The role of fibrillin-1 in arterial thrombus formation.


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Marfan’s syndrome is a dominant autosomal genetic disease, related with fibrillin-1 gene mutation. Most symptoms are probably related to a hyper-activation of the TGF-β factor. Using a Marfan’s Syndrome mice model, it was observed a significant improvement in clinical signals in parallel to a reduction in active TGF-β levels after treatment with losartan. Previous data of our group demonstrate that fibrillin-1 deficient mice required almost double the time of wild mice to form the thrombus. Thus, the main goal of this project was to achieve a better understanding of fibrillin-1 function in the arterial thrombosis process and losartan treatment as well. Wild type and fibrillin-1 deficient mice were treated for 4 weeks with losartan or placebo, and were submitted to a photochemical thrombus induction, to determine thrombosis time. We also analyzed blood pressure, prothrombin time (PT), activated partial thromboplastin time (APTT), platelet aggregation and adhesion and TGF-β levels. Our results showed that losartan was able to recovery normal thrombosis time in the arterial thrombosis assay in fibrillin-1 deficient mice. We observed no significant difference in the active TGF-β levels. Coagulation cascade assays (PT and APTT) as well as platelet aggregation and platelet adhesion assays are still in progress. Finally, the results suggest that losartan plays a role in fibrillin-1 deficient mice physiology changing their occlusion time but the mechanism by which it is acting, remains unknown.

Word Keys: elastic fibers, fibrillin-1 and losartan.
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