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Editorial

Toxoplasmosis: A scenic change and a change of therapy?

The prenatal diagnosis and treatment of congenital Toxoplasma gondii (T. gondii) infection is published in this issue of European Journal of Obstetrics, Gynecology and Reproductive Biology (Schoondermark-van de Ven et al.).

Using rhesus monkeys the authors studied the transplacental transfer of spiramycine and pyrimethamine/sulfadiazine and the effect of treatment at proven fetal infection. The results of these studies were published in paraclinical journals and are also available as a Ph.D. Thesis (Toxoplasmosis – Catholic University, Nijmegen, NL).

To inform our readers the main results from these animal studies are presented as a review article. The results are important for clinical diagnosis and treatment.

Toxoplasma infection can have serious consequences for the fetus. Severe manifestations are hydrocephalus, microcephalus, chorioretinitis, and intracranial calcifications. Non-specific symptoms are intra-uterine growth retardation, hepatosplenomegaly, purpura and jaundice. The frequency of transmission of toxoplasma infection increases from 17% in the first trimester to 65% in the third trimester. The degree of fetal or neonatal morbidity is more severe when infection occurs early in pregnancy.

The diagnosis of fetal Toxoplasma infection is now greatly facilitated by a novel PCR assay. Pyrimethamine and sulfadiazine follow a one compartment model in rhesus monkeys. Both drugs cross the placenta very well. In addition pyrimethamine is found to accumulate in brain tissue with concentrations being three to four times higher than the corresponding concentrations in serum. Thirty percent of the sulfadiazine is found to reach the brain tissue when compared with the corresponding drug concentration in serum.

When administered early after the onset of fetal infection the combination of pyrimethamine/sulfadiazine is clearly effective in reducing the number of parasites in the fetus or amniotic fluid to undetectable levels. One has to realise however that pyrimethamine and sulfadiazine are both strong inhibitors of the enzyme methylene-tetrahydro-folate-reductase (MTHFR) being essential for folate metabolism and thus can impair DNA synthesis and RNA unless folic acid is added.

Pyrimethamine and sulfadiazine only attack tachyzoites. Studies focusing on new drugs crossing the blood-brain barrier and acting on cysts as well are already published (Araujo et al., Antimicrob Agents Chemother 1991, 35, 293–299) and seem promising.

In countries with a low prevalence of T. gondii the policy is to rely on primary prevention. In countries with a high prevalence of T. gondii screening is routinely performed. The improvement of T. gondii prenatal detection by the PCR method and the knowledge that pyrimethamine/sulfadiazine/folic acid combination are clearly effective in the infected fetus are strong arguments in favor of reconsidering the screening in countries that do not have a screening programme.

The therapeutic effect of spiramycine in fetal infection is not to be expected and should be abandoned.

Because the placenta of the rhesus monkey is also of the haemochorial type as in the human, the presented data are probably transferable to the human.

T.K.A.B. Eskes
Chief editor