Endothelin-1 (ET)-induced mobilization of intracellular Ca^{2+} stores from the smooth muscle facilitates sympathetic cotransmission by potentiation of adenosine 5′-triphosphate (ATP) motor activity: Studies in the rat vas deferens

M. V. Donoso, C. G. Montes, J. Lewin, A. Fournier, J. B. Calixto, J. P. Huidobro-Toro

Abstract

Endothelin-1 (ET) enhances nerve-stimulated contractions in epididymal (E) and prostatic (P) halves of the rat vas deferens, in addition to raising the basal tone in E. Whereas the peak increase in basal tone occurs in about 30 s, the maximal enhancement of neurotransmission is observed within 5 min. The latter effect is long lasting and is maintained even after extensive tissue washout. Furthermore, ET potentiates, in a concentration-dependent fashion, the adenosine 5′-triphosphate (ATP) or the adenylylimidodiphosphate (AMP-PNP) but not the noradrenaline (NA)-induced motor activity. The ATP motor response is partially blocked in media without Ca^{2+} plus 0.1mM EGTA or following tissue incubation in buffer containing 10–50nM nifedipine. However, these procedures do not modify significantly the ET-induced potentiation of the ATP contractions. The ET-induced potentiation of the ATP motor response is not modified by tissue preincubation in Ca^{2+}-free buffer plus 10–30 μM ryanodine or 5–20mM caffeine. The ET-induced rise in E basal tension is significantly reduced in the absence of external Ca^{2+} or by nifedipine; ryanodine does not modify this effect. Surgical denervation of the tissues does not obliterate the ET-induced potentiation of the ATP motor responses nor the ET increase in E basal tension in tissues superfused in Ca^{2+}-free media or buffer with 2.5mM Ca^{2+}. Endothelin-1 does not significantly modify the overflow of ^{3}H-NA, following transmural electrical depolarization of tissue nerve terminals. Hoe 140 did not interfere with the ET activity.