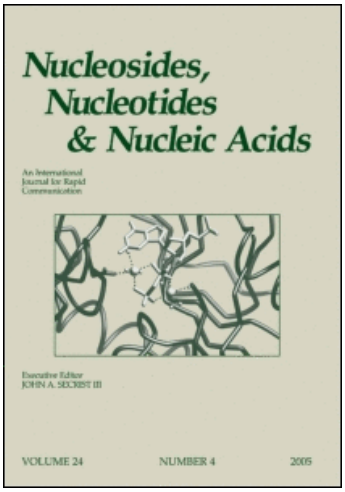

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Kazumasa Shinozuka[a]; Yuta Kobayashi[a]; Keiko Shimoura[a]; Keisuke Hattori[a]
[a] Department of Pharmacology, Shimane Medical University, Izumo, Japan

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REGIONAL DIFFERENCE OF PURINERGIC MODULATION ON ADRENERGIC NEUROTRANSMISSION IN ISOLATED RABBIT PULMONARY ARTERY

Kazumasa Shinozuka*, Yuta Kobayashi, Keiko Shimoura and Keisuke Hattori
Department of Pharmacology, Shimane Medical University, Izumo 693 Japan

Abstract Effects of 2-Chloroadenosine on different parts of pulmonary artery isolated from rabbit were studied,and it was suggested that there was a significant regional difference of purinergic modulation on noradrenaline release between proximal and distal parts of the artery.

The evidence is substantial that adenyl purines such as adenosine and ATP have various actions in blood vessels. Preliminary work in our group with rabbit pulmonary artery indicates the presence of purinoceptors that mediate an inhibition of noradrenaline release (FASEB J., 2: A 1815, 1988). The present studies were performed to seek evidence concerning the regional difference of the prejunctional purinoceptors distribution and nature in the rabbit pulmonary artery.

The preparations, the pulmonary artery trunk(PAT), main extrapulmonary artery branch (EPAB) and main intrapulmonary artery branch (IPAB) isolated from rabbit weighing 2.0 kg,were subjected to electrical stimulation (ES) with 2.0 msec pulses for 20 sec or 3 min at 4 Hz. The contractile responses of the ring preparations were measured isometrically by force-displacement transducer, and noradrenaline (NA) released into bathing solution was quantified by HPLC electrochemical detection.

In PAT,EPAB and IPAB, contractile responses induced by ES for 20sec were abolished by tetrodotoxin at 0.1μM and depressed by bunazosin, α_1-antagonist, at 1μM by 90-95% (data not shown). 2-chloroadenosine (2CA) inhibited the contractile responses of these three preparations to ES in a concentration dependent manner as in FIG.1. The rank order of inhibitory effect was IPAB>EPAB$\gg$PAT. The release of NA evoked by ES for 3 min was reduced by 2CA at 10μM in both EPAB and IPAB by 53.0% and 55.6%, respectively, but not significantly affected in PAT (FIG.2).
Clonidine, α_2-agonist, reduced NA release from both PAT and EPAB, and the inhibition ratios were 37.2% and 41.6%, respectively as in FIG.2.

The inhibitions by 2CA on the contraction and NA release to ES in EPAB were significantly antagonized by 8-sulfophenyl theophylline, P_1-antagonist,at 30μM. In EPAB precontracted with NA at 1μM, 2CA produced relaxation, which was also antagonized by the P_1-antagonist (data not shown). α,β-methylene ATP at 30μM, P_2-desensitizing agent, did not affect the relaxation produced by 2CA at 10μM. But the inhibition by

