Comment

—to: Gardiner TA, Anderson HR, Degenhardt T et al. (2003) Prevention of retinal capillary basement membrane thickening in diabetic dogs by a non-steroidal anti-inflammatory drug. Diabetologia 46:1269–1275

To the Editor: We read with interest the recent paper by Gardiner et al. [1] reporting the effect of a non-steroidal anti-inflammatory drug Sulindac on the early vascular pathology of diabetic retinopathy and some insights into the mechanism by which Sulindac acts in this respect. Gardiner et al. found that Sulindac treatment significantly reduced retinal capillary basement membrane thickening, a common early lesion of diabetic retinopathy, in experimental diabetic dogs. Their study thus reproduced 13 years later the finding of a previous study on diabetic cats [2]. In this previous study the authors had suggested that the effect of treatment with Sulindac may be mediated by inhibition of aldose reductase activity, as Sulindac is a known aldose reductase inhibitor [3].

Whilst investigating the mechanism of the beneficial effects of Sulindac, Gardiner et al. concluded that the treatment benefit is not derived from the inhibition of advanced glycation, the reduction of aldose reductase activity or the improvement of anti-oxidant status. However, they came to this conclusion by assessing the markers of the polyol pathway, advanced glycation and oxidative stress in plasma, serum, erythrocytes and skin collagen. We believe that the conclusion could have been different, if they had investigated these pathological processes in the tissue affected by diabetes, i.e. in the retina [4].

Joussen et al. [5] have previously shown that non-steroidal anti-inflammatory drugs prevent early diabetic retinopathy via TNF-α suppression. They have shown that aspirin and selective cycloxigenase-2 inhibitor meloxicam can reduce blood–retinal barrier breakdown and leucocyte adhesion to diabetic retinal vasculature, at least in part, through the inhibition of TNF-α. Unfortunately, in the study by Gardiner et al. there is no discussion of the possibility of TNF-α-mediated retinal effects of Sulindac. At the end of their discussion the authors mention that the treatment benefit of aspirin in the study by Joussen et al. [5] was clearly derived from its classic anti-inflammatory role as a non-steroidal anti-inflammatory drug. In fact this is only partially true, since the classic mechanism of aspirin as a non-steroidal anti-inflammatory drug involves inhibition of the enzyme cycloxigenase [6]. Moreover, TNF-α suppression is not supposed to be a part of the classic anti-inflammatory mechanism of non-steroidal anti-inflammatory drugs, a factor that has not been appreciated in the study by Gardiner et al.

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