male infertility.

INTRODUCTION

In 1932, McCullagh postulated the existence of a specific hormone of the testis, regulating FSH secretion. He named this hormone "inhibin". We know today, several proteins of the inhibin family are produced in the Sertoli cells. The major product is inhibin B, consisting of an alpha-and a beta-subunit. It is also present in spermatogonia, spermatocytes and early spermatids. The serum levels of inhibin B increase in puberty. In an adult man they are correlated positively to sperm count and testis volume, but negatively to FSH levels^{1,2}. Testicular production of inhibin B is believed to be dependent on the presence of germ cells within the seminiferous tubules³. Currently, serum inhibin B levels, indicating testicular function due directly to its testicular origin, has been used increasingly in assisted reproductive units^{4,5}.

Subfertility affects about 15% of all couples. Assessment of spermatogenesis has a central role in the evaluation of the subfertile couple. Classical markers of spermatogenesis, such as semen analysis, testicular biopsy and endocrine evaluation all have their diagnostic limitations. There is a clear need for accurate additional markers of spermatogenesis. Recently, the serum inhibin B level has emerged as a sensitive endocrine marker of spermatogenesis⁶. The fact that inhibin is a modulator of pituitary FSH, which in turn controls testicular functions, led the andrologists to study any correlation of inhibin with other sex hormones or with sperm count or motility in normal and infertile males^{7,8,9,10}. The effect of inhibin administration to the experimental animals has revealed significant reduction in the number of testicular and epididymal spermatozoa and their motility^{11,12}. On the other hand, in human

being many workders did not find any correlation between serum inhibin and sperm count and motility^{13,14,15}. This study was designed to find out any correlation of serum inhibin with sperm count and sperm motility in fertile and infertile males.

SUBJECTS AND METHODS

Twenty infertile males, between 25-35 years of age, who were referred to pathology laboratory of PGMI for infertility evaluation, were selected for this study. Ten age-matched subjects with proven fertility were included as controls. Semen samples were collected by masturbation in all the subjects and examined for pH, volume, sperm morphology, motility, and count according to the standard procedures¹⁶. Blood samples for serum inhibin estimation were taken between 8-9 am. Serum was separated as soon as possible and stored in aliquots at -20°C ¹⁷. Serum inhibin was estimated by immunoenzymetric assay by Serotec, England.

The data was given as the mean \pm SD. Comparisons of data between fertile, total infertile and different subgroups of infertile subjects were evaluated by Student's *t* test and Wilcoxon's rank sum test. Coefficient of correlation (*r*) was used to calculate the relationship between serum inhibin and parameters of semen analysis namely seprn count and sperm motility.

RESULTS

Infertile subjects were subdivided into three groups depending upon their sperm count.

Oligospermic group comprised of 14 subjects with sperm count below 40 million/ml. Normospermic group, having sperm count above 40 million/ml comprised 4 subjects while azospermic group comprised of 2 subjects. The results are given as follows.

Serum Inhibin Levels

The mean (\pm SD) inhibin levels in fertile and total infertile subjects are compared in figure I. Mean serum inhibin concentrations in infertile subject is higher than fertile subjects, although difference was not statistically significant.

The mean (\pm SD) inhibin levels in different subgroups of infertile subjects are given in figure II. When different groups of infertile subjects were compared with each other or with fertile subjects, no significant difference was found except between azospermic and fertile subjects ($p < 0.05$).

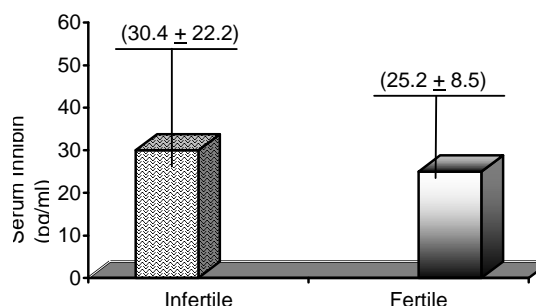


Fig. 1: Comparison of serum inhibin levels of infertile and fertile subjects.

