HYPOXIA ENHANCES THE RELAXING INFLUENCE OF MICE ADIPOSE TISSUE.

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Recent studies propose a paracrine role for perivascular adipose tissue in the regulation of vascular tone. Adipose tissue from different species releases a factor lowering tone of isolated arteries. This factor is called the “adipocyte-derived relaxing factor” (ADRF). The potential influence of hypoxia on the vasorelaxing properties of adipose tissue was investigated. Aorta from male Swiss mice with or without adherent adipose tissue were mounted in a wire myograph for isometric tension recording. Hypoxia (bubbling with 95% N_2, 5% CO_2) relaxed precontracted (norephinephrine, 5 µM) aorta with adipose tissue while only a minimal vasorelaxing effect was observed in arteries without adipose tissue. This effect was also seen after precontraction with prostaglandin $F_{2\alpha}$ (30 µM) or U-46619 (10 nM). Precontraction with 60 or 120 mM K^+, incubation with tetraethylammoniumchloride (3 mM) or glibenclamide (30 µM) significantly impaired the hypoxic response. Glibenclamide (30 µM) enhanced the vasorelaxing effect of NaHS (except at high concentrations of NaHS). Lactate (10 nM to 1 mM) had no effect on preparations with or without adipose tissue. 8-(p-sulfophenyl)theophylline (0.1 mM), zinc protoporphyrin IX (10 µM), 1 H-[1, 2, 4]oxadiazolo[4,3- A]quinoxalin-1-one (10 µM) and removal of the endothelium did not influence the hypoxic relaxation.
In conclusion, our findings indicate that hypoxia has a relaxing influence on mice aorta that is dependent on the presence of adherent adipose tissue. This relaxation is partly mediated by opening K_{ATP} channels and independent of the endothelium and soluble guanylyl cyclase. Neither lactate, adenosine, CO or H_2S seem to be involved in this hypoxic response. However, the involvement of the as yet unidentified "adipocyte-derived relaxing factor" (ADRF) can not be excluded.