Is sulfadiazine alone equivalent (benefit and harm) to spiramycin to treat acute toxoplasmosis in the first trimester of pregnancy?

A sulfadiazina isolada é equivalente (benefício e dano) à espiramicina no tratamento da toxoplasmose aguda no primeiro trimestre da gestação?

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http://dx.doi.org/10.1590/1806-9282.61.06.495

Objective

To evaluate, through a systematic review, if, whenever spiramycin is not available to treat pregnant women with acute toxoplasmosis in the first quarter of gestation, there is an effective and safe treatment option for both mother and fetus, especially in relation to isolated use of sulfadiazine.

Methods

Evidence eligibility criteria

Observational (prospective or retrospective cohort) or experimental (randomized or non-randomized trials) studies comparing forms of treatment of acute toxoplasmosis in the first trimester of pregnancy.

No publication date limit. Languages: English, Portuguese, Spanish and Italian.

Evidence search

Medline was the database consulted, using three different and complementary search strategies: 1. pregnancy AND sulfadiazine (171 studies retrieved); 2. (sulfadiazine) AND Spiramycin AND (comparative study OR epidemiologic methods OR therapy/broad[filter]) (63 studies retrieved); 3. toxoplasmosis AND sulfadiazine AND random (41 studies retrieved).

Result

The combined search strategies led to the retrieval of 224 studies. After applying the eligibility criteria, based on titles and abstracts, 9 studies[1-9] were selected for critical evaluation of texts.

Of the studies, 8 were observational cohorts (7 historical and one prospective) and one systematic review. Patients included in the evidence were pregnant women with acute toxoplasmosis treated prenatally with spiramycin, sulfadiazine, pyrimethamine and folinic acid (PSA), or sulfadiazine and pyrimethamine (SP) combined with spiramycin. The rates of vertical transmission in women infected in the 1st, 2nd and 3rd trimesters of pregnancy were 5, 13 and 32%, respectively. The rates of vertical transmission in those treated only with spiramycin, PSA, or PS combined with spiramycin were 13, 13 and 24% respectively.

No studies have compared spiramycin with sulfadiazine, or even used sulfadiazine as an isolated treatment option.

Discussion

Congenital toxoplasmosis derives from fetal transmission of *Toxoplasma gondii* via placenta, as a result of acute maternal infection. The infection is more severe in the first trimester of pregnancy, although the risk of vertical transmission increases during pregnancy.

Early serological diagnosis in pregnant patients and prenatal treatment, were significant factors to reduce the risk of vertical transmission and the development of sequels in the infected child, including intracranial calcification, eye injury and neurological impairment.

In case of seropositivity, the mother should be immediately treated with spiramycin. There is controversy in the literature regarding the duration of treatment and whether other drugs should be associated. Spiramycin is a macrolide antibiotic, which aims at the prevention of fetal infection. It does not cross the blood-placental barrier and, therefore, has no teratogenic effects to the fetus, or toxicity to the mother. Given that the drug remains at high levels in the placenta, it protects the fetus from contact with the parasite. Spiramycin has no therapeutic effect on already infected fetus.

After 16 weeks of pregnancy, polymerase chain reaction (PCR) of amniotic fluid is performed to confirm the diagnosis of fetal infection. According to the studies, the treatment of choice is the combination of sulfadiazine, pyrimethamine, and folinic acid (PSA), with or without spiramycin. The power of these drugs is higher, because they can cross the blood-placental barrier.

PSA is used only after confirmed or strongly suspected fetal infection and is never administered in the first trimester of pregnancy due to its teratogenic and hematological adverse effects, in addition to symptoms of nausea in the mother. The drug produces aplastic anemia and neutropenia by suppressing the bone marrow. Sulfadiazine and pyrimethamine work synergistically, demonstrating greater efficacy against the tachyzoite form of the parasite. Folinic acid prevents the toxicity of pyrimethamine without activity against Toxoplasma.

None of the treatments mentioned in the literature eradicate toxoplasmosis, because they have no action on the encysted bradyzoite parasite, which may be reactivated later in life. To date, there are no reports of the use of sulfadiazine alone. The reviewed studies found no significant difference between PSA and spiramycin in reducing the risk of vertical transmission.

Risks and benefits of treatment against *Toxoplasma gondii* should be carefully weighed. The high rates of adverse effects of sulfadiazine and pyrimethamine point to spiramycin as the safest drug, with PSA being reserved for confirmed cases of fetal infection only. The patient should be monitored during treatment, and PCR of amniotic fluid should be performed periodically.

Evidence summary

1. Sulfadiazine alone is not a therapeutic option in prenatal care for pregnant women with acute toxoplasmosis;
2. Spiramycin is the treatment indicated in the 1st trimester of pregnancy;
3. PSA, combined or not with spiramycin, is the treatment of choice in cases of fetal infection.

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