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A bacterial lysate (Broncho-Vaxom®[1]) in chronic bronchitis: a multicentre, double-blind, clinical trial

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SUMMARY

Seventy-one adults of both sexes suffering from recurrent chronic bronchitis, whose previous medical histories were well known to the investigators, were observed over a period of six months (autumn-winter 1978-79). During the first three months, 39 of the patients received Broncho-Vaxom® and 32 received a placebo, both in dosage of one capsule per day on 10 days per month. The results of this multicentre trial, conducted on a double-blind basis and analysed statistically, have demonstrated the therapeutic efficacy of immunobiotherapy with Broncho-Vaxom®. The clinical manifestations were improved and the duration of work incapacity diminished. Tolerance was good.

INTRODUCTION

Chronic bronchitis could be defined as a pathological condition in which the principal features are hypersecretion of mucus in the bronchial tree and productive cough that cannot be ascribed to any specific bronchopulmonary lesion. The essential criterion for its diagnosis is the presence of a daily productive cough during three consecutive months in at least two consecutive years. Chronic bronchitis is a serious disease which may lead, if not properly treated, to respiratory failure.

Tobacco and atmospheric pollution are important causal factors in chronic bronchitis. However, respiratory infections play a major role. Acute bronchitic attacks may turn oftenly into chronic bronchitis with hypersecretion of mucus which becomes superinfected thus increasing the severity of the disease.

Therefore, strengthening the body's defence mechanisms against infection is an essential measure in the treatment of chronic bronchitis. For this reason, a trial has been conducted in cases with chronic bronchitis by using a bacterial lysate, whose non-specific immunostimulatory action has already been demonstrated in human (1, 2, 3).

PATIENTS AND METHODS

The trial, which took place over a period of six months during the winter of 1978-79, initially concerned 81 adult patients of both sexes suffering from exacerbations of chronic bronchitis, and whose previous medical histories were well known to the investigators. They were allocated randomly to receive either capsules containing the lyophilized bacterial lysate (LBL) or capsules containing a placebo. All capsules and packages were identical in appearance. Each patient ingested one capsule daily on 10 days per month during the first three months of the trial.

The trial was a multicentre one, but conducted according to a common protocol. Patient particulars

[1] Each capsule contains 7 mg of a lyophilized lysate of Haemophilus influenzae, Diplococcus pneumoniae, Klebsiella pneumoniae and ozaenae, Staphylococcus aureus, Streptococcus pyogenes and viridans, Neisseria catarrhalis.

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recorded included age, gender, tobacco habits, details of respiratory illnesses during the corresponding six months of the previous year (the number, duration, and severity of the attacks, and how they were treated).

Five medical checks were performed, before treatment, at the end of the first, second and third month of treatment, and after the following three-month interval without therapy. At each examination, four clinical manifestations, cough, expectoration, dyspnoea, and abnormal signs on auscultation, were assessed on a five-point severity scale (0 to 4).

The same variables that were recorded for previous respiratory illnesses were recorded during the six months of the trial. Each investigator made a general evaluation of the treatment, based upon observation of the results as a whole. The results were analysed statistically. Tolerance to the preparation was noted.

RESULTS

Out of the 81 patients who began the trial, two unaccountably failed to attend for their second medical check. There thus remained 79 patients, 45 in the LBL group and 34 in the placebo group.

One patient in the LBL group stopped taking the drug because of alleged "burning sensations" in his head, another patient was eliminated from the assessment because he took all his capsules during the first month instead of over three months, and five patients (three from LBL group, two from placebo group) were eliminated because they had taken antibiotics throughout the entire period of the trial. Statistical analysis of the results therefore concerned 72 patients, 40 in the LBL group and 32 in the placebo group.

The mean age of the patients in the LBL group was 54.6 years and in the placebo group 55.5 years. There was no significant difference between the two groups as regards gender, use of tobacco, or previous history (such as number and severity of attacks of respiratory illness). In contrast, the number of days absent from work had been significantly higher in the LBL than in the placebo group before the start of the trial period (Behrens-Fisher test for comparison of means: $p<0.05$).

The investigators' general assessment (Table I) in 71 patients (one assessment was missing) revealed good results in 61.5% of the patients treated with the LBL and in 31.3% of those given the placebo. The difference between the groups was statistically significant (Lehmann's rank-sum test: $p<0.05$).

Table I. — General assessment of the results.

