2.4. Effect of treatment of the infected pregnant woman and her foetus

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Introduction

If primary Toxoplasma infection is identified in a pregnant woman today, antiparasitic treatment is mandatory. The aim is primarily to prevent the mother-to-foetal transmission and secondly to treat or reduce any damage in an already infected foetus. Whenever foetal infection is diagnosed, two options are considered: pregnancy termination or continuation of pregnancy with antiparasitic treatment of the infected maternal-foetal unit.

Problems in evaluating the benefit of treatment

For 40 years two antiparasitic regimens (spiramycin and/or pyrimethamine-sulphonamides) have been employed in the therapeutic approach. Their effect on preventing vertical transmission and congenital disease has been discussed for years. Admittedly, the efficacy of antenatal treatment has been difficult to evaluate since it depends on factors such as the antenatal screening procedure, the gestational stage of maternal seroconversion and how soon after acquisition the infection is recognised. Another important factor is whether or not fetal infection is diagnosed before the start of treatment [1].

Today prenatal diagnosis may be offered to every newly infected pregnant woman, and it may thus be possible to establish if vertical transmission has occurred before initiation of treatment. Antenatal treatment studies not taking into account fetal infection can only be used to evaluate if treatment is effective on the parasitic infection in the placenta, and on the development of symptoms, signs and complications in infected children.

It should be born in mind that congenital toxoplasmosis exhibits great variation in severity and outcome, and that long term follow-up studies have to be required for proper evaluation of effectiveness. The main problem is however, the lack of randomised placebo controlled trials [2]. Moreover, such treatment studies are not likely to be carried out because it is considered unethical to withhold therapy from an infected foetus [3].
Drugs used in pregnancy

The drugs that have been used in the treatment of pregnant women are spiramycin and pyrimethamine together with sulphonamides (P+S) [4]. The usual regimen, dosage and duration of therapy are given in Table 1.

**Table 1. Treatment of Toxoplasma infection in pregnant women**

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Pregnant women</th>
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</thead>
<tbody>
<tr>
<td>Spiramycin</td>
<td>3 g = 9 MIU /day</td>
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<tr>
<td></td>
<td>or</td>
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<tr>
<td>Pyrimethamine (P)</td>
<td>25 mg /day (First day: double dose)</td>
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<tr>
<td>Sulfadiazine (S)</td>
<td>50-100mg /day (Initially: double dose)</td>
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<td>or</td>
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<tr>
<td>Fansidar</td>
<td>2 tablets/week</td>
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<td></td>
<td>(25 mg pyrimethamine + 500 mg sulphadoxine tablet)</td>
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</tbody>
</table>

During pyrimethamine therapy
- Folinic acid 5-15 mg twice weekly
- Blood cells counts (platelet, white cells) every 1-2 weeks

**Indications**

- Pregnant women with primary infection
  - Before conception: No need for treatment
  - Suspected cases: Spiramycin until diagnosis
- Proven cases of maternal infection:
  - 1st trimester: Spiramycin continuously
  - 2nd, 3rd trimester: Spiramycin continuously, or P+S (3 weeks), then Spiramycin (3 weeks)
- Evidence of foetal infection (positive amniotic fluid): Repeated courses until delivery.
  - P+S (3 weeks), then Spiramycin (3-6 weeks)
  - or
  - Fansidar: 2 tablets weekly

*Spiramycin*

This drug is a macrolide, which is completely safe to use in pregnancy. It concentrates markedly in the tissue, and its concentration in placenta is found to be five times higher than that of the corresponding maternal serum. Transplacental passage has been confirmed with accumulation of the drug in all fetal organs except the brain [5].

In the 1960s’ the antenatal treatment program comprised one 3-weeks course of spiramycin or repeated courses at different intervals [6]. However Daffos and colleagues [7] indicated that continuous daily treatment throughout pregnancy was more effective. It is shown that spiramycin slowly reduces the *Toxoplasma* load in the tissue requiring administration for at least three weeks to be effective [8].