NEURAL TUBE DEFECTS

Overview and prevalence

Globally, approximately 300,000 pregnancies are affected every year by a neural tube defect (NTD) -

- The term is used for a group of birth defects that affect the brain or the spinal cord, and lead to a wide range of minor to major neurological disabilities
- Approximately 8-9 in every 10,000 pregnancies in Europe (≈ 3.7% of all congenital anomalies) are affected by NTDs

Understanding Spina Bifida

Spina Bifida

Spina bifida is the most common neural tube defect, counting for over 50% of all NTDs. It is not a single condition, but has three major sub-types:

<table>
<thead>
<tr>
<th>Spina bifida occulta</th>
<th>Meningocele</th>
<th>Myelomeningocele</th>
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</thead>
<tbody>
<tr>
<td>- The mildest type of spina bifida</td>
<td>- A sac of fluid comes through an opening in the back, however the spinal cord is not in this sac</td>
<td>- The most serious type of spina bifida</td>
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<td>- Sometimes called “hidden” spina bifida – since it is not usually discovered until late childhood or adulthood</td>
<td>- Usually little or no nerve damage</td>
<td>- With this condition, a sac of fluid comes through an opening in the back, and contains a part of the spinal cord and nerves</td>
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<td>- Does not usually cause any disabilities</td>
<td>- Causes minor disabilities</td>
<td>- The nerves are usually damaged</td>
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<tr>
<td>- Anatomically there is a small gap in the spine, but no opening or sac on the back. The spinal cord and the nerves are usually normal</td>
<td></td>
<td>- Causes moderate to severe disabilities</td>
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- 50.3% of pregnancies with NTDs in Europe are classified as spina bifida
- 37.6% of spina bifida pregnancies result in live births
  - Equivalent to approximately 4.9 in every 10,000 pregnancies in Europe, or ~2% of all congenital anomalies
- Risk of NTDs can be reduced by 70% by the use of periconceptional folate supplements (like provided for example in Femibion®)
Neural Tube Defects

Neural tube defects (NTDs), including spina bifida, affect approximately 8-9 in every 10,000 pregnancies. Clinical severity of NTDs varies greatly ranging from minor neurological handicaps to lethal malformations such as anencephalus and encephalocele. As neural tube closes between 21 to 28 days of embryonic development, NTDs occur very early in pregnancy but are only traditionally detected with high precision in the 2nd trimester. As a result, information is shared with the mother very late in the pregnancy. By this time, the mother can already feel the child’s movement, making it harder to emotionally prepare for the future. This delays any potential conversation with a doctor about the consequences of diagnosis.

There is no known single cause of NTDs, and, as such, the aetiology is multi-factorial. Modern research suggests that there is a multi-gene predisposition, together with environmental factors such as diabetes, obesity, exposure to exogenous factors like antiepileptics and folate status which is one of the best characterised, and modifiable factors.

Ultrasound screening

Non-invasive ultrasound screening is used to check on a number of different foetal health factors, besides gestational age and the detection of multiple pregnancies, it is also used for the detection of foetal anomalies including neural tube defects. When screening for spina bifida, specialists look for tell-tale echoes known as banana and lemon signs.

If an NTD is suspected following ultrasound, physicians may offer the mother an amniocentesis, where fluid is removed from the amniotic sac around the foetus. This procedure is invasive and increases the risk of miscarriage (risks quoted as ranging from 1 in 100 to 1 in 500. Latest estimates even put the risk as low as 1 in 1,600).

Recent Advances

A recent study by Chen et al (Multicenter Berlin intracranial-translucency (IT)-study) was the first prospective, long term large scale study to assess the early diagnostic potential of non-invasive sonographic measures related to the observable features affected by NTDs. It showed that in the hands of experts open spina bifida can be reliably diagnosed during first trimester screening (weeks 11-13) by an evaluation of the whole posterior brain, with its characteristic four line view and the hypoechoic structures of the fourth ventricle, particularly the cisterna magna. Additionally, the use of cut-off values for the main parameters enabled a high degree of detection sensitivity.

Prevention of NTDS

For a number of years the role of folates, such as folic acid or L-5-MTHF (available as calcium salt Metafolin), in the prevention of NTDs has been known, and in some countries there is mandatory fortification of common food types (e.g. cereals).

An early interventional study from 1991 showed that folic acid supplementation (compared to supplementation with other vitamins) led to a relative risk reduction of 72% in women at high risk of having a pregnancy with NTD. This figure has been upheld by a more recent review of five clinical trials, which showed that a periconceptional supply of folate has been reported to reduce the incidence of NTD by more than 70% (risk ratio (RR) 0.28, 95% confidence interval (CI) 0.15 to 0.52), underlining the essentiality of peri-conceptional folate supplementation.

References


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