Serum Inhibin B Concentration as a Prognostic Factor for Prediction of Sperm Retrieval in Testis Biopsy of Patients with Azoospermia

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**Background:** This study was conducted to determine if serum inhibin B concentration can predict spermatogenesis in azoospermic infertile men.

**Methods:** This cross-sectional study included 70 patients with male-factor infertility referred to Alvand and Vali-e-Asr Infertility Centers, Tehran, Iran. All patients had azoospermia. Standard evaluation consisted of history and physical examination with extreme attention to sexual history and testis examination including testis size, consistency, and presence of varicocele. Laboratory evaluation done for all cases consisted of FSH, testosterone, LH, prolactin, and inhibin B. Testis biopsy was performed in all cases with acceptable testis volume and FSH. The mean inhibin B level was compared in groups with positive and negative sperm retrieval.

**Results:** The mean±SEM age of 70 azoospermic patients was 32.1±6.2 (range: 20 – 50) years. All couples had primary infertility with a mean±SEM duration of infertility of 74.3±7.7 months. The mean±SEM testicular volume was 10.14±0.75 mL. The mean±SEM FSH and LH levels were 17.55±1.68, and 11.33±0.99 mIU/mL, respectively. The mean±SEM serum prolactin and testosterone levels were 308.77±17.35 and 5.45±0.91 ng/dL, respectively. The mean±SEM serum inhibin B concentration was 138.23±28.58 (range: 15 – 1500) pg/mL. Sperm was not retrieved in 82% of the patients; in 13% of the cases, biopsy revealed spermatogenesis. The mean±SEM serum FSH level of positive and negative groups was 9.78±2.13 and 22.56±2.46 mIU/mL, respectively (P<0.05). The mean serum LH, prolactin, and testosterone levels were not statistically different between the two groups. The mean±SEM serum inhibin B was 129±45.46, and 158.93±47.24 pg/mL in positive and negative groups, respectively (P>0.05).

**Conclusion:** Inhibin B concentration is not an appropriate predicting factor for testicular spermatogenesis.

**Keywords:** Azoospermia • inhibin B • sperm retrieval

**Introduction**

According to WHO, “infertility” is defined as an inability to conceive after one year of unprotected intercourse.1 Infertility treatment in azoospermic males is based on sperm retrieval. Several factors have been proposed to predict sperm retrieval in testicular biopsy noninvasively. The serum FSH and testis size are currently proven predictors of sperm retrieval, but neither is completely reliable.

This study was conducted to assess the value of serum inhibin B level in prediction of sperm retrieval. Inhibin, a 32-kD glycoprotein hormone secreted primarily by Sertoli cells, suppresses FSH secretion by negative feedback. Inhibin B selectively suppresses FSH secretion in gonadotropes by inhibiting transcription of the gene encoding the β-subunit of FSH. The clinical use of inhibin B as a marker of impaired testicular function is controversial.

Vernaeve and colleagues2 performed a study on 185 men with nonobstructive azoospermia and concluded that inhibin B alone or in combination with FSH cannot predict biopsy results. On the
other hand, Ballesca and colleagues\(^3\) performed the same study on 17 nonobstructive men and concluded that inhibin B is a good predictor of sperm retrieval. Brugo-Olmedo et al.\(^4\) compared the predictive value of inhibin B in 78 nonobstructive, 15 obstructive, and 10 normal control men. Those with nonobstructive azoospermia had significantly higher FSH, and lower inhibin B levels. The mean inhibin B value in nonobstructive azoospermia was higher when sperm had been retrieved compared with those with negative biopsy, while FSH failed to show such a relation. They concluded that inhibin B has a higher predictive value compared with FSH. These conflicting results made us to conduct this study to determine if inhibin B can predict sperm retrieval in azoospermic males.

### Patients and Methods

This cross-sectional study included 70 men presenting with azoospermia to Alvand and Vali-e-Asr Infertility Centers, Tehran, Iran for treatment of infertility from December 2004 through December 2005. Fertility history and physical examination including measurement of testis size were obtained in all patients along with routine laboratory evaluation of hormones including serum FSH, LH, prolactin, testosterone, and inhibin B levels (Oxford Bio-Innovation UK kit). Biopsy was performed in all patients with testicular volume >5 mL and FSH <2-fold the normal value, regardless of the inhibin B concentration. Patients with very small testis (<5 mL), and FSH value >2-fold the normal value were exempted from biopsy and excluded from the study as performing biopsy may impair androgen production. Every patient who met these inclusion criteria for testis biopsy entered the study. The patients were categorized into two groups according to their biopsy results. The inhibin B level was then compared in those with retrieved sperm (in either testis) and those without it.

Parameters were presented as mean±SEM. Independent-sample Student’s \(t\)-test was used to compare the means. Binary logistic regression analysis was also used to test the effect of combined main variables with pathology results. A \(P\) value<0.05 was considered statistically significant. The sample size of 38 patients was determined according to the standard deviation (4.7 pg/mL) and the accuracy (1.5 pg/mL) of the Oxford inhibin B kit assuming a 95% confidence interval.

### Results

The measured parameters are summarized in Table 1. Unilateral testis atrophy was evident in only four patients while 61.4% of the patients had bilateral testis atrophy. Of 70 patients studied, 44.3% had no previous history of illness related to infertility; 12.9% had unilateral and 5.7% had bilateral varicocele; 4.3% and 1.4% had history of bilateral and unilateral orchiopepsy, respectively; 2.9% underwent herniorrhaphy; and 1.4% had received chemotherapy. History of urinary tract infection was positive in 1.4% and of orchitis was positive in 2.9% of the patients. Sperm was retrieved in 12.9% of the patients and 81.6% failed to show complete spermatogenesis.

Patients with positive pathology results have been married for a mean±SEM of 89.33±24.01 months.

The mean age of those with negative biopsy results was not significantly different from those with positive results (Table 1, \(P=0.38\)). Patients with negative biopsy have been married for a mean±SEM of 78.02±11.11 months, which had also no significant difference with the positive group (\(P=0.66\)).

The mean serum FSH level had significant difference with that of the positive group (Table 1, \(P<0.0001\)). The mean serum LH, prolactin, testosterone, inhibin B, and testicular volume in those with negative results did not have a

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All patients</th>
<th>Spermatogenesis</th>
<th>No spermatogenesis</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>70</td>
<td>9 (81.4%)</td>
<td>40 (81.6%)</td>
<td>0.38</td>
</tr>
<tr>
<td>Age</td>
<td>32.14±0.75 (yr)</td>
<td>33.78±2.36</td>
<td>31.68±1.63</td>
<td>0.45</td>
</tr>
<tr>
<td>Duration of infertility</td>
<td>74.33±7.72 (mo)</td>
<td>89.33±24.01</td>
<td>78.02±11.11</td>
<td>0.66</td>
</tr>
<tr>
<td>Testis volume</td>
<td>10.14±0.75 (mL)</td>
<td>10.94±1.88</td>
<td>9.44±0.95</td>
<td>0.49</td>
</tr>
<tr>
<td>Testosterone</td>
<td>5.45±0.91 (ng/dL)</td>
<td>3.81±0.46</td>
<td>4.66±1.61</td>
<td>0.51</td>
</tr>
<tr>
<td>Prolactin</td>
<td>308.77±17.35 (ng/mL)</td>
<td>363.38±86.98</td>
<td>302.19±18.94</td>
<td>0.51</td>
</tr>
<tr>
<td>LH</td>
<td>11.33±0.99 (mIU/mL)</td>
<td>7.62±1.61</td>
<td>13.43±1.54</td>
<td>0.058</td>
</tr>
<tr>
<td>FSH</td>
<td>17.55±1.68 (mIU/mL)</td>
<td>9.78±2.13</td>
<td>22.56±2.46</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Inhibin B</td>
<td>138.23±28.58 (pg/mL)</td>
<td>129±45.64</td>
<td>158.94±47.24</td>
<td>0.77</td>
</tr>
</tbody>
</table>

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**Table 1.** The measured parameters in the study groups.
statistically significant difference with those of the positive group (Table 1).

In binary regression model, only FSH level had significant correlation with sperm retrieval results ($P=0.03$); the testis size and inhibin B level did not have any significant correlations with sperm retrieval ($P=0.63$, $P=0.53$, consecutively). It means that combination of inhibin B with FSH and testis size would not improve the predictability.

**Discussion**

So far, several studies have been performed to examine the predictability of serum inhibin B concentration for prediction of sperm retrieval in men with azoospermia. In our study, serum inhibin B level could not predict the outcome of biopsy in men with azoospermia. Jensen and colleagues\(^7\) in 1997 reported that in nonselective men of healthy fertile couples, inhibin B level has a significant correlation with FSH and sperm density. In our study, however, all patients were azoospermic. Although FSH could predict sperm retrieval, inhibin B failed to do that. Ballesca and coworkers\(^8\) in 2000 compared 17 men with nonobstructive azoospermia with some fertile men with obstructive azoospermia and concluded that inhibin B can predict sperm retrieval in nonobstructive azoospermia. This result was confirmed by Vernaeve and colleagues\(^6\) in 2002. Brugo-Olmedo and colleagues\(^4\) recognized that inhibin B is a good marker for prediction of spermatogenesis in nonobstructive azoospermia. We thought of dividing the positive cases into two groups but it would decrease the study power. Furthermore, dividing patients into obstructive and nonobstructive is only possible when the results of the biopsy are available, while we were looking for a marker that predicts the results of biopsy before it is performed. So, we did not divide the positively retrieved cases into obstructive and nonobstructive. In 1999, von Eckardstein and coworkers,\(^7\) in a study on 91 patients concluded that inhibin B only in conjunction with FSH can predict spermatogenesis. Accordingly, Bohring and colleagues\(^8\) in 2002 declared combination of FSH and inhibin B as the best marker of spermatogenesis. Binary logistic regression showed that only FSH is statistically correlated with the retrieval and the model in our study did not show that inhibin B in combination with FSH or testis size would increase the predictability.

It seems that the testis size $>5$ mL would lead to no significant correlation with sperm retrieval and that if all azoospermic cases had been studied regardless of their testes size, the variable would then become significant, although limited number of cases or combination of obstructive and nonobstructive patients might distort the statistics.

The only proven predictor of sperm retrieval is FSH. Therefore, when FSH value is $>2$-fold the normal value, biopsy should be performed with caution. Testis size $>5$ mL does not significantly predict the result of the biopsy. Therefore, biopsy should be advised in every azoospermic patient with testis size $>5$ mL. Serum inhibin B level is not a good predictor of sperm retrieval alone or in combination with FSH and testis size and should not be used for exclusion of patients from doing biopsy.

**References**