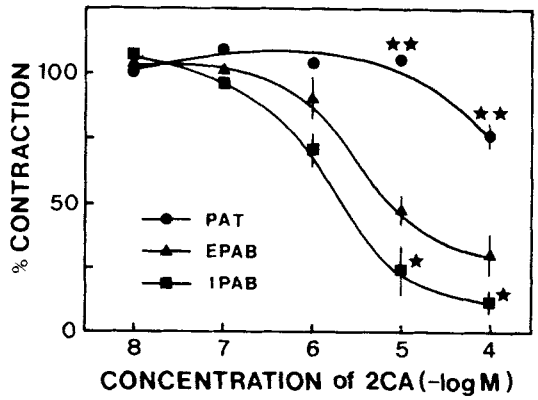

FIG.1 Concentration related effects of 2-chloroadenosine (2CA) on electrically(4Hz,20sec) evoked contractions of the pulmonary artery trunk (PAT), extrapulmonary artery branch(EPAB) and intrapulmonary artery branch (IPAB), isolated from rabbit.

Ordinate expresses percent of control contraction to electrical stimulation.

*p<0.05,**p<0.01 from EPAB(N=4-6)

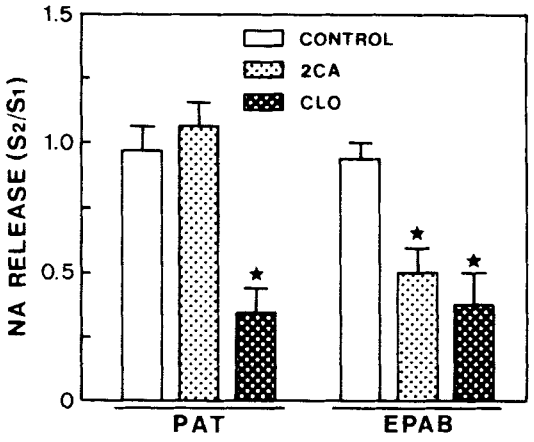

FIG.2 Inhibitory effects of 2-chloroadenosine(2CA,10μM) and clonidine (CLO,0.1μM) on electrically (4 Hz,3 min) induced noradrenaline (NA) release from the pulmonary artery trunk (PAT) and extrapulmonary artery branch (EPAB).

Ordinate expresses noradrenaline release as S2/S1 ratio. Drugs were added to the tissues 3 min before the second stimulation(S2).

*p<0.05 from each control (N=4-8)

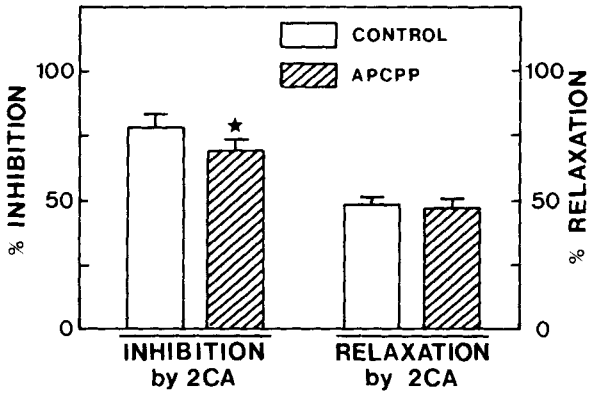

FIG.3 Influence of α,β-methylene ATP (APCPP,30μM) on the inhibitory and relaxant effects of 2-chloroadenosine(2CA,10μM) in the intrapulmonary artery branch.
Left ordinate expresses percent inhibition of each control contraction to electrical stimulation at 4 Hz for 20 sec. (N=8)
Right ordinate expresses percent relaxation of each contraction to noradrenaline (1μM). (N=4)
*$p<0.05$ from control,paired t-test

2CA on the contraction to ES was attenuated by α,β-methylene ATP significantly (FIG.3).

Generally,it is accepted that small blood vessels take an important role in the control of local circulation and blood pressure. The present results show that there is a significant difference the prejunctional inhibition by purines between the pulmonary artery trunk and its branch, and suggest one possibility that purinergic modulation may be more important in peripheral part of the artery than the proximal part. Furthermore, the prejunctional purinoceptor in this artery seems to have similar property to P_3-receptor (Naunyn-Schmied.Arch.Pharmacol.,338:221, 1988; J.Pharmacol.Exp.Ther., in press, 1990).