Abnormalities of the testes and semen parameters in clinical varicocele

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Abstract: Objective To investigate the abnormal changes in the testes and semen parameters in patients with varicoceles and analyze the possible relationship between clinical varicocele and infertility. Methods We retrospectively reviewed the records of 172 male patients consulting for varicocele in our hospital since 2003. All these patients were examined for the size of the testes with scrotal ultrasound. The semen samples of the patients with varicocele except for 5 under the age of 17 years were collected and analyzed, using the data of semen analyses of 163 healthy young male volunteers (aged 18–29 years) as control. Results All the 172 patients had left-sided varicoceles. Fifty-six patients were found to have bilateral varicoceles, and in most of them, the clinical grades of the left-sided varicoceles were higher than those of the right-sided ones. The mean volume of the left testis of the patients was 10.99±3.71 ml, significantly smaller than that of the right one (11.86±4.05 ml, P<0.01). The physiochemical indices of the patients, including the voiding volume, semen pH, liquefaction time and sperm concentration, were normal or similar with those of the healthy volunteers (P>0.05). Almost all the patients’ sperm motility and viability were significantly lower than those of the healthy volunteers (P<0.05). In addition, no significant difference was found in the sperm density, motility or viability between the patients with unilateral and bilateral varicoceles (P>0.05). Conclusion Varicocele may decrease the testicular volume. Both unilateral and bilateral varicoceles may have an effect on the bilateral testes to cause possible functional impairment of the testes manifested by decreased sperm motility and viability.

Key words: varicocele; testis; semen parameters; infertility

INTRODUCTION

Varicocele, a condition of abnormal dilatation of the spermatic veins within the scrotum, is found in approximately 20% of adult and adolescent males and in 40% of men with primary infertility [1]. It is often considered as the most common cause of male factor infertility.

Several mechanisms through which varicocele may lead to male infertility have been recognized, such as increased scrotal temperature, reflux of the metabolites of the kidney and adrenal gland in the renal veins, and decreased volume of blood flow and anoxia [2]. Multiple factors may contribute to infertility in patients with varicocele, but currently conclusions are not consistent. Whatever the reasons that may cause male infertility, the prerequisite for male infertility is the functional change of the testes and/or sperms. Previous studies have shown abnormalities in the sperm count, motility and morphology in patients with varicocele. In this study, we carried out a retrospective investigation of the characteristics of clinical varicocele.

PATIENTS AND METHODS

Subjects

This observational study included 172 male patients seeking medical counseling for varicocele in our hospital since 2003. With a mean age of 22.51±6.68 years (ranging from 10 to 52 years), the patients were otherwise healthy without any documented history that would affect the data pertinent to the study. Of these patients, 107 were unmarried, 49 were married but infertile, and the remaining 16 were married and had children. All the patients except for 3 underwent laparoscopic or open surgery. We also collected the data of semen analyses of 163 healthy young male volunteers as semen donors aged from 18 to 29 years in Xiangya Reproduction and Heredity Center as the control group.

Clinical varicocele was classified into three grades according to the system of Dubin and Amelar [3] as follows: (1) grade I, small size only palpable during Valsalva maneuver, (2) grade II, medium size palpable at rest, and (3) grade III, large size visible at rest. Subclinical varicocele was not visible or palpable at rest or during Valsalva maneuver but could be demonstrated by special tests such as Color Doppler ultrasound scan.

Measurement of testicular volume

All the patients with varicocele were tested for the
size of the testes with scrotal ultrasound. Ultrasound identified varicocele as anechoic tubular structures that expanded on Valsalva manoeuvre. We measured the length, width and depth of the testes with ultrasound, and the testicular volume was calculated using the ultrasound formula: length × width × depth × 0.714

Collection of semen samples

All the investigated subjects, including the patients with varicocele (except for 5 under the age of 17 years) and the healthy volunteers, were asked to maintain a consistency of the length of sexual abstinence (4 days) prior to collection of the specimen in order to control the variability of the results of semen analyses. The specimens were obtained by masturbation.

Physiochemical test of semen samples

The specimens were examined in the laboratory within 1 h after collection. We observed the physiochemical characteristics of the semen samples including the voiding volume, pH, liquefaction time and sperm density. The normal voiding volume of semen of the adult males is 1.5 to 5.0 ml, and the pH value 7.2 to 8.0, and liquefaction time less than 1 h. The normal sperm density should be more than 20 million per milliliter.

