Antagonism of acetylcholine-induced bronchospasm by WG 253, a new sympathomimetic amine

WG 253, [erythro-(3,4-dihydroxyphenyl)(2-piperidyl) methanol hydrobromide], a member of a new series of sympathomimetic amines cyclized about the α-carbon atom gave longer protection against histamine-induced bronchospasm than did isoprenaline when administered by aerosol to human volunteers (Griffin & Turner, 1971). In addition, isoprenaline had much greater cardiovascular effects as measured by pulse rate, blood pressure and electrocardiographic changes.

A within-subjects double-blind comparison of aerosol preparations of isoprenaline, orciprenaline, salbutamol and WG 253 in protecting human volunteers against acetylcholine induced bronchospasm has now been made. Eight normal subjects of either sex (aged 20–36 years) took part, and the order of treatments within subjects was determined from two latin squares, the tests being carried out at intervals of 7 days. On each test day, two control measurements of FEV_1 were made on each subject using a Vitalograph. The subject then inhaled 500 μg of acetylcholine from a pressurized aerosol delivering 250 μg/puff. Measurements of FEV_1 were then made at 30 s after inhalation of acetylcholine and at 1 min intervals for 10 min. Two h after the first inhalation of acetylcholine, two further control measurements of FEV_1 were made, then the subject was given from an aerosol preparation one metered dose of isoprenaline (100 μg/dose), orciprenaline (750 μg/dose), salbutamol (100 μg/dose) or WG 253 (500 μg/dose), according to the randomization schedule. (The aerosol dispensers were not distinguishable one from another.)

Five min after receiving the bronchodilator aerosol the subjects were challenged again with 500 μg of acetylcholine, the FEV_1 being measured as previously. The changes in FEV_1 from baseline control values were determined for acetylcholine alone and for acetylcholine given after pretreatment with a bronchodilator aerosol. These values were subjected to a multivariate analysis of dispersion followed by calculation of T^2 for all contrasts between pairs of drugs (Smart, Sneddon & Turner, 1967; Cherrington & Smart, 1971).

The ½ min values were significantly greater than zero, indicating that all drugs had reduced the fall in FEV_1 produced by acetylcholine. All the other values up to 10 min were significantly greater than zero, except for salbutamol which was not significantly different from zero after 6 min. There was no difference between the other treatments at any of the times measured.

Thus all four compounds exerted a significant protection against bronchospasm induced by acetylcholine within half a minute of inhalation, and the effect was maintained for at least 10 min for all drugs except salbutamol under the experimental conditions and in the doses used.

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