Effects of carbamazepine on semen parameters in men with newly diagnosed epilepsy

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Keywords
Carbamazepine, Epilepsy, Semen, Men

Abstract
Background: We investigated the effects of carbamazepine (CBZ) on semen parameters in men with newly diagnosed epilepsy, by performing semen analysis before starting any antiepileptic drugs, and then after starting CBZ, to determine the role and effects of CBZ in creating abnormalities in sperm analysis in these patients.

Methods: In this prospective study, eight male patients 20-40 years of age who were referred to the outpatient epilepsy clinic at Shiraz University of Medical Sciences, Iran, from 2009 to 2012, due to new-onset seizure(s) were studied. A semen analysis was performed. CBZ was started and after at least 3 months of taking CBZ, another semen analysis was requested to determine the changes in semen quality. Statistical analyses were performed using non-parametric Wilcoxon test.

Results: Mean age of the patients was 28.5 ± 3.5 years. 7 (87.5%) patients had temporal lobe epilepsy and 1 (12.5%) had parietal lobe epilepsy. The mean follow-up period was 5.5 ± 0.9 months. We observed that semen quality (concentration, progressive motility, morphology) has significantly changed in patients with newly-diagnosed epilepsy after being treated with CBZ (P = 0.012 for all indices).

Conclusion: This study shows the direct effects of CBZ in causing changes in semen quality in men with epilepsy. Abnormalities in sperm concentration, morphology and motility, which were observed in the current study, might play a significant role in causing reduced fertility in men with epilepsy.

Introduction
Reproductive disorders are more common among men with epilepsy than in the general population.¹ Both epilepsy and antiepileptic drugs (AEDs) may play a role in creating these problems, however, the underlying mechanisms have not yet been identified clearly and separating the direct effects of epilepsy versus AEDs has always been difficult.² Infertility, morphological changes in testes and abnormalities in sperm analysis have been reported in patients taking sodium valproate.³⁵ Carbamazepine (CBZ) had negative effects on sperm analysis in both animal and human studies.⁶⁸

In this study, we investigated the effects of CBZ on semen parameters in men with newly diagnosed epilepsy, by performing semen analysis before starting any AEDs, and then after starting CBZ, to determine the role and effects of CBZ in creating abnormalities in sperm analysis in these patients.

Materials and Methods
In this prospective study, eight male patients, who were referred to the outpatient epilepsy clinic at Shiraz University of Medical Sciences, Iran, from January 2009 to January 2012, due to new-onset seizure(s) were studied. Inclusion criteria were patients aged 20-40 years at the time of referral; whose seizures were considered to be epileptic in nature [based on the clinical grounds and the
Sex hormones and carbamazepine

Reproductive disorders are common among men with epilepsy. The etiology of reproductive and sexual dysfunction in men with epilepsy has been attributed to a number of possible etiologies; including psychosocial stress, AEDs, and epilepsy itself. Separating the direct effects of epilepsy versus AEDs have always been difficult. Role of AEDs in sexual dysfunction among patients with epilepsy has been investigated repeatedly. It has been speculated that AEDs can induce various hormonal abnormalities; in particular, the use of the liver enzyme inducing AEDs, such as phenytoin and CBZ, which increases serum sex hormone binding globulin concentrations. This increase leads to diminished bioactivity of testosterone, which may result in diminished potency and thus reduced fertility. In a number of studies, it has been reported that men with epilepsy treated with CBZ, had altered semen quality compared with healthy controls. However, no human study has ever investigated the semen quality in patients with epilepsy, before and after treatment with any AEDs. In the current study, we observed that semen quality has significantly changed in patients with newly-diagnosed epilepsy after being treated with CBZ. This shows the direct effects of CBZ in causing changes in semen quality in men with epilepsy. Abnormalities in sperm concentration, morphology and motility, which were observed in the current study, might play a significant role in reduced fertility in men with epilepsy. Our findings are concordant with the observation of reduced fertility among male patients with epilepsy reported in previous studies. Further, larger studies with CBZ and other AEDs, particularly new AEDs, are necessary to determine the role of each AED in causing reproductive disorders among men and women with epilepsy.

Results
Eight patients were studied. Mean age of the patients was 28.5 ± 3.5 years. 7 (87.5%) patients had temporal lobe epilepsy and 1 (12.5%) had parietal lobe epilepsy. The mean follow-up period was 5.5 ± 0.9 months. The results of the semen analyses of the patients before and after CBZ therapy are summarized in table 1.

Discussion
Reproductive disorders are common among men with epilepsy. The etiology of reproductive and sexual dysfunction in men with epilepsy has been attributed to

<table>
<thead>
<tr>
<th>Semen parameters Before starting CBZ (mean ± SD)</th>
<th>While taking CBZ (mean ± SD)</th>
<th>Percentage change between means (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean volume (ml)</td>
<td>3.25 ± 1.46</td>
<td>3.50 ± 1.22</td>
<td>7.70</td>
</tr>
<tr>
<td>Mean concentration (million/ml)</td>
<td>78.37 ± 25.99</td>
<td>54.50 ± 32.36</td>
<td>−30.45</td>
</tr>
<tr>
<td>Mean progressive motility (%)</td>
<td>50.75 ± 9.25</td>
<td>41.75 ± 14.50</td>
<td>−17.73</td>
</tr>
<tr>
<td>Mean normal morphology (%)</td>
<td>35.00 ± 6.80</td>
<td>28.62 ± 9.27</td>
<td>−18.23</td>
</tr>
<tr>
<td>Mean motile sperm count (million/ml)</td>
<td>42.65 ± 20.75</td>
<td>26.66 ± 21.88</td>
<td>−37.49</td>
</tr>
<tr>
<td>Mean functional sperm count (million/ml)</td>
<td>26.54 ± 16.99</td>
<td>15.48 ± 15.63</td>
<td>−41.67</td>
</tr>
<tr>
<td>Mean sperm motility index</td>
<td>214.25 ± 70.82</td>
<td>152.12 ± 85.91</td>
<td>−28.99</td>
</tr>
</tbody>
</table>

Table 1. Semen parameters before and after taking carbamazepine (CBZ) in men with newly-diagnosed epilepsy

CBZ: Carbamazepine; SD: Standard deviation

Conclusion
This study shows the direct effects of carbamazepine in causing changes in semen quality in men with epilepsy. Abnormalities in sperm concentration, morphology, and motility, which were observed in the current study, might play a significant role in reduced fertility in men with epilepsy.

Limitation
The main limitation of this study is the small number of the patients enrolled in the investigation.

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Conflict of Interests
The authors declare no conflict of interest in this study.

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References