

Shockwave induces up-regulation of endogenous VEGF-R2 during early hindlimb ischemiareperfusion injury

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Device and producing company:

OW 180

Introduction:

Different strategies have been developed to reduce ischemia/reperfusion injury. Shockwave therapy has been gaining increasing interest, not only for lithotripsy, but also in wound healing. This study investigates the *in vivo* expression of VEGF-R2 during early murine hindlimb ischemia/reperfusion and its alteration by shockwave application.

Methods:

Transgenic FVB/N-Tg (Vegfr2-luc) Xen mice (n=12/group) were used for noninvasive, real-time assessment of the VEGF-R2 (Flk-1/KDR) expression. Ischemia was induced by a tension controlled (250g) hindlimb tourniquet and was verified by laser Doppler imaging (LDI, Moor Instruments Inc.) technique. Ischemia was maintained for 2 hours with subsequent reperfusion for 24 hours. Control animals received no treatment, whereas the animals of the shockwave group received 50 percutaneous impulses on the ischemic hindlimb 15 minutes prior to reperfusion. The contralateral leg was used as an internal control. At different time-points LDI was done to check hindlimb perfusion; bioluminescence detection was done to observe VEGF-R2 expression (VivoVision® IVIS®, Xenogen).

Results:

Applying the tourniquet resulted in reproducible ischemia, as verified by a reduction of leg perfusion to approximately 10% in all groups. Ischemia was maintained for the entire 2 hours. Furthermore, restoration of blood flow was seen to 85% of baseline in the control group after 24 hours of reperfusion. Increased perfusion levels were observed in the shockwave group (108%). Edema was found in all groups in the injured hindlimb. In the control group, VEGF-R2 expression was increased in the ischemic hindlimb only after 24 hours of reperfusion. The shockwave group showed significantly increased VEGF-R2 expression levels after 4 hours compared to the control group. The 24h levels exceeded the control group as well.

Discussion:

This ischemia/reperfusion model in transgenic mice enables *in vivo* observation of the VEGF-R2 expression, a key receptor in angiogenesis. VEGF-R2 is up-regulated in the reperfusion period after severe ischemic conditions.

Conclusion:

Shockwave application results in a substantial increase in endogenous VEGF-R2 expression indicating enhanced angiogenesis.