Quantitative Analysis of Testicular Biopsies in Acquired Obstructive Azoospermic Patients


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Abstract

Objectives: To assess quantitative deterioration of the testicular spermatogenic capacity in Obstructive Azoospermia (OA) in relation to the duration of obstruction and the patients' age.

Methods: Retrospective analysis of forty seven histopathology testicular biopsy slides of acquired obstructive azoospermic patients who underwent TESE/ICSI, were analyzed using Johnsen score and late spermatid score. Biopsies with sperm granulomas were recorded.

Results: The mean patient age was 41.8 years with a mean obstructive duration of 12 years. Only five slides showed the presence of sperm granuloma. No statistical correlation was found between Johnsen score and interval of obstruction (p=0.574) nor the age of the patient (p=0.506). No correlation was found between late spermatid score and interval of obstruction (p=0.113) or the patient's age (p=0.401).

Conclusion: Duration of obstruction, patient's age and presence of sperm granulomas do not affect spermatogenic capacity proved by 2 quantitative analyses for the first time.

Key Words: Obstructive azoospermia – Quantitative analysis – Johnsen score – Late spermatid score – Spermatogenesis.

Introduction

OBSTRUCTIVE Azoospermia (OA) is the complete absence of spermatozoa in the ejaculate despite normal spermatogenesis. It is considered a common andrological condition which accounts for 6.1% to 13.6% of patients presenting for fertility evaluation [1].

Causes of obstructive azoospermia might be either congenital (lifelong) such as bilateral absence of vas or acquired, due to infection or iatrogenic causes.

The most common cause for obstruction in the developing countries would be infection, while vasectomy is the leading cause in developed countries [2]. Iatrogenic injury other than vasectomy was shown to be the cause of obstruction in 8-19% of patients diagnosed with obstructive azoospermia [3].

Achieving fertility in obstructive azoospermic patients depends on multiple factors, including: etiology, level of obstruction, duration and the pathology of obstruction. Taking the previous factors into consideration, the most appropriate therapeutic line could be either corrective surgery (vasoepididymostomy, vasovasostomy, transurethral resection of the ejaculatory ducts) or Testicular Sperm Extraction (TESE) and Intracytoplasmic Sperm Injection (ICSI) [4]. The main advantage of surgical intervention, is giving the couple the chance for future spontaneous normal conception with less cost and reduced risks [5].

Does the duration of obstruction really affect the competency of the testicular tissue? Herein we tried to find an answer for this question.

Patients and Methods

Retrospective analysis and review of our records for ICSI/TESE patients in the last 10 years were done. Patient records showing an obstructive azoospermia diagnosis were selected and critically reviewed. Patients with congenital obstruction such as Bilateral Congenital Absent Vas (BCAV) or congenital mid line prostatic cyst, were excluded from the study. Forty seven patients with history of normal semen that deteriorated into azoospermia following infection or related surgical procedure in which testicular histopathology was done during ICSI/TESE were included in the study. Twenty
seven males were found to be related to previous genitourinary infection. 10 due to iatrogenic injury either hernioplasty or hydrocelectomy, one case following vasectomy and no specific cause was found for the remaining nine cases. All slides were evaluated using quantitative methods described by Johnsen (1970) [6] and Silber and Rodriguez-Rigau (1981) [7]. Presence of sperm granuloma was also determined. Detection of the date of obstruction was done using date of last normal semen, date of the surgery-hernia repair, bilateral hydrocelectomy or vasectomy.

**Results**

The mean patient age was 41.8 years with a mean obstructive duration of 12 years. Five slides (10.6%) showed sperm granuloma with no deterioration of spermatogenic capacity.

Correlation between various variables was done using Pearson moment correlation equation for linear relation in normally distributed variables and Spearman rank correlation equation for non-normal variables/non-linear monotonic relation. \( p \)-values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) (Release 15 for Microsoft Windows (2006)).

Table (1): Pearson moment correlation between late spermatid score and both duration of infertility and age of the patients.

<table>
<thead>
<tr>
<th>Duration</th>
<th>Age</th>
<th>Pearson correlation</th>
<th>( p )-value</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.234</td>
<td>-0.125</td>
<td>0.113</td>
<td>-0.401</td>
<td>47</td>
</tr>
</tbody>
</table>

Table (2): Pearson moment correlation between Johansen score and both duration of infertility and age of the patients.

