Letter to the Editor

Neovascular membrane and pregnancy. Treatment with bevacizumab

Membrana neovascular y embarazo. Tratamiento con bevacizumab

Dear Sir:

I would like to congratulate Dr. Gómez Ledesma et al.1 for the excellent Clinical Case which sparks off an increasingly frequent debate in daily clinical practice due to the broad range of indications for antiangiogenic therapy (idiopathic, myopic or inflammatory membranes, diabetic edema, vascular occlusions, etc.). Accordingly, ophthalmologists must take into account the possibility of pregnancy and possible side effects of this therapy, i.e., ocular neovascularization and its treatment in pregnant women, some of whom do not yet know they are pregnant or do not report it believing that no current medication cannot affect their pregnancy. The adequate development of the embryo requires the formation of new vessels (vasculogenesis) involving various growth factors, notably VEGF. The suppression or reduction of VEGF levels can affect both the mother (the mean concentration of VEGF in non-pregnant woman is of 1.10 µ/l [0.91–1.30] and of 2.13 µ/l [1.62–2.77 in pregnancy] as well as the fetus, involving sequels dependent on the pregnancy stage. Said concentrations are one of the factors regulating the cardiovascular adaptation of the mother to the pregnancy.2 During conception and the first 3 months (critical phases) this can be associated to spontaneous abortion, while in the second quarter it could involve malformations incompatible with life and in the third quarter could bring about retarded development of different organs. A limited number of studies have researched in detail the use of drugs during pregnancy. However, there are no studies with pregnant women on the use of antiangiogenics the month prior to pregnancy, the implantation of the zygote and the first quarter (critical phases) and accordingly no recommendations can be given.

At present, ranibizumab and bevacizumab are the most widely used antiangiogenics in ophthalmology. Both are category C drugs, comprising fetal teratogenicity demonstrated in animal studies. Even though there are no studies on humans and despite the risks, antiangiogenics could be beneficial in pregnant women in specific circumstances: 1.25 mg of intravitreal bevacizumab has a mean life of 10 days with a peak at 2–5 days and a concentration between 80 and 170 µ/g/ml, and in serum it reaches a concentration between 20 and 687 ng/ml with a mean life of 1.5 months and a peak at 5 days. In turn, intravitreal ranibizumab (0.5 mg) has a mean life of 10 days, reaching in serum a concentration between 0.79 and 2.90 ng/ml with peak at one day.3 The clinically relevant part of this is that at dosages above 10 ng/ml antiangiogenics block the VEGF-systemic effect4 and for this reason ranibizumab would be the choice against bevacizumab in pregnant women to be treated. Pegaptanib, an aptamere, is highly selective and inhibits isoform 165. Theoretically it is a safe choice. Pegaptanib is in category B, not teratogenic in rats although no studies have been carried out on humans.

In fertile women, antiangiogenics must be applied with caution. For medical-legal reasons, pregnancy tests should be routinely performed, discussing possible risks with the patient, the pediatrician and gynecologist. A better knowledge of the parameters which determine teratogenicity-abortion would allow the ophthalmologist greater certainty concerning risks and benefits of these drugs when applied during pregnancy.

REFERENCES


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