Risk-Benefit Assessment of Anticonvulsants in Women of Child-Bearing Potential

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Contents

Summary
1. Side Effects of Anticonvulsant Drugs
   1.1 Appearance
   1.2 Contraception
   1.3 Fertility
2. Pregnancy
   2.1 Seizure Frequency in Pregnancy
   2.2 Effect of Seizures on the Mother and Fetus
   2.3 Malformations
      2.3.1 Anticonvulsants
      2.3.2 Phenytoin
      2.3.3 Valproic Acid
      2.3.4 Carbamazepine
      2.3.5 Mechanism of Teratogenicity
      2.3.6 Conclusions Regarding Anticonvulsant Teratogenicity
      2.3.7 Other Factors Associated with Malformations
   2.4 Postpartum Bleeding Disorders
   2.5 Breastfeeding
   2.6 Care of the Child
   2.7 Postnatal Growth Retardation and Intellectual Development
3. Risk-Benefit Assessment of Anticonvulsants in Pregnancy
4. Management of Epilepsy Before and During Pregnancy
5. Conclusion and Recommendations

Summary

Problems with anticonvulsants in women of child-bearing potential include potential adverse effects on appearance, contraception and pregnancy. These effects must be weighed against the overwhelming benefits of anticonvulsant treatment in the majority of women with epilepsy.

Coarsened features, hirsutism and acne may occur in both men and women, particularly if they are exposed to phenytoin. Valproic acid may cause weight gain and hair loss, while carbamazepine treatment carries a significant risk of skin rashes. Anticonvulsants which are liver enzyme inducers (phenytoin, phenobarbital, primidone and carbamazepine) reduce the efficacy of the oral contraceptive pill. No 'pill failure' has been reported with valproic acid.
There is a risk of increased seizure frequency in pregnancy irrespective of whether anticonvulsant treatment is taken. Individual seizures carry little risk to the mother or fetus but status epilepticus has a significant maternal and fetal mortality. The risk of status epilepticus must be taken into account when deciding whether to stop anticonvulsant treatment before pregnancy.

There is a 2 to 3 times increased malformation rate in the offspring of epileptic women on treatment. This is primarily due to the drug treatment, but epilepsy itself may also increase the malformation rate. Most malformations are mild and include facial clefts, congenital heart disease and skeletal abnormalities. Valproic acid, however, carries a 1% risk of causing neural tube defects: women receiving this drug who become pregnant should have an ultrasound and α-fetoprotein estimation at 16 to 18 weeks of pregnancy. If any abnormality is detected then amniocentesis should be carried out.

Women with epilepsy should be counselled before conception and during pregnancy. Before achieving pregnancy a woman should be on optimum treatment, preferably on one anticonvulsant. Consideration should be given to withdrawal of anticonvulsant drugs in any woman who has been seizure free for 2 years or who has only mild and infrequent seizures. Folate supplementation should be started prior to conception and should continue during pregnancy. There is a tendency for anticonvulsant drug concentrations to fall during pregnancy, and the dose may need to be increased if clinically indicated. Over 90% of epileptic women who become pregnant will have uneventful pregnancies and will produce healthy infants.

1. Side Effects of Anticonvulsant Drugs

The main concern about anticonvulsants centres around pregnancy, and in particular the risk of malformations in the offspring of women with epilepsy. However, there are other aspects to be considered and these include their effects on appearance, contraception and fertility.

1.1 Appearance

Both epilepsy and anticonvulsants may affect appearance, which is a concern to many individuals, and the details are listed in table II. Coarsened features in patients with epilepsy have been recognised for many years and the changes

<table>
<thead>
<tr>
<th>Effect</th>
<th>Anticonvulsants</th>
<th>Epilepsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Child care</td>
<td>O</td>
<td>+</td>
</tr>
<tr>
<td>Contraception</td>
<td>+</td>
<td>O</td>
</tr>
<tr>
<td>Fertility</td>
<td>O</td>
<td>+</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>++</td>
<td>+</td>
</tr>
</tbody>
</table>

Key: + = adverse effect; O = no effect or beneficial effect.