Effect of labetalol on adrenergic transmission in the rat anococcygeus muscle

S.A. DOGGRELL & D.M. PATON

Department of Pharmacology, University of Alberta, Edmonton, Alberta, Canada

Labetalol has been reported to block α- and β-adrenoceptors in several tissues (Brittain & Levy, 1976). In the present study we have compared the α-adrenoceptor blocking actions of labetalol, prazosin and phentolamine in the rat anococcygeus muscle. Contractile responses of the rat anococcygeus muscle were recorded isometrically as described by Gillespie (1972). Mean vales were determined from at least 5 observations and are expressed ± s.e. mean.

Labetalol (10^{-5}M and 10^{-6}M) induced marked spontaneous activity which was abolished by phentolamine (5×10^{-6}M). After this spontaneous activity had disappeared (2-3 h), labetalol (10^{-5}M and 10^{-6}M) alone, or in the presence of nortriptyline (10^{-6}M), had no effect on responses to (-)-noradrenaline. In the presence of nortriptyline (10^{-6}M), phentolamine (10^{-6}M) and prazosin (10^{-8}M) inhibited responses to (-)-noradrenaline with pA_2 values of 6.76 and 8.86, respectively. Labetalol (10^{-6}M) did, however, inhibit responses to (-)-noradrenaline in the presence of guanethidine (6×10^{-6}M)); the pA_2 value being 6.76. Labetalol (10^{-6}M) abolished responses to field stimulation (1 ms, supramaximal voltage) at 0.1-2 Hz, and reduced responses at higher frequencies. In the presence of nortriptyline (10^{-6}M) this inhibitory effect of labetalol was significantly reduced. Guanethidine (6×10^{-6}M) abolished responses to field stimulation at 0.1-2 Hz and reduced responses at higher frequencies; this effect was partially reversed by nortriptyline (10^{-6}M). Both labetalol and guanethidine were thus less potent inhibitors of responses to field stimulation in the presence of nortriptyline. By contrast, all responses to field stimulation (0.1-40 Hz) were inhibited by phentolamine (10^{-6}M) and prazosin (10^{-7}M), in the presence of nortriptyline (10^{-6}M).

Maximum responses to tyramine in the absence of other drugs, and in the presence of 10^{-5}M and 10^{-6}M labetalol were 98% ± 6, 9% ± 9, and 61% ± 5, respectively, of the maximum response to (-)-noradrenaline. In the presence of phentolamine (10^{-6}M), responses to tyramine were abolished.

These results suggest that labetalol releases (-)-noradrenaline in the rat anococcygeus muscle. A depletion of noradrenaline stores or an impairment of release may explain why labetalol is a more potent inhibitor of responses to field stimulation and tyramine than of (-)-noradrenaline in this tissue.

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References

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Factors influencing the inhibitory effectiveness of clonidine on adrenergic transmission: the relationship between clonidine-induced inhibition and the duration of interval between stimuli

O.A. IDOWU & M.A. ZAR

Department of Pharmacological Sciences, The Medical School, The University of Newcastle upon Tyne, NE1 7RU

It has been reported earlier (Idowu & Zar, 1976) that clonidine inhibits the adrenergic motor transmission in the anococcygeus by presynaptic mechanisms. In the present investigation we have ascertained the effect of the duration of the interval between stimuli upon the clonidine-induced inhibition of the adrenergic transmission.

Isolated anococcygii from male rats were set up in 10ml organ baths between parallel platinum electrodes in Krebs-Henseleit solution at 37°C and contractions were recorded isometrically. For electrical field stimulation, 5 pulses of 1 ms duration at 10 Hz were delivered at supramaximal voltage, at variable intervals (3, 7.5, 15, 30, 60 s). The inhibitory effect of clonidine on adrenergic motor transmission was most marked at 60 s intervals and declined as the interval between the delivery of the 5-pulse trains decreased (Table 1). A possible explanation (Starke, 1972) for this relationship between clonidine-induced inhibition and the interval between stimuli might lie in a feed-back inhibition of transmitter release by endogenous noradrenaline (NA); with shorter intervals between stimuli, larger biophase concentrations of NA is to be expected and is likely to produce a greater degree of feed-back inhibition, thus masking the effectiveness of clonidine. This possibility is sup-