

STUDIES OF NEW SYMPATHOMIMETIC BETA-RECEPTOR STIMULATING DRUGS IN ASTHMATIC PATIENTS. IV. A COMPARATIVE TRIAL OF SUBCUTANEOUS TERBUTALINE (BRICANYL) AND SALBUTAMOL (VENTOLIN)

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SYNOPSIS

A comparative study of the bronchodilator and cardiovascular effects of subcutaneous terbutaline (0.5 mg.) and salbutamol (0.2 mg.) was carried out. Both drugs produced a rapid and pronounced broncholytic effect. Terbutaline gave better bronchodilatation but also caused a greater increase in heart rate at the dosages used. An analysis of the ratio of the relative maximum increase in peak expiratory flow rate to the relative maximum increase in heart rate for each drug revealed no significant difference between the two drugs.

Salbutamol (Ventolin, Glaxo Laboratories Ltd., U.K.) and terbutaline (Bricanyl, AB Astra, Sweden) are two widely used bronchodilator drugs for the relief of airways obstruction in asthmatic patients. Both drugs are more selective bronchodilators (beta₂ adreno-receptor stimulants) with relatively little cardiovascular side effects (Cullum *et al*, 1969; Warrell *et al*, 1970; Formgren, 1970; Arner *et al*, 1970 and Da Costa and Goh, 1973a). Terbutaline has been shown to be highly effective in acute asthma when rapid parenteral administration is desirable (Da Costa and Goh, 1973b). As the effects of subcutaneous salbutamol have not been previously compared with terbutaline, we report such a study in 14 asthmatic patients.

MATERIALS AND METHODS

Fourteen patients (8 males and 6 females) with bronchial asthma were investigated. Their mean age was 29 years (range 11—72 years). The reversibility of their airways obstruction was tested the day before the start of the trial. After two inhalations of orciprenaline aerosol (1.5 mg. orciprenaline), they had to show an increase in peak expiratory flow rate (PEFR) of at least 15 percent. No other bronchodilator drug was given later than ten hours before the start of the trial. Six patients who were on oral steroid therapy continued to receive the same dose during the trial. The tests were performed between 9

a.m. and 3 p.m. on two consecutive days as far as possible. A subcutaneous dose of 0.5 mg. terbutaline or 0.2 mg. salbutamol was given on different days, consecutively. The drugs were injected slowly over 3 minutes. PEFR was recorded using a Wright's peak flow meter (Wright *et al*, 1959) before, and at 15 and 30 minutes and 1, 2, and 3, 4 hours after injection. All measurements were made with the same apparatus while the subjects were seated. The best value of three measurements at each time period was used for the calculations. The heart rate was measured at the same periods before and after each injection and any side effects experienced by the patients were also recorded.

For each parameter (PEFR and Heart Rate) we have used Analysis of Variance to assess the following aspects:

- (a) Increase in the parameter measurement at each time of measurement.
- (b) Maximum increase, regardless of when it occurred.
- (c) Average increase throughout measurement period (i.e. a weighted average taking account of the time intervals between measurements).

RESULTS

The results are summarised in Tables I and II. In terms of Peak Flow, terbutaline 0.5 mg. subcutaneously exerts a better bronchodilating effect than 0.2 mg. salbutamol. The result being statistically significant 1 and 2 hours after drug administration. However, when the changes in heart rate are compared, salbutamol was better, the difference being statistically significant up to 1 hour after drug administration.

To determine which drug might be better to use, we have analysed the ratio of the relative maximum increase in PEFR to the relative maximum increase

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TABLE I
PEAK EXPIRATORY FLOW RATE (PEFR) IN THE
ASTHMATIC PATIENTS BEFORE AND AFTER
SUBCUTANEOUS INJECTION OF TERBUTALINE AND SALBUTAMOL

Aspect	Estimate for:— (litre/min)		Difference between Estimates that would be significant at P < 0.05
	terbutaline	salbutamol	
Increase at 15 min	63.7 a	51.3 a	16.5
Increase at 30 min	70.7 a	57.7 a	18.2
Increase at 60 min	80.3 a	57.7 a	19.8
Increase at 120 min	68.3 a	37.7 b	21.8
Increase at 180 min	45.0 a	27.3 a	24.5
Maximum Increase	83.3 a	65.7 b	16.2
Average Increase	64.5 a	43.0 b	17.1
Mean Basal value	241.5	236.5	—

Note: For any Aspect (i.e. in any one row) two estimates with the same letter are not significantly different.

TABLE II
HEART RATE IN THE ASTHMATIC PATIENTS BEFORE
AND AFTER SUBCUTANEOUS INJECTION OF
TERBUTALINE AND SALBUTAMOL

Aspect	Estimate for:— (beats/min)		Difference between Estimates that would be significant at P < 0.05
	terbutaline	salbutamol	
Increase at 15 min	22.3 a	11.6 b	5.0
Increase at 30 min	20.4 a	10.3 b	6.2
Increase at 60 min	12.8 a	6.5 b	5.1
Increase at 120 min	4.7 a	-0.5 a	5.3
Increase at 180 min	3.6 a	-1.9 a	5.7
Maximum Increase	25.7 a	12.7 b	5.1
Average Increase	9.8 a	3.4 b	3.6
Mean Basal value	90.8	91.2	—

Note:— For any Aspect (i.e. in any one row) two estimates with the same letter are not significantly different.

in Heart Rate, i.e. for each drug:—

$$\text{Ratio} = \frac{\text{Maximum PEFR after drug}}{\text{Basal PEFR}} \div \frac{\text{Maximum Heart Rate after drug}}{\text{Basal Heart Rate}}$$

(a ratio greater than 1 would be desirable)

The means of these ratios for both drugs are:

Terbutaline 1.08

Salbutamol 1.11

The difference is not statistically significant.

Table III shows the side effects which were encountered. It is seen that terbutaline, in the dosage

used, produced more side effects than salbutamol although these were not at any time severe.

DISCUSSION

Both salbutamol and terbutaline were shown to produce marked bronchodilatation. Although the latter was better in this respect it however also caused a greater increase in the heart rate. Thus the results obtained are closely comparable with little to choose between either drug. It is interesting to com-

TABLE III
SIDE EFFECTS ENCOUNTERED AFTER
ADMINISTRATION OF SUBCUTANEOUS
TERBUTALINE AND SALBUTAMOL

Side effect	After Terbutaline (patients)	After Salbutamol (patients)
Slight palpitation	2	2
Moderate palpitation	4	—
Slight giddiness	1	—

pare these results with those of a similar comparative trial (Choo-Kang *et al*, 1973) of these two drugs administered as aerosols. Similar dosages were also used and both drugs were found to be equipotent bronchodilators producing negligible cardiovascular side effects by this route of administration. Thus either drug is suitable for the treatment of acute or chronic asthma, the aerosol being the more useful mode of administration, especially in chronic asthma.

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