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THE POSSIBLE EFFECT OF NITRIC OXIDE ON RELAXATIONS AND NORADRENALINE RELEASE IN THE ISOLATED RABBIT URETHRA

Aims of Study

There are reports demonstrating that nitric oxide (NO) is one of the neurotransmitters released from the nitrergic component of non-adrenergic, non-cholinergic nerves Recently, NO has been identified as a nitrergic neurotransmitter contributing to relaxation in various mammalian urethra However, some reports have suggested that neurotransmitters released from nitrergic nerves do not appear to be free radical NO only, and may include NO-containing compounds (1) Recently, we found a new class of NO scavenger, i e , a series of derivatives of carboxy-2-phenyl-4,4,5,5,-tetramethylimidazoline-1-oxyl-3-oxide (PTIO), that showed a unique radical-radical reaction with NO Using this compound, we have analyzed the pathophysiological roles of NO in vivo and vitro (2) In the present study, assuming that part of the nitrergic nerve-mediated urethral relaxation relates to free radical NO and NO-containing compounds, we attempted to investigate the effects of water soluble carboxy derivative of PTIO (carboxy-PTIO) on relaxations induced by electrical field stimulation (EFS) in rabbit urethral smooth muscles In addition, we examined the effects of carboxy-PTIO on noradrenaline release from prejunctional adrenergic nerves endings in rabbit urethra, using high-performance liquid chromatography (HPLC) with electrochemical detection (ECD) coupled with a microdialysis procedure, since several reports demonstrated that the endogenous free radical NO has a prejunctional action in inhibiting excitatory neurotransmitter transmission in several tissues (3)

Methods

Rabbit urethral smooth muscle strip, which was suspended in a 20 ml muscle bath filled with Krebs-Henseleit solution, was connected to an isometric force displacement transducer, and an isometric tension development was recorded In the relaxation experiments, we investigated the effects of N^{ω}-nitro-L-arginine (L-NNA) and carboxy-PTIO on EFS (supramaximum voltage, 2 0 ms pulse duration, 0 1-15 Hz and 3 s train)-induced relaxations of rabbit urethral smooth muscles precontracted with 1 0 μM phenylephrine In the noradrenaline release experiments, the microdialysis probe was inserted into the strip, and Ringer solution was perfused into the probe The dialysate during EFS (supramaximum voltage, 0 5 ms pulse duration, 40 Hz and 3 s train at 1 min interval for 10 min) was collected, and the amount of noradrenaline released in the dialysate was measured by HPLC with ECD The effects of pretreatment with carboxy-PTIO and L-NNA on noradrenaline release in urethral strips were evaluated

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Results

EFS caused frequency-dependent relaxations in rabbit urethral smooth muscles precontracted with phenylephrine. The relaxation responses were significantly inhibited by pretreatment with L-NNA (10-100 μM) or carboxy-PTIO (10-100 μM) The inhibitory effect of carboxy-PTIO was significantly weaker than that of L-NNA (Fig 1) EFS caused significant noradrenaline releases from adrenergic nerve endings in the rabbit urethra Pretreatment with carboxy-PTIO (100 μM) significantly enhanced EFS-induced noradrenaline release, and simultaneous application of L-NNA (100 μM) and carboxy-PTIO (100 μM) did not cause further enhancement of noradrenaline release in the rabbit urethra (Fig 2)

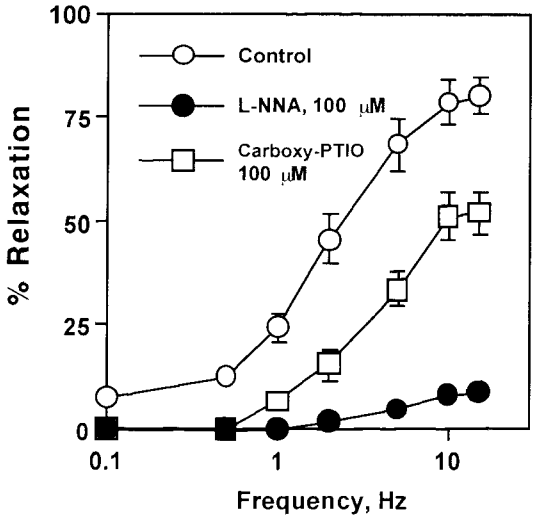

Fig. 1 Effects of L-NNA and carboxy PTIO on frequency dependent curve for EFS-induced relaxation

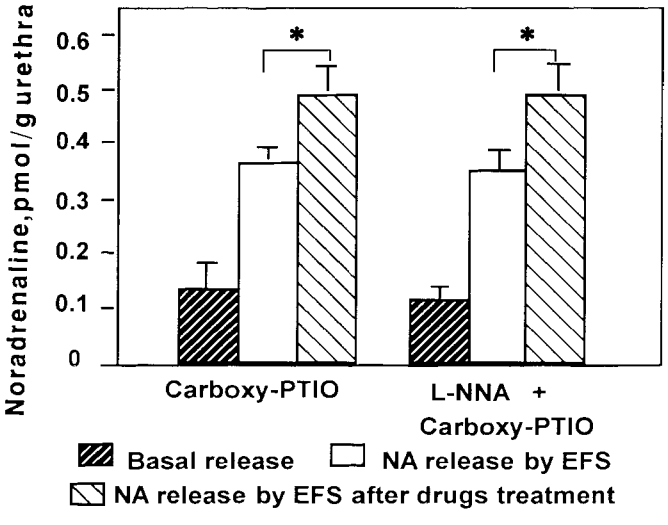

Fig. 2 Effects of L-NNA and carboxy-PTIO on EFS induced noradrenaline releases in rabbit urethra

Conclusions

As carboxy-PTIO reacts only with the free radical NO, the present data indicate that both free radical NO and NO containing compounds are involved in the L-NNA sensitive nitrergic nerve-mediated relaxation in the rabbit urethra At the same time, free radical NO may have a prejunctional inhibitory action on noradrenaline release from adrenergic nerve endings

References

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