FEMORAL HEAD ARTERY WALL TENSION ENHANCED BY METHYL PREDNISOLON AND ENDOTHELIN

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Introduction: The initial pathogenesis of steroid induced Femoral Head Necrosis (FHN) is thought to be local ischemia. The FH is supplied mainly by the lateral epiphyseal arteries as described by Trueta [4]. This study aimed to investigate if long term steroid treatment enhances the vasocontractive effect of endothelin-1 or noradrenaline, or diminishes the vasodilative effect of bradykinin on FH lateral epiphyseal arteries [3].

Materials and Methods: From 24 domestic pigs from 12 litters, 12 animals were randomly allocated to a test group receiving steroid treatment while their 12 sister pigs served as controls. Methylprednisolone 100 mg daily was orally given to the test group animals for a period of 3 months. The pigs were sacrificed with intravenous injection of 20 ml pentobarbital. A random FH was excised, and cut into frontal slices from which lateral epiphyseal arteries were isolated (Fig. 1).

These arterial segments were threaded onto two stainless steel wires 40 μm in diameter, and mounted as ring preparations on a small vessel myograph for measurement of isometric wall tension (Fig. 2).

The arteries were stimulated cumulatively with noradrenaline (0.02-10 μM in 0.3 log-unit steps at 2-min intervals) to obtain its dose-response curve. From this curve, the noradrenaline concentration resulting in 80% of maximal contraction was estimated to induce a submaximal precontraction. After 6 min submaximal precontraction with noradrenaline, increasing concentrations of bradykinin (10-11-10-6 M) were added cumulatively. After wash-out, endothelin-1 was added cumulatively (10-12-10-7 M). Isometric wall tension was quantified by the EC50, the vasoconstrictor concentration resulting in halfmaximal contraction.

Results: 38 artery segments could be harvested in total, 21 from the control and 17 from the test group animals. Noradrenaline elicited a concentration-dependent vasocontraction in all arteries. The maximal active tension, and the EC50 of noradrenaline were not significantly different in the control and the test group. Bradykinin elicited a concentration-dependent relaxation in all arteries without differences in steroid and control vessels. The endothelin-1 dose-response curve displayed a shift to the left for the steroid group in relation to the controls (Fig. 3). This was reflected by a significantly lower EC50 of 2.17*10^-9 M for the steroid vessels compared to 10.5*10^-9 M for the control vessels (p<0.005).

Discussion: Endothelin-1 is a potent vasoconstrictor having receptors in vascular smooth muscle [1, 2]. This study showed that endothelin-1 mediated contraction of femoral head epiphyseal arteries was enhanced in pigs treated with long term steroids (Fig. 3).

This effect could be explained by steroids downregulating the expression of endothelial nitric oxide (NO) synthase. This can lead to increased vascular tension as NO is an important mediator of vasodilatation [5]. Contraction of FH lateral epiphyseal arteries can diminish femoral head blood flow, and be a relevant cofactor in the early pathogenesis of steroid induced femoral head necrosis.

References: