TACSM Abstract

Vasodilation to PTH 1-84 in Bone Resistance Arteries of Rats Occurs via Endothelium-dependent, Rather than Endothelium-independent Signaling

TYLER J BENSON[1] and RHONDA D PRISBY[2]

[1]Department of Kinesiology, University of Texas at Arlington; Arlington, TX
[2]Bone and Microcirculation Laboratory; Department of Kinesiology and Applied Physiology; Newark, DE

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ABSTRACT

Parathyroid hormone (PTH) is a potent vasodilator, causing systemic hypotension. Previous investigations concluded that vasodilation to PTH in a variety of vascular beds occurs via inhibition of L-type calcium channels in smooth muscle cells. Further, removal of the endothelium in aortic strips and tail arteries did not inhibit relaxation to PTH, suggesting that vasodilation in these vessels does not require nitric oxide (NO) or vascular endothelial cells (Pang et al., 1985; Nickols 1987; Nickols et al., 1986; Crass et al., 1988). We have previously shown that PTH 1-84 augments vasodilation to ~52% of maximum diameter in the femoral principal nutrient artery (PNA; the primary conduit for blood flow to long bones). Further, vasodilation was nearly obliterated with blockade of NO production with the endothelial nitric oxide synthase inhibitor L-NAME, suggesting that vasodilation in the bone vasculature occurs exclusively via NO-mediated signaling. Thus, to confirm these findings, the purpose of this study was to determine whether vasodilation to PTH 1-84 occurs in the absence of endothelial cells. *METHODS:* Right femoral PNAs were dissected from 4 month-old male Wistar rats (453 g; n=6), denuded (i.e., removed of the endothelial cells) and cannulated on glass micropipettes. PNAs were considered adequately denuded if they dilated ≤ 20 µm to a bolus dose of acetylcholine ($5x10^{-5}$ M). Vasodilation to PTH 1-84 (10^{-13} – 10^{-8} M) was assessed in the presence of 1) PSS buffer, 2) PSS buffer with L-NAME, and 3) PSS buffer with L-NAME + indomethacin (Indo; a cyclooxygenase inhibitor). To ensure that the smooth muscle cells were not damaged during endothelial cell removal, endothelium-independent vasodilation to sodium nitroprusside (SNP; 10^{-10} – 10^{-4}) was determined. *RESULTS:* Vasodilation to cumulative doses of PTH 1-84 peaked at 5% of maximum diameter. Inhibition of NO production with L-NAME completely inhibited vasodilation and caused a slight vasoconstriction, while combined inhibition with L-NAME + Indo did not constrict the femoral PNA; however, neither response differed from the PTH 1-84 response. Vasodilation to SNP rose to 69% of maximal diameter, indicating that smooth muscle cell responsiveness was not altered with endothelial denudation. *DISCUSSION*: These preliminary data support our contention that vasodilation of the bone resistance vasculature occurs via endothelium-dependent, rather than endothelium-independent signaling pathways. This novel finding suggests that, contrary to vasodilator mechanisms in blood vessels from other tissue beds, bone blood vessels require the vascular endothelial cell lining for vasodilation to PTH 1-84.

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