Diurnal Variation in the Onset of Branch Retinal Vein Occlusion: Early Morning Blood Pressure Surge as a Possible Risk Factor

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Oh et al. [1] observed that branch retinal vein occlusion (BRVO) symptoms were often apparent between 6.00 a.m. and noon in their patients, suggesting that these retinovascular events occurred during sleep or in the initial hours after awakening. To explain this finding, the authors referred to the hypothesis that nocturnal arterial hypotension is an instigator of ocular ischaemic events. However, discussions on the diurnal variability of retinal vein occlusion might also acknowledge the 'early morning blood pressure surge' (EMBPS) [2] when considering mechanisms.

The EMBPS is a normal circadian phenomenon whereby systemic arterial pressure is boosted in most persons from awakening to about 4–6 h thereafter [3]. This 'supercharging' of the circulation is believed to explain the well-noted pattern of early morning stroke and myocardial infarction [4].

Notably, with increasing age, the EMBPS becomes more pronounced and furthermore meets a retinal end-arteriolar system that has a decreased reflex response to variations in systemic arterial pressure [2, 5]. Hence, the combination of an enhanced EMBPS and an age-related weakening of retinal autoregulation can conceivably lead to pathogenic rheology in the retina.

Artery-over-vein crossings are at special risk of damage from disordered haemodynamics. Even in normotensive persons, the artery-over-vein complex has characteristics which affect blood flow, such as focal venular constriction and an abrupt deflection of the associated vein [6]. The obstructive effect of these sites in the microvasculature is exaggerated in the hypertensive state, the risk factor par excellence of BRVO. Therefore artery-over-vein crossings represent sites in the retinal circulation where there is potential for venular endothelial injury secondary to fluctuations in perfusion. In this regard, Meyer et al. [7] have remarked that 'venous endothelial damage increases the potential role of haemostatic risk factors in the pathophysiology of retinal vein occlusion'.

In essence, the 'high-flow' hypothesis professed here (to explain the apparent diurnal variation in onset of BRVO) states that the combination of an EMBPS and weakened retinovascular autoregulation favours venous intimal injury. A *damaged* endothelial surface at a site of stenosis (arteriovenous crossing) creates an optimal environment for thrombosis.

Previously, the literature has considered only venous hypoperfusion in the pathogenesis of retinal vein occlusion (the prothrombotic 'low-flow' state presumed to arise from nocturnal hypotension). However, the EMBPS, already characterised as a

risk factor in systemic vascular events, may also be relevant in the pathogenesis of BRVO and might explain why in some patients this retinovascular event occurs during certain hours in the circadian cycle.

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Reply

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We would like to thank Jagdeep Singh Gandhi for the comment on our article entitled 'Diurnal variation of the incidence of symptomatic branch retinal vein occlusion (BRVO)' [1]. Gandhi stresses the early morning blood pressure surge (EMBPS) as the mechanism of its diurnal variation.

The fact that cardiovascular accidents usually occur in the morning and our results that patients with symptomatic BRVO frequently noted their visual deterioration in the morning suggest that the diurnal variation in the onset of BRVO may be influenced by variation in arterial pressure [2, 3]. We acknowledge that there are some doubts about how the results based on arterial diseases like stroke and myocardial infarction can be applied to a venous disease like BRVO. However, recent studies that systemic arterial pressure can influence retinal venous flow support our suggestion that the variation of arterial flow could have an effect on the diurnal variation in the onset of BRVO [4, 5].

Gandhi supposes that the BRVOs really occur in the morning and stresses

EMBPS as a factor that influences the diurnal variation of BRVO onset. We agree that EMBPS has an effect on the fluctuation of ocular perfusion and possibly influences the diurnal variation in the onset of BRVO. However, our results could not directly show that BRVOs occur more frequently in the morning. Even though visual deterioration is often noticed in the morning in many vascular diseases, there is a strong suggestion that the visual loss may actually occur during sleep and the patient only becomes aware of it when he/she has to use their vision. We suggested that nocturnal arterial hypotension may be combined with a rise of the intraocular pressure during sleep, and this may produce a fall of the perfusion pressure in a vein that has been already stenosed and so influences the diurnal variation of BRVO onset.

Further studies are needed to elucidate when BRVOs really occur and how the fluctuation of systemic blood flow influences the diurnal variation of BRVO onset.

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