SMOOTH MUSCLE-SPECIFIC DELETION OF NITRIC OXIDE-SENSITIVE GUANYLYL CYCLASE IS SUFFICIENT TO INDUCE HYPERTENSION IN MICE

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BACKGROUND: Arterial hypertension is one of the major diseases in industrial countries and a major cause of mortality. One of the main vascular factors responsible for the relaxation of blood vessels and regulation of blood pressure is nitric oxide (NO). NO acts predominantly via NO-sensitive guanylyl cyclase (NO-GC), which is made up of 2 different subunits (alpha and beta). Deletion of the beta(1) subunit leads to a global NO-GC knockout, and these mice are hypertensive. However, global deletion of NO-GC in mice does not allow identification of the cell/tissue type responsible for the elevated blood pressure. METHODS AND RESULTS: To determine the relative contribution of smooth muscle cells to the hypertension seen in NO-GC knockout mice, we generated smooth muscle-specific knockout mice for the beta(1) subunit of NO-GC using a tamoxifen-inducible system. Male mice were investigated because the Cre transgene used is located on the Y chromosome. Tamoxifen injection led to a rapid reduction of NO-GC expression in smooth muscle but did not affect that in other tissues. Parallel to a reduction in NO-induced cGMP accumulation, NO-induced relaxation of aortic smooth muscle was gradually lost after induction by tamoxifen. Concomitantly, these animals developed hypertension within 3 to 4 weeks. CONCLUSIONS: We generated a model in which the development of hypertension can be visualized over time by deletion of a single gene in smooth muscle cells. In sum, our data provide evidence that deletion of NO-GC solely in smooth muscle is sufficient to cause hypertension. **[Circulation 2010; 121(3):401-409]**

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THE EFFECT OF CAROTID STENTING ON RHEOLOGICAL PARAMETERS, FREE RADICAL PRODUCTION AND PLATELET AGGREGATION

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INTRODUCTION: Carotid artery stenting has become a possible treatment of significant carotid stenosis. The risk of stent occlusion and restenosis might be increased by abnormal rheological conditions amplified platelet aggregation and free radical production during the operation.Aims: The aim of our study was to assess the changes in hemorheological parameters, platelet aggregation, and catalase activity after endovascular treatment of carotid stenosis. METHODS: 18 patients (11 men, ages 68 +/– 9 years and 7 women, ages 62 +/– 8 years) suffering from significant carotid stenosis and treated with carotid endovascular intervention were examined. Alteration in hemorheological parameters as well as epinephrine-, ADP-, and collagen-induced platelet aggregation were evaluated. Antioxidant reserve was characterized by the determination of catalase activity. The measurements were carried out directly before and after the procedure and 1, 2, 5 days and 1 month following the intervention. Preceding the operation the patients were administered a maximum dose (300 mg) of clopidogrel. RESULTS: Hematocrit, plasma fibrinogen concentration (PFC) and whole blood-, and plasma viscosity values (WBV and PV) significantly decreased immediately after stenting ($p<0.001$). By the fifth day following the intervention the PFC, WBV, PV, red blood cell (RBC) aggregation and ADP-induced platelet aggregation significantly increased ($p<0.0001$) compared to values measured postprocedurally. At 1 month follow-up these parameters, except whole blood viscosity, decreased significantly compared to measurements made on the 5th day. On the other hand, catalase activity showed significant elevation by the end of the first month. CONCLUSION: Hemorheological parameters and platelet aggregation showed specific changes following carotid stenting. Abnormal changes of the rheological conditions and increasing platelet activation are the most pronounced in the first week following stenting, which may lead to early stent occlusion. Oxidative stress production returned to baseline levels only by the end of the first month [**Clin Hemorheol Microcirc 2009; 43(3):209-217]**

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