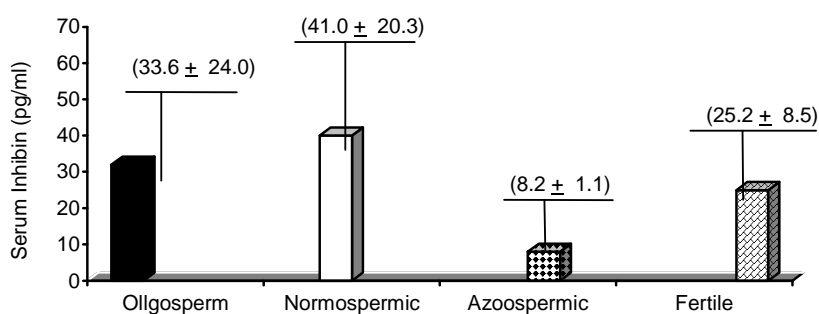


Fig. 2: Comparison of serum inhibin levels of subgroups of infertile male subjects.

Sperm Count

Mean (\pm SD) sperm count and their range values for study and control groups are shown in table I. The difference of sperm count between fertile and infertile groups was statistically significant ($p < 0.01$). When different subgroups of infertile subjects were compared with each other or with fertile subjects the difference was statistically significant.

Table 1: Sperm count of fertile and infertile males given as mean \pm SD. Figures in parenthesis are the range values.

Subjects	Sperm Count (million/ml)
Total Infertile Subjects (n=20)	24.0 \pm 20.1 (0-80)
Oligospermic Infertile Subjects (n=14)	14.2 \pm 11.8 (0.05-30)
Normospermic Infertile Subjects (n=04)	63.0 \pm 17.4 (40-80)
Azospermic Infertile Subjects (n=02)	0
Fertile Subjects (n=10)	70.6 \pm 11.0 (50-85)

Sperm motility

The motility of spermatozoa of infertile and fertile subjects was studied immediately after

liquefaction. The motility was distributed into motile and immotile. Motile spermatozoa were further distributed into active (progressive) and sluggish (non progressive). Mean (\pm SD) sperm motility and their range values for study and control groups are shown in table II.

a. Active (Progressive) Motility:

The difference of active motility between fertile and infertile subjects was statistically highly significant ($p < 0.001$). In addition, when different subgroups of infertile subjects were compared with fertile subjects, difference was statistically highly significant.

b. Sluggish (Non-Progressive) Motility:

No significant difference of sluggish motility was found between fertile and infertile subjects. When different subgroups of infertile subjects were compared with fertile subjects, significant difference was found between oligospermic vs. fertile and normospermic vs. fertile subjects.

c. Immotile Spermatozoa:

A highly significant difference ($p < 0.001$) of immotile sperms was found between fertile and infertile subjects. When different subgroups of infertile subjects were compared with fertile subjects, highly significant difference was found between oligospermic vs. fertile and normospermic vs. fertile subjects.

Table 2: Sperm count of fertile and infertile males given as mean \pm SD. Figures in parenthesis are the range values.

Subjects	Immediate Sperm Motility (%)		
	Progressive (Active)	Non-Progressive (Sluggish)	Immotile
Total Infertile Subjects (n=20)	12.5 \pm 10.9 (0-40)	29.0 \pm 24.4 (0-70)	48.5 \pm 30.0 (0-95)
Oligospermic Infertile Subjects (n=14)	15.7 \pm 11.0 (5-40)	38.9 \pm 22.3 (0-70)	45.3 \pm 23.0 (20-90)
Normospermic Infertile Subjects (n=04)	7.5 \pm 6.4 (0-15)	8.7 \pm 7.5 (5-20)	33.7 \pm 11.1 (70-95)
Azospermic Infertile Subjects (n=02)	0	0	0
Fertile Subjects (n=10)	70.5 \pm 5.5 (60-80)	91.0 \pm 4.6 (10-30)	9.0 \pm 4.5 (5-20)

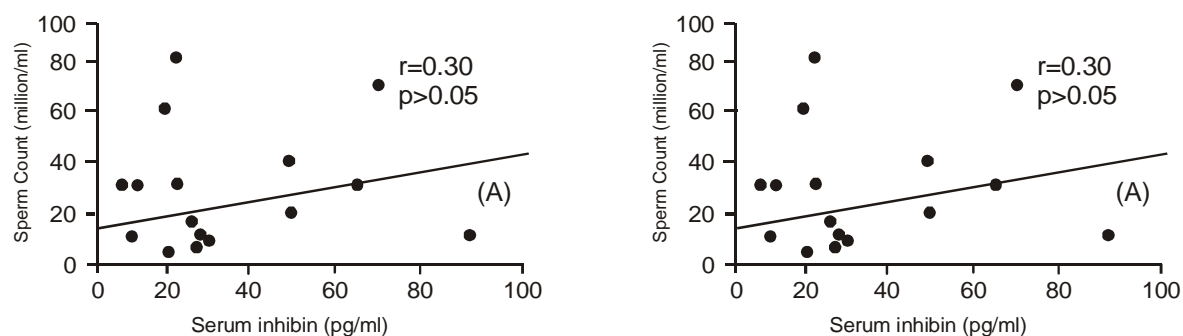


Fig. 3: Correlation of serum inhibin with sperm count in fertile (A) and infertile (B) male subjects.

