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A double-blind trial of bromocriptine in steroid dependent asthma

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The pilot study of Newman Taylor *et al* (1976) in which, by adding bromocriptine to the full medical treatment, they improved the symptoms of three out of four asthmatic patients, prompted us to carry out this study. Bromocriptine is a dopaminergic agonist that is used in acromegalic patients, as well as an inhibitor of prolactin in doses of 5 to 20 mg a day. We decided to use 15 mg a day, which is usually without major side effects.

Methods and results

The trial was designed as a controlled double-blind cross-over study with bromocriptine (A) against placebo (B). Patients were randomised in two parallel groups for treatment in combinations A-B and B-A.

The bromocriptine and placebo capsules were identical. In each period the drug was given in an initial dose of one capsule (2·5 mg) a day and was slowly increased to two capsules three times a day. Each patient received each preparation for 12 weeks. Between the two periods the initial medical treatment was given for one week.

The clinical effect of the treatment was evaluated by:

(1) Titrating the oral daily dose of prednisone by reducing the actual dose by 2·5 mg a day if the patient improved. In cases of deterioration the prednisone dose was increased.

(2) Actual decrease/increase in additional symptomatic bronchodilator requirements (xanthines and beta-2-stimulating drugs) were registered for each treatment period. Each additional tablet, suppository, or aerosol inhalation was considered as one dose.

(3) Change in daily peak flow rate (PEF), measured by the patients before the first and last daily medical intake.

Wilcoxon's matched paired signed rank test for differences was used with the bromocriptine period as positive rank against the placebo period.

The 23 outpatients (12 from the chest clinic, Aalborg County Hospital and 11 from the medical department, Middelfart Hospital) were all patients with longstanding chronic asthma in whom the conventional treatment with aminophylline and beta-2-stimulating drugs had to be supplemented by oral prednisone for at least six months before the trial. (Eleven of the patients also received a beclomethasone inhaler.) All patients gave informed consent to participating in the trial. Three patients left the trial for reasons unconnected with bromocriptine. Twenty patients (10 men, 10 women) were finally included in the study. Age range was 33 to 75 years, mean 55·6. Mean daily prednisone dose before the trial was 10·65 mg.

The mean daily prednisone dose and the mean daily dose of bronchodilators did not differ between the two treatment periods and the average daily PEF did not differ between the two periods (see table).

Discussion

The lung contains large concentrations of dopamine, but the part played by this substance is not known. A possible relation between bronchial asthma and low dopamine concentration has been suggested by Barbeau (1970), who showed an extremely low urinary excretion of dopamine in many patients with asthma. Three patients who had required corticosteroid for more than two years were treated with a daily dose of 3 g levodopa for from three to nine months. In two patients the required dose of corticosteroids was decreased from an average of 30 mg a day to less than 5 mg. A similar hypothesis was the background of the pilot study by Newman Taylor *et al* (1976) of four patients with disabling asthma, who failed to respond to conventional treatment with bronchodilators and corticosteroids. Bromocriptine was given in a maintenance dose of 20 mg a day. This treatment permitted a reduction in the dose of corticosteroids and a decrease in symptomatic bronchodilator requirements in three patients, while the fourth patient showed no improvement. However, in our controlled study, bromocriptine, a dopamine agonist, did not produce any improvement in the condition of severe corticosteroid-dependent asthmatic patients.

Daily dosage of prednisone and bronchodilators with PEF measurements

Patient no	*I Average steroid requirement mg a day*		*Difference*	*II Mean daily dose of additional symptomatic bronchodilator requirements*		*Difference*	*III PEF measured by the patient*				*Difference**
							Morning		*Night*		
	A	*B*	*A–B*	*A*	*B*	*A–B*	*A*	*B*	*A*	*B*	*A–B*
1	8·65	10·55	−1·90	0·12	0·25	−0·13	192	179	202	188	27
2	7·50	7·50	0	2·27	2·23	0·04	237	281	286	281	− 39
3	7·85	6·67	1·20	0·02	0	0·02	319	356	330	389	− 96
4	10·90	10·90	0	0·92	0·55	0·37	232	225	237	231	13
5	19·35	14·23	5·12	2·73	3·15	−0·42	292	355	329	401	−135
6	8·07	9·33	−1·25	10·23	9·77	0·46	225	221	288	284	8
7	8·25	6·52	2·23	0·55	0·78	−0·23	163	172	196	219	− 32
8	7·50	2·50	5·00	0·87	0·85	0·29	174	171	219	204	18
9	4·80	4·58	0·22	0·01	0·01	0	259	276	251	273	− 39
10	7·50	9·17	1·67	0	0	0	134	126	140	130	18
11	6·67	4·14	2·50	0	0	0	219	210	266	264	11
12	18·10	18·80	−0·70	1·58	1·28	0·30	144	152	243	214	21
13	5·23	4·81	0·42	0·21	0·31	−0·10	238	236	323	313	12
14	15·39	16·99	−1·60	0	0	0	191	192	259	265	− 7
15	6·61	6·21	0·40	0·93	0·25	0·68	97	88	181	204	− 14
16	23·75	27·47	−3·72	5·20	3·30	1·90	129	143	136	149	− 27
17	7·17	6·77	0·40	1·16	2·73	−1·57	186	196	197	229	− 42
18	4·93	5·95	−0·98	0	0	0	257	236	256	236	41
19	5·63	7·02	−1·35	1·26	2·76	−1·50	233	208	268	232	61
20	11·55	14·90	−3·35	5·62	6·58	−0·96	113	98	135	119	30
			N 18 ΣR 171 t_+ 79			N 15 ΣR 120 t_+ 60					N 20 ΣR 210 t_+ 94·5

A = Bromocriptine period; B = Placebo period.
*Difference of morning + night values of PEF in periods A and B.

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