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A comparison of the effects of Salbutamol, Fenoterol, and Placebo Aerosols on Airway Resistance in Asthmatics

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SUMMARY

The reduction in airways resistance, assessed by measurements of forced expiratory volume in one second, vital capacity and peak expiratory flow rate was estimated before and after inhalation of fenoterol, salbutamol or placebo aerosols in nine asthmatic subjects. This study showed that fenoterol is significantly better than salbutamol in terms of magnitude and duration of response.

INTRODUCTION

The usefulness in asthma of adrenergic drugs administered orally, parenterally or by aerosol inhalation is undoubted. (Siegmund et al. 1947; Barger and Dale, 1910, Konzett, 1940). However this usefulness has been limited by their short duration and by excessive cardiovascular side effects (Lands, 1966, Speizer et ai., 1968, Liefer and Wittig, 1975).

The solution of these problems was stimulated by the discovery of two different Beta adrenergic receptors (Lands et al. 1964, 1967 (a), 1967 (b) Furchgott. 1967; Collier and Dornhorst, 1969· Dunlop and Shanks, 1968). Beta – 1 receptors increase cardiac rate and force, relax smooth muscle and stimulate lipolysis whilst the Beta-2 receptors cause relaxation of bronchial, uterine and vascular smooth Muscle and stimulate glucogenolysis.

This discovery led to the development of Beta-2 Symphathomimetic drugs of which several are now available.

This study reports a comparison of salbutamol, an established Beta-2 symphathomimetic agent with the more recently introduced Fenoterol (Berotec, Boehringer Ingelheim) and placebo aerosols.

METHOD

Nine adult asthmatic subjects, four women and five men were studied on successive days. All regular bronchodilator therapy was stopped 24 hours before the trial took place. The asthma was stable during the period of the study as an exacerbation led to withdrawal of the subject from the trial. Measurements of forced expiratory volume in one second ($F.E.V._1$) and forced vital capacity (F.V.C.) were made by means of a Lode D-51 Spirograph and peak Expiratory Flow Rate (P.E.F.R.) was measured using a standard Wright Peak flow meter before and at regular intervals for six hours after the randomized double blind administration of aerosol. The pulse rate and blood pressure were measured at the same time as the pulmonary function studies were performed and an electrocardiogram was done before and half an hour after aerosol administration.

$F.E.V._1$/F.V.C.% and P.E.F.R. were chosen as the indices of airways obstruction as their measurement requires only simple easily maintained equipment, is quickly and easily performed by relatively unskilled technicians, is not distressing to the patient and compares well both for accuracy and airways obstruction.

RESULTS

The pooled results for all nine patients are represented in tables I and II.

These show that the reduction in airways resistance estimated both by $F.E.V._1$/F.V.C.% and by P.E.F.R. is significantly higher for both salbutamol and fenoterol than the placebo ($P < 0.01$) (Table IV) and for fenoterol when compared with salbutamol ($P=0.02 - 0.01$) (Table IV). These results are set out graphically in figs. I and II which clearly show that although there is a faster initial response to salbutamol when P.E.F.R. is used as the index of airways obstruction the greatest response and the longest duration of effect is found with fenoterol when either measurement is used.

As we are really interested in the duration as well as magnitude of bronchodilation probably the the best method of assessing response is to measure the areas of the graphs which is the product of these two values. If we do this (table III) the results again show a greater improvement with fenoterol than with salbutamol or placebo.

TABLE I

CHANGES IN FEV1/F.V.C. AFTER INHALATION OF BRONCHODILATOR AEROSOLS.

	Pre-inhalation	½hr	1hr	2hr	3hr	4hr	5hr	6hr
Salbutamol								
Mean FEV1/FVC	55	66	63	59	69	56	57	58
S.D.	13.1	11.4	13.3	9.2	10.5	9.0	7.2	10.4
% of pre-inhalation	100	122	117	109	115	104	106	107
Fenoterol.								
	Pre-inhalation	½hr	1hr	2hr	3hr	4hr	5hr	6hr
Mean FEV1/FVC	51	56	66	64	63	61	64	62
S.D.	14.8	13.8	11.7	8.3	7.3	10.6	12	11.8
% of pre-inhalation	100	110	129	125	124	120	125	122
Placebo.								
	Pre-inhalation	½hr	1hr	2hr	3hr	4hr	5hr	6hr
Mean FEV1/FVC	61	61	63	62	57	59	59	56
S.D.	10.5	10.0	7.6	9.1	11.0	10.7	8.9	11.7
% of pre-inhalation	100	100	103	102	93	97	97	92

