VEGF and pathology

The predominant role of VEGF-A in the development of pathological angiogenesis, such as that occurring in tumours and ischaemic and inflammatory processes was widely demonstrated in the last decade(18).

In hypoxic states, VEGF is secreted by RPE cells(19).

This factor induces endothelial cell proliferation and increases vascular permeability.

It has been shown in several models that VEGF-A is required and sufficient for development of new blood vessels in the retina and the iris.

s already mentioned, VEGF-A has been identified as a primordial factor in the neovascular response induced by retinal ischaemia.

Therefore, VEGF-A levels are increased in the vitreous and retina of patients with neovascularization secondary to proliferative diabetic retinopathy, venous occlusion or retinopathy of prematurity(20-23). In clinical practice, observed blood VEGF levels are increased in AMD patients(24).

Many studies have revealed VEGF overexpression in neovascular membranes during autopsy procedures or after surgical extraction(25,26).

Since 1996, immunohistochemistry studies of frozen sections of neovascular membranes have shown significant VEGF levels in highly vascularized regions, although lower immunoreactivity has been observed in fibrotic membrane regions(28,29).

Drusens and basal linear deposits have also been associated with high VEGF levels(30).

Therefore, vascular endothelial growth factor A (VEGF-A) regulates angiogenesis and vascular permeability in the eye, both in physiological and pathological processes.

This growth factor selectively influences endothelial cell growth, being particularly responsible for increased vascular permeability.

It also plays a role in the survival of many cells. Inhibition of neovascularization – the cause of exudative or neovascular AMD – was the basis of some disease-modifying therapies, since anti-VEGFs may delay or even halt disease progression.

The vascular endothelial growth factor is a secreted protein that induces angiogenesis and increases vascular permeability and inflammation, which appear to contribute to neovascular AMD progression. Naturally, VEGF is the target of investigational drugs for the treatment of AMD(31,32).

It is possible to inhibit every step of the angiogenesis cascade induced by VEGF: VEGF synthesis may be inhibited by inhibiting the synthesis of the corresponding mRNA or by inhibiting transcription[(33)].

The effect of VEGF may also be directly inhibited , by inhibiting protein action.

This is the mechanism used in anti-VEGF therapies[(34,35)]. Angiogenesis may also be inhibited after VEGF binding, as occurs with anecortave acetate and squalamine lactate [(36-38)].

Treatment of AMD with anti-VEGFs is thus considered to be a turning point since its emergence has allowed a more direct approach to choroidal neovascularization and its selective inhibition.

Therefore, anti-VEGF treatments offer new hope to thousands of neovascular AMD patients, a disease that used to be understood as an untreatable condition associated with ageing before the emergence of anti-VEGF drugs.

These drugs are particularly effective in the early stages of the disease, when newly formed blood vessels are less mature: inhibition of their growth allows photoreceptors to remain viable, as well as reducing the risk of central fibrosis and delaying progressive loss of vision.

Three drugs in this class are currently used in the treatment of AMD: pegaptanib (Macugen®), ranibizumab (Lucentis®) and bevacizumab (Avastin®), of which only the first two have been approved for this therapeutic indication.

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