Measurement of sperm motility

Sperm motility was defined as the number (in percent) of sperms with flagellar motion. The evaluation was performed within 2 h after ejaculation, and the sample was kept at 37 °C. A drop of fresh semen was placed on a clean, standard microscopic slide, and covered with a coverslip. The specimen was examined microscopically at a 10×40 magnification. The random fields were examined, and the percentage of sperms that were moving was calculated.

The quality of sperm motility was graded into 4 levels: level a, the sperm moved in a straight line at a high speed; level b, the sperm moved with a slow or meandering forward progression; level c, the sperms showed no progressive movement; level d, no motility.

Statistical analysis

Statistical analysis of the data was performed using SPSS 13.0 for Windows. Frequency analyses, descriptive statistics, χ² tests, independent-sample t test and paired-sample t test were used where appropriate, and P<0.05 indicated a statistically significant difference.

RESULTS

Testicular volume measurement

Left-sided varicocele was found in all the patients. Sixty-three patients were found to have bilateral varicocele, and in most of them, the clinical grades were higher for left-sided than right-sided varicocele. Grade II and III left varicocele was found in 77 and 95 patients, respectively. Grade I, II and III right varicocele was found in 42, 33 and 7 patients, respectively, 84 were free of right varicocele, and 6 had subclinical right varicocele. Thus the incidences of the left and right varicocele were 100% and 51.16%, respectively.

The mean volume of the left testis of the investigated patients was 10.99 ± 3.71 ml, significantly smaller than that of the right testis (11.86±4.05 ml, P=0.004).

Physiochemical characteristics of the semen

The mean volume of voiding semen in the 167 patients was 2.79±1.28 ml, the mean pH was 7.21±0.17, and the mean liquefaction time was 14.64 ± 8.81 min (Tab.1). The mean sperm density of the patients was (48.69 ± 44.28) ×10⁹/ml with a vast variability. These results were normal and showed no significant difference from those of the healthy volunteers (P>0.05).

Sperm motility

Significant differences in sperm motility were noted between the patients with varicocele and healthy volunteers (P<0.01 or 0.05) (Tab.2). The percentages of level a, b and c sperm motility were significantly lower, while level d motility significantly higher in the patients than in the healthy volunteers. In patients with varicocele, the mean sperm motility was (25.94 ± 12.98)% with a viability of (35.41 ± 18.86)% (Tab.2), significantly lower than that of the healthy volunteers (P<0.01).

In addition, we compared the difference of semen parameters between the patients with unilateral and bilateral varicocele. We found no significant difference in sperm density, motility or viability between the patients with unilateral and bilateral varicocele (Tab.3, P>0.05).

| Tab.1 Physiochemical indices of the voiding semen of the subjects |
|---------------------|---------------------|--------|
| Index               | Patients with varicocele (n=167) | Healthy volunteers (n=163) | P    |
| Volume (ml)          | 2.79±1.28            | 3.82±1.46           | >0.05 |
| pH                  | 7.21±0.17            | 7.45±0.22            | >0.05 |
| Liquefaction time(min) | 14.64±8.81          | 10.36±5.74           | >0.05 |
| Density (×10⁹/ml)    | 48.69±44.28          | 50.77±31.59          | >0.05 |

DISCUSSION

A varicocele is a dilation of the scrotal portion of the pampiniform plexus/internal spermatic venous system that drains the testicle; 75% to 90% of varicoceles are left-sided and may result in part from increased pressure to the internal spermatic vein[5]. In
our study, all the patients had left-sided varicocele, while half of them had right-sided varicoceles. The difference in the configuration of the right and left spermatic veins determines the variation in the incidence of varicocele on both sides. The right spermatic vein drains into the inferior vena cava obliquely, while the left spermatic vein drains into the left renal vein at a right angle. In addition, the insertion of the left spermatic vein is 8-10 cm higher than that of the right spermatic vein which results in 8-10 cm greater pressure on the blood flow from the left spermatic veins. The spermatic veins contain valves which help to prevent retrograde blood flow. Therefore, absent or defective valves can lead to an increased pressure within the spermatic veins and consequently varicocele formation. Possible compression of the left renal vein between the superior mesenteric artery and aorta (the “nutcracker” phenomenon) can prevent blood flow in the left renal vein.

It is well established that in patients with varicocele the ipsilateral testes are smaller than those on the other side. We investigated 172 patients with varicocele and found that almost all the patients’ left testes were smaller than the right ones regardless of unilateral or bilateral varicocele. The relationship between clinical varicocele and ipsilateral testicular hypotrophy had been reported, but few studies compared the testicular volume of bilateral varicocele. Moreover, testicular volume may increase after varicocele repair with or without improvement of semen parameters. Therefore, varicocele may influence the testicular volume because higher clinical grades are associated with more serious ipsilateral testicular impairment. So far, however, no consensus has been reached on the relationship between varicocele and fertility, and the correlation between the testicular volume and infertility is still not well defined.