TABLE II

CHANGES IN P.E.F.R. AFTER INHALATION OF BRONCHODILATOR AEROSOLS

	Pre-inhalation	½hr	1hr	2hr	3hr	4hr	5hr	6hr
		Salbutamol						
Mean P.E.F.R.	266	317	326	321	309	294	295	275
S.D.	76.7	63.6	90.3	82.9	75.7	78.6	94.7	95.5
% of pre-inhalation	100	119	123	121	116	111	111	103
		Fenoterol.						
	Pre-inhalation	½hr	1hr	2hr	3hr	4hr	5hr	6hr
Mean P.E.F.R.	218	294	329	313	312	295	297	278
S.D.	88.2	93.0	99.9	114.2	1000.5	91.2	83.0	85.7
% of pre-inhalation	100	135	151	144	143	135	136	128
		Placebo						
	Pre-inhalation	½hr	1hr	2hr	3hr	4hr	5hr	6hr
Mean P.E.F.R.	298	288	320	275	272	262	245	227
S.D.	105	89	91	98	84	102	98	86
% of pre-inhalation	100	97	107	92	91	88	82	76.

TABLE III

AREA OF THE GRAPHS

FEV1/FVC

SALBUTAMOL	=	636
FENOTEROL	=	709
PLACEBO	=	562

P.E.F.R.

SALBUTAMOL	=	662
FENOTEROL	=	805
PLACEBO	=	431

TABLE IV

LEVELS OF SIGNIFICANCE (t-test)	
FEV1/FVC %	
SALBUTAMOL Vs PLACEBO	P < 0.01
FENOTEROL Vs SALBUTAMOL	P = 0.02 - 0.01
P.E.F.R.	
SALBUTAMOL Vs PLACEBO	P < 0.01
FENOTEROL Vs SALBUTAMOL	P = 0.02 - 0.01

Side effects

In no patient was there an increase of more than 5mm Hg for either systolic or diastolic blood pressure nor were any electrocardiographic changes observed.

Only in one patient receiving fenoterol was there a rise in pulse rate of more than 10 beats/minutes (from 76/min to 95/min). This slight tachycardia persisted for one hour only and the pulse rate returned to pre-inhalation levels. No other adverse effects were observed during this study.

FIG.I

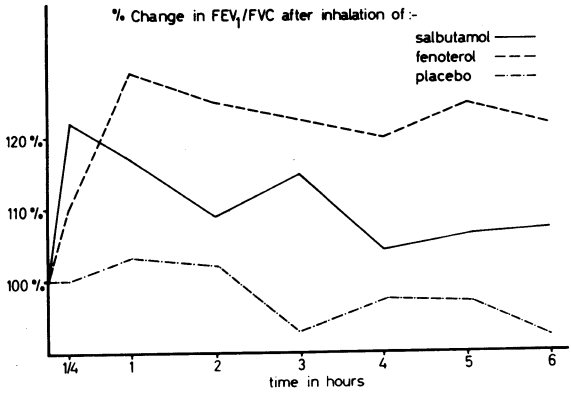
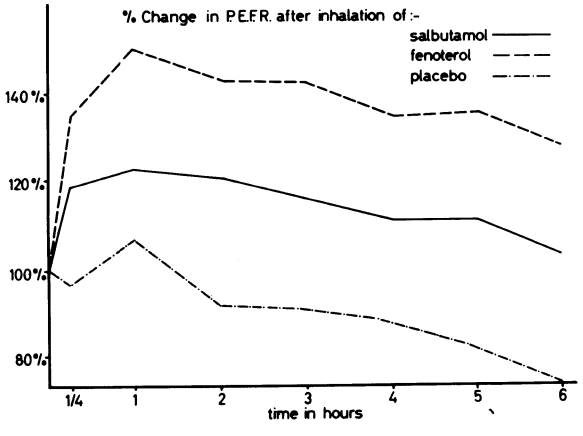


FIG. II



CONCLUSION

This study demonstrated that in asthmatics fenoterol (Berotec, Boehringer Ingelheim) is superior to placebo and salbutamol both in the magnitude of the reduction in airways resistance and in the duration of this effect.

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