Result	No. of patients	
	Placebo (n = 32)	LBL (n = 39)
Good	10 (31.3%)	24 (61.5%)
Moderate	8 (25.0%)	5 (12.8%)
Nil	14 (43.8%)	10 (25.6%)

Statistically significant difference between Placebo and LBL ($p < 0.05$; Lehmann's rank-sum test).

Statistical analysis of the severity of the clinical features at the different stages of the six-month trial (Table II) showed LBL to be better than placebo on expectoration and dyspnoea (rank-sum test: $p<0.1$) after one month of therapy. For dyspnoea the improvement was more significant ($p<0.05$) after two months. This is confirming the favourable effect of LBL on the acute episodes in chronic bronchitis. The differences were not demonstrable statistically at the later stages, because of general abatement of the clinical manifestations in both groups. The improvement in cough, expectoration and dyspnoea in the LBL group was over 30% at the end of month 1 and rose to over 40% at the end of month 6. Improvement after placebo was never as great as after LBL, apart from the signs on auscultation at the end of the second month.

Days of incapacity for work during the corresponding period of the year preceding the trial had been statistically more numerous in the patients subsequently treated with LBL than in those assigned to receive the

Table II. — Changes in the severity of the clinical features of chronic bronchitis at different stages of a six-month clinical trial (three months on LBL or Placebo, three months follow-up).

Clinical feature	*Treatment*	*Before treatment*		*After 1 month*			*After 2 months*			*After 3 months*			*After 6 months*		
		n	Index of sever.	n	Index of sever.	Δ %	n	Index of sever.	Δ %	n	Index of sever.	Δ %	n	Index of sever.	Δ %
COUGH	LBL	40	2.00	40	1.38	-31.0	39	1.21	-39.5	36	1.25	-37.5	35	1.11	-44.5
	PLACEBO	32	2.25	32	1.75	-22.2	28	1.64	-27.1	27	1.41	-37.3	20	1.25	-44.4
EXPECTORATION	LBL	40	2.00	40	1.33*	-33.5	39	1.28	-36.0	36	1.25	-37.5	35	1.09	-45.5
	PLACEBO	32	2.06	32	1.81	-12.1	28	1.71	-17.0	27	1.48	-28.2	20	1.65	-19.9
DYSPNOEA	LBL	40	2.05	40	1.43*	-30.2	39	1.23**	-40.0	36	1.22	-40.5	35	1.20	-41.5
	PLACEBO	32	2.13	32	1.84	-13.6	28	1.64	-23.0	27	1.56	-26.8	20	1.45	-31.9
ABNORMAL SIGNS OF AUSCULTATION	LBL	40	1.95	39	1.49	-23.6	36	1.44	-26.2	36	1.25	-35.9	34	1.18	-39.5
	PLACEBO	32	2.16	31	1.77	-18.1	29	1.55	-28.2	27	1.44	-33.3	20	1.50	-30.6

The index of severity was determined from the following severity scale: 0 = absent; 1 = mild; 2 = moderate; 3 = severe; 4 = very severe.
Values are means for the number of patients (n) indicated.
Δ % = difference (%) from the index of severity before treatment.
* = $p < 0.1$ (rank-sum test). ** = $p < 0.05$ (rank-sum test).

placebo ($p<0.05$). After treatment with LBL they fell from an average of 23.3 days per patient to 1.5 days per patient. The fall in the placebo group from 4.9 to 2.4 days per patient was not statistically significant.

TOLERANCE

As regards tolerance, the incidence of side effects was 6.6% in the LBL patients and 5.8% in the placebo patients, a difference which is not statistically significant. Apart from the patient who stopped taking LBL because of headache, one patient complained of gastric upset, and one of exacerbation of cough. In the placebo group, allergic asthma developed in one patient and tiredness in another.

DISCUSSION

This double-blind study has demonstrated the efficacy of an immunostimulatory preparation in the treatment of chronic bronchitis. The general effect of LBL in such a condition which is often refractory to therapy, was significantly superior to that of the placebo. Its curative effect became evident in the early months of its administration. The symptoms typical of the acute episode of chronic bronchitis, expectoration and dyspnoea in particular, were relieved. Because of the need for a standard treatment schedule, LBL was given in courses of 10 days per month for three consecutive months, but the curative effect of a longer course during the acute phase in the first month merits study (4).

The significant reduction, already noted by other investigators (3, 5) in working days lost because of sickness that resulted from LBL therapy forecasts for this product an important role in the long-term prevention of acute episodes in chronic bronchitis.

All the results of this trial show, in fact, that LBL deserves a place among therapeutic measures of recognised value in chronic bronchitis.

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