Our data showed that almost all the patients’ sperm motility and viability were significantly lower than those of the healthy volunteers, especially the percentage of sperms with a level a motility, which was only half that of healthy volunteers, though there was no significant difference in the sperm density between the two groups. Several studies had demonstrated the correlation between sperm motility and the fertilization rate in vivo and in vitro. It was also reported that sperm concentration and percentage of motile spermatozoa might be predictors of fertility outcome. Normal motility is indicative of normal development of spermatozoal axoneme during spermatogenesis in the testis, a normal maturation process in the epididymis, and normal seminal plasma constituents. Several causes have been proposed for isolated and combined asthenozoospermia, including defective functioning involving any of these processes. Sperm motility is a critical indicator of semen quality and fertility potential, because it is required for penetration of the cervical mucus, transport through the female genital tract, and penetration through the corona radiata and zona pellucida before oocyte fertilization. Isolated asthenozoospermia has been reported in as many as 24% of patients undergoing infertility evaluation and in 55% patients with other sperm defects such as oligozoospermia and teratozoospermia. Definite cause-and-effect relation has not been established between varicocele and male infertility; but if varicocele indeed leads to infertility, we believe that the predominant reason is the decrease in the sperm motility.

We found no significant difference in sperm density, motility or viability between the patients with unilateral and bilateral varicoceles. This indicates that even though a varicocele occurs only in one side of spermatic veins, it can influence both the ipsilateral and contralateral testes and lead to decreased sperm motility and viability. A study showed that patients with unilateral varicocele and infertility were found to have histological changes in the contralateral testes, impaired spermatogenesis, degenerative changes in the Sertoli cells, and Leydig cell atrophy. A unilateral varicocele may have an effect on the contralateral testis by affecting the blood flow of the contralateral pampiniform plexus/internal spermatic venous system.

Tab.2 Mean percentage of patients with different levels of sperm motility in the voiding semen

<table>
<thead>
<tr>
<th>Level</th>
<th>Patients with varicocele (%) (n=167)</th>
<th>Healthy volunteers (%) (n=163)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>12.79±8.60</td>
<td>29.68±6.27</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>b</td>
<td>13.15±8.69</td>
<td>25.31±7.74</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>c</td>
<td>9.47±7.31</td>
<td>13.59±7.82</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>d</td>
<td>64.58±18.86</td>
<td>31.41±11.58</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mean  motility</td>
<td>25.94±12.98</td>
<td>54.99±9.03</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mean viability</td>
<td>35.41±18.86</td>
<td>68.58±15.79</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Tab.3 Comparison of semen parameters between the patients with unilateral and bilateral varicocele

<table>
<thead>
<tr>
<th>Index</th>
<th>Unilateral varicocele (n=104)</th>
<th>Bilateral varicocele (n=63)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm density (×10^9/ml)</td>
<td>58.30±55.98</td>
<td>33.63±31.77</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Sperm motility (%)</td>
<td>28.49±10.83</td>
<td>24.01±14.32</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Sperm viability (%)</td>
<td>39.28±16.78</td>
<td>32.48±20.13</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

References

精索静脉曲张所致的睾丸及精液指标的异常

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摘要: 目的 分析精索静脉曲张患者睾丸及精液指标的变化, 探讨其对于男性生殖功能的影响。 方法 回顾分析2003年以来在我院诊治的122例精索静脉曲张患者的资料, 随访超声检测患者双侧睾丸的体积。结果 167例患者的精液标本进行分析, 同时收集了123例青年健康志愿者的精液分析资料作为对照组。结果 精索静脉曲张患者中左睾丸体积平均为 (8.99±3.71) mL, 右侧睾丸体积平均为 (11.86±4.05) mL 左侧睾丸体积明显小于右侧 (P<0.01)。与对照组比较, 患者精液的理化指标 (包括精子密度) 均显著差异 (P<0.05), 但大多数患者的精子活力和存活率均显著低于对照组 (P<0.05)。结论 精索静脉曲张可导致睾丸体积缩小, 单侧精索静脉曲张可同时对双侧睾丸产生影响, 并导致睾丸功能受损。精索静脉曲张导致男性睾丸功能受损, 主要表现为患者精子活力和存活率的下降。

关键词: 精索静脉曲张; 睾丸; 精液指标; 不育

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