Abstract

Diabetic retinopathy (DR) is a multifactorial disease characterized by reactive gliosis and disbalance of angiogenesis regulators, contributing to endothelial dysfunction and microvascular complications. This study was organized to elucidate whether poly(ADP-ribose) polymerase-1 (PARP-1) inhibition could attenuate diabetes-induced damage to macroglia and correct angiogenic disbalance in diabetic rat retina. After 8 weeks of streptozotocin (STZ)-induced diabetes, Wistar male rats were treated with PARP-1 inhibitors, nicotinamide (NAm) or 3-aminobenzamide (3-AB) (100 and 30 mg/kg/daily i.p., respectively), for 14 days. After the 10-weeks experiment period, retinas were undergone an immunohistochemical staining for glial fibrillary acidic protein (GFAP), while western blots were performed to evaluate effects of PAPR-1 inhibitors on the levels of PARP-1, poly(ADP-ribosyl)ated proteins (PARs), GFAP, and angiostatin isoforms. Diabetes induced significant up-regulation and activation of retinal PARP-1, reactive gliosis development, and GFAP overexpression compared to non-diabetic control. Moreover, extensive fragmentation of both PARP-1 and GFAP (hallmarks of apoptosis and macroglia reactivation, respectively) in diabetic retina was also observed. Levels of angiostatin isoforms were dramatically decreased in diabetic retina, sustaining aberrant pro-angiogenic condition. Both NAm and 3-AB markedly attenuated damage to macroglia, evidenced by down-regulation of PARP-1, PARs and total GFAP compared to diabetic non-treated group. PARP-1-inhibitory therapy prevented formation of PARP-1 and GFAP cleavage-derived products. In retinas of anti-PARP-treated diabetic animals, partial restoration of angiostatin’s levels was shown. Therefore, PARP-1 inhibitors counteract diabetes-induced injuries and manifest retinoprotective effects, including attenuation of reactive gliosis and improvement of angiogenic status, thus, such agents could be considered as promising candidates for DR management.