treatment at a dose of 2.5 mg (0.1 ml) in patients with acute (≤1 month after the occlusion was diagnosed) central/hemiretinal vein occlusions (C/HRVOs). Of these patients, 50% had ischaemic C/HRVOs. Initially, the treatment consisted of 4 consecutive IVB injections, each injection given approximately 45 days apart. Thereafter, the IVB therapy was flexible, and subsequent injections were administered on pro re nata (PRN) basis until stabilization of the BCVA score lasting ≥6 months was achieved. There were no events of endophthalmitis, retinal tears or retinal detachment and no serious non-ocular adverse events. The results of this study showed, for the first time, the evidence suggesting that early treatment applied immediately after the clinical onset of venous occlusion provides significant and sustained improvements in visual acuity and FT in most phakic patients with acute C/HRVOs, making this treatment option a rational and viable therapeutic strategy. These findings are consistent with the 12-month results reported in the Swedish trials (Epstein et al. 2012a, b). Bevacizumab was more effective in patients with ischaemic occlusions who required a significantly higher number of injections (9.7 versus 8.7 injections).

In conclusion, the standard injection scheme during the first year of IVB therapy [1.25 mg (0.05 ml)] for MO due to CRVO was clearly set by the level 1 evidence of the Swedish trials (Epstein et al. 2012a,b), that is, IVB injections given off-label every 6 weeks for 48 weeks, which was proven to significantly improve vision and reduce MO. Considering our currently acquired experience with intravitreal injections of 2.5 mg (0.1 ml) bevacizumab (Călugăru & Călugăru 2015), we believe that after an initial aggressive treatment with four consecutive injections administered off-label approximately 45 days apart, the therapy may be continued with subsequent dosing given PRN until stabilization of the BCVA score. CRVO should be considered, and ophthalmic emergency therapy with anti-VEGF agents must be promptly applied as soon as possible after the CRVO onset. Any delay in treatment will adversely affect the restoration of visual functions.

References


Reduced vitreal concentration of periostin after vitrectomy in patients with proliferative diabetic retinopathy

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In an earlier study, we identified periostin, a 90-kDa-secreted matricellular protein involved in wound repair (Kudo et al. 2007), as a molecule whose expression is enhanced in proliferating epiretinal fibro(vascular) membranes (FVMs) and in the vitreous of patients with both proliferative diabetic retinopathy (PDR) and proliferative vitreoretinopathy (PVR; Ishikawa et al. 2013). These results identified periostin as an important molecule for FVM formation. However, to the best of our knowledge, there is little direct evidence on how vitrectomy affects the periostin-mediated fibro(vascular) proliferation. Thus, the purpose of our study was to determine whether vitrectomy changes the levels of periostin in the vitreous of eyes with PDR.

In our University Hospital, we have been using a two-step surgical strategy for the treatment of patients with severe PDR (Yoshida et al. 2012). It was decided that patients with severe PDR would undergo vitrectomy without the insertion of an IOL at the initial surgery, and an IOL would be implanted only after confirming that the activity of retinopathy had calmed down after the initial vitrectomy.

We collected vitreous samples from 54 eyes of 54 patients with macular hole as control and 36 eyes of 33 patients with PDR without IOL implantation. We obtained 36 samples from the same patients at the time of the IOL implantation during a second vitrectomy. The interval between the initial vitrectomy and IOL implantation was 3.1 to 25.7 (mean 6.7) months.

The mean concentration of periostin in the vitreous was significantly higher in the 36 vitreous samples collected from 33 patients with PDR (11.44 ± 2.62 ng/ml) than in the vitreous of the control patients (0.12 ± 0.03 ng/ml, p < 0.001, Fig. 1A). At the time of the IOL implantation, the periostin level was significantly higher (3.39 ± 1.33 ng/ml, p = 0.007) than that in the control patients, but the periostin level was significantly lower than the level in the vitreous collected at the initial vitrectomy (11.4 ± 2.56 ng/ml, p < 0.001, Fig. 1A). Finally, the periostin level was significantly and inversely correlated with the interval between the first vitrectomy and the second
that a successful vitrectomy may suggest periostin and VEGF for a long time (Yoshida et al. 2012; Fig. 1B). The periostin level is significantly higher in eyes with PDR at the time of initial vitrectomy than in MH patients (p < 0.001). The periostin level at the time of the second vitrectomy for IOL implantation is also higher than in the controls (p = 0.007), but is significantly lower than that in the vitreous samples at the time of initial vitrectomy. (*p < 0.001). PPV, pars plana vitrectomy. (B) Correlation of vitreous periostin levels at the second vitrectomy for IOL implantation surgery with days after initial vitrectomy in 36 patients with PDR. There is significant intermediate negative correlation between the periostin concentration and days after the initial vitrectomy (r = −0.38, p = 0.02).

Fig. 1. Vitreous concentrations of periostin. (A) Periostin concentrations in the vitreous samples of non-diabetic patients (MH), PDR patients, and vitrectomized PDR patients at the time of the IOL implantation after an earlier vitrectomy (PDR after PPV). Periostin concentration is determined. Because the level of periostin protein was reduced in a time-dependent manner (Fig. 1B), one possible explanation is that there is an increase in the diffusion of periostin away from the retina by the replacement of the vitreous gel with less viscous saline. Another reason for the quieting effects of vitrectomy may be the removal of FVMs because we have shown that the smooth muscle cells and M2 macrophages in FVMs actively produce periostin as well as a variety of adhesion molecules (Yoshida et al. 2011).

Anti-VEGF therapy is being used to treat neovascular diseases of the eye, and its use has led to significant advances in the management of PDR. However, this treatment turns on an ‘angiobiotic switch’ to favour a fibrotic phase, and tractional retinal detachment have been reported in PDR patients following the administration of anti-VEGF agents in spite of the neovascular inhibition (Sohn et al. 2012). This indicates that anti-VEGF therapy is not effective in inhibiting fibrotic proliferation. Our findings that successful vitrectomy can reduce both periostin and VEGF for a long time (Yoshida et al. 2012; Fig. 1B) suggest that a successful vitrectomy may inhibit both angiogenesis and subsequent fibrosis by reducing the level of these molecules.

References


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Editor,

Recreational users of poppers must be informed about the risk of developing poppers-associated maculopathy and the possible cumulative risk when taking poppers in combination with sildenafil. We suggest that it is an accumulative increase in cGMP which is harmful for the photoreceptor cells and may cause poppers-associated maculopathy (Fig. 1). A possible association between the use of poppers and maculopathy with visual loss was first described in 2004 (Pece et al. 2004). Poppers is the popular name for alkyl nitrite which is a short-acting, volatile drug used by inhalation. To better understand this possible association, we looked into the medical history and drug use of 10 patients with poppers-associated maculopathy. Seven patients (70%) were HIV positive, for which one patient was treated with a protease inhibitor at time of onset. Sixty per cent used sildenafil in combination with poppers: three were HIV positive and three were HIV negative.

It may be that patients, who use poppers most, are those who get HIV and are more prone to the development of a maculopathy due to a higher cumulative dose of poppers. However, if poppers alone were a sufficient cause of maculopathy, far more women and heterosexual men would be expected among a cohort of

Do not turn a blind eye to alkyl nitrite (poppers)!

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