Losartan treatment and Arterial Thrombus formation in MAGP1-deficient Mice


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Microfibril-Associated GlycoProtein 1, MAGP1, is a ∼22 KDa protein present in vessel wall elastic fibers. Even though its biological function is not clear, studies using Zebrafish demonstrated that changes in this protein expression are associated with decreased integrin/extracellular matrix interactions causing vascular defects in MAGP1 morphants. On the other hand, MAGP1-deficient mice are viable and have normal development. Recently, our group determined that MAGP1-deficient mice have prolonged thrombosis time when challenged in a photochemical arterial thrombosis assay. Recent data has shown that MAGP1 can bind active forms of BMP-7 and TGF-β. Considering that TGF β is released by activated platelets during thrombus formation we decided to treat wild-type and MAGP1-deficient mice with losartan, that blocks Angiotensin II AT1 receptor and decreases TGF β signaling. To verify the involvement of MAGP1 deficiency and TGF β in thrombus formation, mice were treated for four weeks with losartan, captopril or placebo and submitted to photochemical arterial thrombus induction. We also analyzed blood pressure, prothrombin time (PT), activated partial thromboplastin time (APTT) and platelet aggregation and adhesion. Both treatments were effective in decreasing thrombosis time to normal levels in MAGP1-deficient mice. Coagulation cascade assays (PT and APTT) as well as platelet aggregation and platelet adhesion assays are still in progress.

Keywords: MAGP1, TGF-β, Arterial Thrombosis, Losartan
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