The use of anti-VEGF (vascular endothelial growth factor) in retinal vascular conditions has experienced significant growth in recent years, and is being applied to an increasing number of diseases. The vascular physiopathological basis of retinopathy of prematurity (ROP) supports its use. However, the indiscriminate application of a new therapeutic resource involves risks. For this reason, the use of anti-VEGF must answer a number of questions.

**Is the use of anti-VEGF justified for retinopathy of prematurity?**

Without a doubt the physiopathology of ROP is based on an increase of VEGF. The existence of a higher concentration of VEGF in the vitreous of ROP patients has been demonstrated and compared with those who do not develop the disease. Accordingly, the use of anti-VEGF is a physiopathological treatment which, on principle, is recommended more frequently for all conditions, with the advantage of a single peak which, once brought under control, does not recur. Anti-VEGF has demonstrated its efficiency in experimental animals with ROP models and in adult diseases is similar to ROP. In addition, at present there are sufficient publications describing its use in prematures as well as in isolated cases and small series. A clinical trial has been published recently. All this data constitute scientific endorsement for its use.

**Should anti-VEGF treatment substitute current conventional diode laser treatment?**

No. In the early nineties, laser photocoagulation was a very important development for treating ROP which displaced cryotherapy because it is less aggressive, less painful and less iatrogenic and exhibited a significant reduction in the proportion of unfavorable evolutions, mainly because it could be applied at earlier stages of the disease. At present, successful outcomes are achieved in nearly 100% in pre-threshold stages and of 90% average in the threshold stage. With this proportion of success at each stage, it is difficult for a new therapy to displace laser because it should demonstrate similar efficiency rates and lower iatrogeny. Diode laser has hardly produced any complications like cataracts or vitreous hemorrhage, and even though it is true that the laser destroys the retina, long-term studies have shown that in the early stages or with the involvement of areas 2 or 3, the laser does not have a significant repercussion in the visual field. Finally it is free of repercussions at the general level except those derived from anesthesia although it can be applied under sedation. Even with the...
use of general anesthesia, morbidity and mortality are very low. Laser has been utilized for nearly 2 decades, and even though some alterations have been described in the treated-untreated retinal interface, no significant complications have been found in the long term. Anti-VEGF intravitreal injections are not innocuous and, even though some authors propose it as a replacement for laser treatment because it avoids retinal destruction, its advantages over laser have yet to be demonstrated in a long series. On the other hand, local complications have already been described such as retinal detachment due to contraction of the fibrovascular membranes, and there is a risk of endophthalmitis, detachment due to retinal puncture, vitreous hemorrhage, cataracts, etc. Finally, the possibility of repercussions in the normal development of the retina and at the systemic level has yet to be determined in patients with highly specific characteristics such as prematures.

ROP cases with posterior involvement (zone 1), particularly with plus signs, must be considered separately. In these cases, the efficiency of laser is significantly diminished and the retinal destruction is considerably greater. Mintz-Hittner et al. demonstrated that anti-VEGF treatment is more efficient than later in cases of zone 1 stage 3+. However, the efficiency is similar in posterior zone 2.

What is the current indication for anti-VEGF in ROP?

As explained above, the use of anti-VEGF should be considered in: (a) cases in which laser cannot be applied due to opacification, poor midriasis, etc., utilizing anti-VEGF as the first choice; (b) in cases in which laser has been applied completely and vascular activity persists as a co-adjuvant treatment, provided there is no marked fibrous component to avoid retina detachment due to membrane contraction; and (c) in cases with advanced zone 1 retinopathy, where anti-VEGF can be considered as a first choice or as a co-adjuvant treatment for laser.

Which anti-VEGF should be utilized?

Bevacizumab. The anti-VEGF drug should be utilized as a compassionate use and must be supported with sufficient references. Bevacizumab is backed by greater experience and use. The most recommended dosage is 0.65–0.70 mg in 0.03 ml. At present there is no sufficient literature to support the use of other anti-VEGF drugs.

REFERENCES