The influence of cyclic GMP on contractions of guinea-pig bronchial muscle

DRAGINJA ANDJELKOVIĆ*, I. ANDJELKOVIĆ, *Department of Pharmacology, PF 662, Medical Faculty, 11000, Belgrade, Yugoslavia*

Earlier observations have indicated acetylcholine-like drugs and other agents which stimulate contractions also enhance the accumulation of cyclic guanosine 3′5′-monophosphate (cGMP) on various isolated smooth muscle preparations (Lee et al 1972; Schultz et al 1973; Dunham et al 1974; Andersson et al 1975). It was also observed that cGMP increased contractions of the guinea-pig vas deferens caused by noradrenaline and electrical stimulation. These results were explained by hypothesis that cGMP may act as a co-mediator with calcium to promote contraction (Wikberg & Andersson 1978). However, there are no data on the possible influence of cGMP on contraction of bronchial muscle. We therefore have examined the influence of cGMP on the bronchoconstrictor effects of acetylcholine, histamine, 5-hydroxytryptamine (5-HT) and prostaglandine $F_{2\alpha}$ on the guinea-pig bronchial muscle, in vivo.

Guinea-pigs of either sex, 450–600 g, were anaesthetized with urethane (0·7 ml of 25% solution/100 g s.c.). The bronchoconstriction was recorded by 'Bronchospasm tranducer 7020', Ugo Basile.

Freshly prepared solution of acetylcholine (20 μg kg^{-1}), histamine hydrochloride (1 μg kg^{-1}), 5-HT (5 μg kg^{-1}) and prostaglandin $F_{2\alpha}$ (3 μg kg^{-1}) were injected through a polyethylene catheter into the jugular vein. Dibutyryl cyclic guanosine 3′5′-monophosphate (db-cGMP) was injected in the same way in a dose of 2 mg kg^{-1} 10 min before the bronchoconstrictors.

After administration of db-cGMP the acetylcholine effect was strongly potentiated (about 600% compared with the control). Ten min later, the acetylcholine effect returned to the control value (Fig. 1). This kind of effect was obtained in 15 out of 20 experiments. In the remaining experiments the db-cGMP potentiation of acetylcholine bronchoconstriction was longer, lasting 1 or more hours. On the contrary, db-cGMP did not change the bronchoconstriction caused by either histamine, or 5-HT and prostaglandine $F_{2\alpha}$. 5′-GMP was ineffective in these experiments.

Our results show that cGMP potentiated only the acetylcholine bronchoconstriction. This potentiation agrees with the finding that cGMP may stimulate cholinergic neurons (Puglisi et al 1972; Folco & Wikberg 1974). It was also suggested that cGMP acts as intracellular mediator for acetylcholine-like substances (Goldberg et al 1973). It is possible, also, that a kind of positive feedback mechanism between cGMP and Ca^{2+} may be involved in the contractile process of the smooth muscle (Andersson et al 1975).

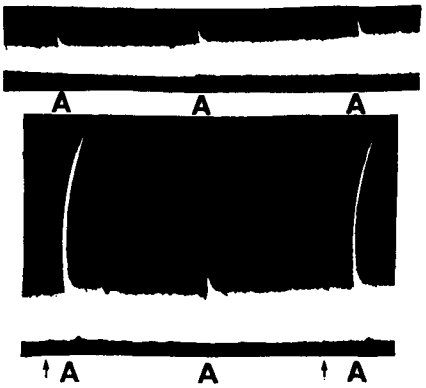

Fig. 1. The influence of db-cGMP on the acetylcholine contraction of the guinea-pig bronchial muscle. At 'A': acetylcholine injected i.v. in a dose of 20 μg kg^{-1}. At arrows: injection of db-cGMP.

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* Correspondence.

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