<table>
<thead>
<tr>
<th>Duration</th>
<th>Age</th>
<th>Pearson correlation</th>
<th>( p )-value</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.084</td>
<td>-0.099</td>
<td>0.574</td>
<td>0.506</td>
<td>47</td>
</tr>
</tbody>
</table>

From (Tables 1,2), by using Pearson moment correlation equation for linear relation in normally distributed variables no statistical correlation was found between Johnsen score and duration of obstruction \((p=0.295)\) nor the age of the patient \((p=0.187)\). No correlation was found between late spermatid score and interval of obstruction \((p=0.314)\) nor the age of the patient \((p=0.269)\).

Table (3): Spearman rank correlation equation between late spermatid score and both duration of infertility and age of the patients.

<table>
<thead>
<tr>
<th>Duration</th>
<th>Age</th>
<th>Spearman's rho</th>
<th>( p )-value</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.156</td>
<td>-0.196</td>
<td>0.295</td>
<td>0.401</td>
<td>47</td>
</tr>
</tbody>
</table>

Table (4): Spearman rank correlation equation correlation between Johansen score and both duration of infertility and age of the patients.

<table>
<thead>
<tr>
<th>Duration</th>
<th>Age</th>
<th>Spearman's rho</th>
<th>( p )-value</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.150</td>
<td>-0.165</td>
<td>0.314</td>
<td>0.269</td>
<td>47</td>
</tr>
</tbody>
</table>

**Discussion**

It has long been speculated that obstruction causes an increase in the intraluminal pressure and this might precipitate functional deterioration in the testis [8].

Most animal studies focused on the effect of vasectomy as a major cause of obstruction on the sperm functions and the accompanying histopathological alterations in the epididymis, which include, decreased sperm motility, increased incidence of sperm granuloma, increased epididymal tubular lumen diameter and increased inflammatory infiltrate in epididymal tissue [9,10].

Human studies on the testicular histopathological changes accompanying acquired obstructive azoospermia other than vasectomy cases are limited.

In our study, we found that there is no statistical correlation between either Johnsen or LSS scores and duration of obstruction or the age of the patient. These results match the results of both Magheli, et al. [11] and Xiang, et al. [12]. Quantitative analysis using late spermatid score was done to 330 patients whom underwent vasectomy reversal by Magheli, et al. in 2010. It showed no spermatogenic capacity affection related to either the duration of obstruction or the age of the patient. Sperm granuloma were present in 19.6% of the patients with no statistically significant correlations with late spermatid score. Xiang, et al. in 2013 studied the long-term effect of vasectomy on spermatogenesis. They included 51 patients that underwent bilateral inguinal hernia repair, 25 control males and 26 males with history of bilateral vasectomy. Morphometric examination
and comparison between the two groups was done using light microscope and computer with stereology image system. The system calculated the volume fraction of the seminiferous tubules in the testis, the diameter of the tubules and the basement membrane thickness. Calculated percentage of the tubules with late spermatids and tubules with round spermatids in the lumen was documented. Comparison between the two groups was done, and concluded that equilibrium between sperm production and removal/degradation could result in preserved intratubular pressure which could explain the preserved testicular function [12].

Also paucity of sperm granuloma in the testis coincides with Magheli, et al. [11] as the testis is an immunologically privileged site while the most susceptible site for immunological injury and sperm granuloma is the epididymis, being the least immunologically privileged site [13].

On the other hand, Matsuda, et al. included 34 patients divided into two groups. Group one included males with obstructive azoospermia following childhood bilateral inguinal hernia repair (n=15), and group two included obstructive azoospermia patients following vasectomy (n=19). Testicular biopsies were analyzed histologically in a quantitative manner and comparison between both groups was done. This study showed there was a significant negative correlation between the duration of obstruction and total germ cells per tubule and the tubular diameter was larger in the second group. They contributed this difference to the longer duration period of obstruction in group one [14]. However, we suggest that this difference may come from interruption of the blood supply to the testes by injuring the vasal arteries that may occur during the procedure.

Conclusion:
Obstruction causes no alteration in the spermatogenic capacity of the testis but it may cause some architectural disorganization.

References