Comparison of the Broncholytic and Cardiovascular Responses of Asthmatic Patients to Aerosol Dose of Isoproterenol and Fenoterol

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Because lung function measurements per se do not reflect an interplay of desirable and unwelcome effects, we compared the beta₂ specificity of four doses of fenoterol and isoproterenol in a randomized double-blind evaluation of cardiac and pulmonary responses in 24 patients (mean age 54.9 years) with moderately severe bronchial asthma. All had demonstrated potential reversibility on prior isoproterenol inhalation testing. Maximum expiratory flow-volume (MEFV) curves generated the lung function information. Arterial blood pressure, pulse and respiratory rates were monitored...
clinically, and a 9-lead electrocardiogram was recorded on each test day at baseline and 5, 15, 30, 60 and 120 minutes after individual coded treatments. A parallel-line bioassay was used to determine the relative potencies of the two drugs for their respiratory and pulse rate functions, defining relative potency as the ratio of the dose of isoproterenol to a given dose of fenoterol producing an equal response; a quantitative selectivity ratio was computed from these data. A second index was determined by calculating the ratio of percentage changes in ventilatory function to percentage changes in pulse rate at all test points for the four doses of the two aerosols.

**Results:** Both aerosols produced a significant bronchodilatation. At all levels of inhalation dosage, fenoterol induced a shorter and less marked cardioacceleration than isoproterenol (Fig 1). One inhalation of fenoterol was as effective as 1.16 inhalations of isoproterenol in improving the FEV1,0, whereas more than three inhalations of the former were needed to speed the pulse as much as one whiff of isoproterenol; these data furnish a quantitative selectivity ratio for fenoterol of 3.86. Similar treatment of the MEF and pulse rate figures yielded a selectivity ratio for bronchodilatation versus tachycardia for these variables of 3.70. When the same data are tabulated as percentage change in ventilatory function over percentage change in pulse rate, the overall results emphasize the superiority of fenoterol in standard clinical doses as a selective bronchodilator. Both approaches suggest that inspection of the FEV1,0, MEF and PEFR indices in relation to pulse rate values furnishes a practical method of assessing the beta2 properties of bronchodilators.

Neither aerosol changed the blood pressure significantly. CNS and cardiovascular manifestations, the principal side effects, were more frequent after isoproterenol inhalations. Digestive, musculoskeletal and central activity appeared only with 8 inhalations (1.6 mg) of fenoterol. The ventilatory advantages of fenoterol, the minimal undesirable effects when given in one or two inhalations, and the difference between bronchodilator and tachycardic potencies indicated by quantitative selectivity ratios computed using simple lung function tests, indicate that this agent surpasses isoproterenol in the beta2 selectivity of its action.