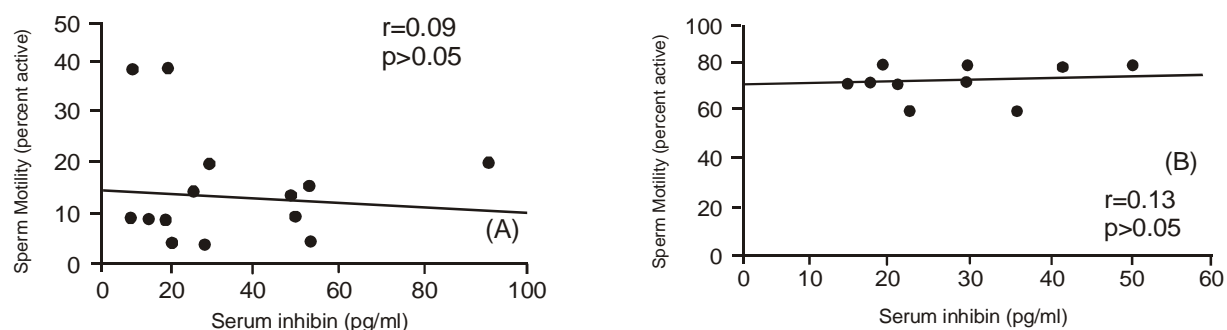


Fig. 4: Correlation of serum inhibin with sperm motility in fertile (A) and infertile (B) male subjects.

Correlation of Serum Inhibin with Sperm Count and Sperm Motility:

No statistically significant correlation of serum inhibin with sperm count or sperm motility was observed in both, fertile as well as infertile subjects (figure III and IV).

DISCUSSION

The predominance of inhibin secretion into the eminiferous tubule during testicular maturation suggested that it might have an important paracrine or autocrine role in the developmental biology of spermatogenesis¹⁸. The inhibin measurements in serum and its correlation with sperm count and motility and with other male sex hormones have been a subject of interest for the last so many years^{2,12,15,19}. There is no consensus on where the limit of abnormally low sperm count should be set in order to be a cause of infertility. However, it has been documented that conception rate decreases significantly below a sperm count of 20 million/ml^{20,21}. Sperm count is usually used

as the basis for characterizing the semen into different groups, namely oligospermic, normospermic and azospermic. However, sperm motility is probably the most important parameter of the semen analysis for fertility prediction²².

In this study mean serum inhibin concentration was higher in infertile as compared to fertile subjects, however this difference was not significant statistically. Similar observation was made by many other workers^{14,15,23} which among the subgroups of infertile subject mean serum inhibin concentration was significantly lower in azospermic than fertile subjects. Azoospermia in our subjects was due to testicular atrophy, which was shown on biopsy. However, further studies in this respect are suggested in which serum inhibin may be implicated to differentiate between obstructive and non-obstructive azoospermia^{9,24}.

In this study no significant correlation of serum inhibin with sperm count and sperm motility was observed both, in fertile and infertile

subjects. This finding is in agreement with many earlier studies^{9,14,15} while against many others^{4,10,12,25,26}. In fact control of inhibin secretion by healthy spermatogenesis and in turn effect of serum inhibin on sperm maturation has been a matter of great debate over the years and different workers obtained different results. The reason for this difference, as suggested in earlier studies, was lack of availability of a purified, homogeneous inhibin preparation for standardization of inhibin immunoassays. However later it was also suggested that inhibin may also be differentially regulated and contribution of sex glands may limit the use of inhibin as a marker of spermatogenesis¹⁰.

We conclude that serum inhibin levels may be a serum marker of Sertoli cell function, but the prediction of the quality of spermatogenesis is not superior to that of other conventional parameters like serum FSH and sperm count and motility. In summery although inhibin B is a valuable index of spermatogenesis, the measurement of serum inhibin is still of limited clinical relevance for individual patient.

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