BASAL BLOOD FLOW TO CORTICAL BONE IS PARTIALLY CONTROLLED BY ALPHA ADRENERGIC RECEPTORS

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Introduction: The fundamental question of clinical importance is, “What physiologic factors control bone blood flow?” The goal of the present study was to determine if endogenous norepinephrine, acting via alpha adrenergic receptors, regulates cortical bone blood flow in vivo. The overall experimental approach was to assess the change in blood flow to the intact rat tibia after pharmacological inhibition of alpha adrenergic receptors. The extent to which blood flow increased after alpha receptor blockade would reflect the extent to which endogenous norepinephrine was tonically constricting the vasculature of cortical bone.

Methods: Male Sprague Dawley rats (250 – 350 g) were anesthetized with Inactin (100 mg/kg, i.p.) and body temperature was maintained at 37 ± 0.5 °C. The carotid artery was cannulated to measure arterial blood pressure. The left iliac artery was cannulated and the tip was advanced to the bifurcation of the aorta. The left iliac artery was then occluded to stop blood flow to the left hindlimb. This allowed drugs to be delivered preferentially to the right hindlimb. A laser doppler flow probe was placed against the shaft of the right tibia (periosteum removed) for measurement of cortical bone blood flow. The first series of experiments determined the dose of alpha receptor antagonist, phentolamine, which would significantly inhibit the constrictor effect of exogenous norepinephrine on tibia cortical blood flow. A dose-response curve to exogenous norepinephrine (NE) was generated by injecting 5 doses of NE into the left hindquarter and quantitating the change in cortical bone blood flow and blood pressure. After a 30-min recovery period, the NE dose-response protocol was repeated after injection of phentolamine (17 µg/kg) into the hindquarter circulation prior to each NE injection.

The second series of experiments determined the effect of alpha adrenergic receptor blockade on resting cortical bone vascular resistance. In this series, phentolamine (17 µg/kg) was injected 5 times at 6-min intervals while measuring blood pressure and cortical bone blood flow. In both series, cortical bone vascular resistance was calculated from the blood pressure and blood flow values at specific time points during the experiments. Changes in cortical bone vascular resistance were expressed as a percentage of the vascular resistance during the pre-drug control periods. Group data were calculated as Mean ± SEM values.

Essential Results: Exogenous NE caused a dose-dependent decrease in cortical bone blood flow and an increase in systemic blood pressure. The highest NE dose decreased bone blood flow by 30 – 60% and increased blood pressure by 10-12 mmHg. Phentolamine inhibited by 50% the decrease in bone blood flow caused by NE but had no significant effect on the systemic pressor effect of NE. Thus, the selected phentolamine dose effectively inhibited constriction to exogenous NE that was mediated by alpha adrenergic receptors. When phentolamine alone was injected into rats of series #2, cortical bone vascular resistance decreased by 20-25% during the first 5 min. Subsequent injections of phentolamine further decreased vascular resistance by as much as 35% to indicate that there is alpha adrenergic receptor control of baseline cortical bone blood flow.

Discussion: Previous studies have demonstrated that bone vascular resistance increases in response to the administration of exogenous norepinephrine. The present study demonstrate that pharmacological inhibition of alpha adrenergic receptors results in a significant decrease in cortical bone vascular resistance. We conclude that endogenous norepinephrine plays a significant role in the regulation of cortical bone blood flow by exerting a tonic constrictor effect on supply vessels.

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