Immunobiotherapy with Broncho-Vaxom®* in the prevention of postoperative respiratory infections. Report of a double-blind trial

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Eighty patients about to undergo various surgical operations were divided into two groups, of which one received the immunobiotherapeutic agent Broncho-Vaxom® and the other received a placebo, for 15 days before the operation. The number of postoperative respiratory infections and the length of stay in hospital after operation were noted in each group. The infection incidence was lower, especially in patients with a history of previous respiratory disease, and the period of hospitalisation shorter (5.57 days versus 6.84 days) in the Broncho-Vaxom® than in the placebo patients, and the differences were statistically significant. Tolerance to the administered products was excellent in both the treated and the placebo patients.

Introduction

Respiratory infections often cause postoperative complications (1) requiring antibiotics, which are not always well tolerated, and prolonging hospitalisation at rising cost to the community.

It was therefore thought of interest to investigate the effect of the new immunobiotherapeutic preparation *Broncho-Vaxom®** in patients submitted to gastrointestinal operations. *Broncho-Vaxom®* has already been shown to reduce recurrence of respiratory infections and to be well tolerated in other categories of patients (2, 3, 4). Its immunostimulatory properties have been demonstrated in animals by *Fontanges* (5) and *Parès Farras* et al. (6) and in man by *Girard* and *Fleury* (7), *Clot* (8) and *Puigdollers* et al. (9).

Investigation of the efficacy of immunostimulation by *Broncho-Vaxom®* in reducing postoperative morbidity required a trial conducted on the double-blind principle.

A second aim of this study was to define more clearly the incidence of postoperative respiratory infections in patients with and without known previous respiratory disease.

Patients and methods

The trial concerned 80 patients, 42 men and 38 women. Their respiratory histories were known and recorded.

We were supplied with randomly numbered boxes of identical appearance containing 15 white capsules of either the immunobiotherapeutic preparation *Broncho-Vaxom®* or a placebo. Each *Broncho-Vaxom®* capsule contained 7 mg of a freeze-dried bacterial lysate of each of the following species : Haemophilus influenzae ; Diplococcus pneumoniae ; Klebsiella pneumoniae ; Klebsiella ozanae ; Staphylococcus aureus ; Streptococcus pyogenes ; Streptococcus viridans ; Neisseria catarrhalis.

During the 15 days before the operation all the patients ingested one capsule daily, in the morning on an empty stomach.

Broncho-pulmonary past history of each patient was noted.

The number of days spent in hospital after the operation and the incidence of respiratory infections during that time were noted.

When the code was broken on termination of the trial it was seen that 42 patients, 22 men and 20 women, mean age 42.8 years, had received *Broncho-Vaxom®* and 38 patients, 20 men and 18 women mean age 43.8 years, had received the placebo.

Out of the 42 patients who received *Broncho-Vaxom®*, 20 had previous respiratory disease (P.R.D.) and 22 had no previous respiratory disease (N.P.R.D.). The corresponding figures for the 38 placebo patients were 22 and 16. "P.R.D." included conditions such as chronic bronchitis, sequelae of tuberculosis, and the effects of excessive use of tobacco.

The numbers of operations performed in the *Broncho-Vaxom®* patients and in the placebo patients were as follows:

Type of operation	*Broncho-Vaxom®*	*Placebo*
Biliary passages	14	14
Stomach and duodenum	8	6
Hiatus hernia	3	2
Parietal hernia	13	12
Colon	4	4
Total	42	38

The *Broncho-Vaxom®* and the placebo patients were thus comparable statistically, and also as regards respiratory history and type of operation.

Each type of operation was performed by a uniform technique ; type of incision, postoperative respiratory therapy, and duration of gastric drainage were the same. Only patients undergoing colonic surgery received antibiotics. All the patients with P.R.D. did the same active and passive respiratory exercises during the postoperative period.

The criteria for the presence of respiratory complications were pyrexia,cough or dyspnoea, abnormal auscultatory findings, and in the doubtful cases abnormal radiological appearances.

Results

There were fewer respiratory infections after operation in the *Broncho-Vaxom®* patients (4 out of 42 or 9.5 %) than in the placebo patients (13 out of 38 or 34.2 %) (Table 1). This difference was statistically significant ($p<0.01$) according to χ^2-test.

In the P.R.D. group, postoperative respiratory infections occurred in 15 % of the *Broncho-Vaxom®* patients and in 50 % of the placebo patients, a difference of high statistical significance ($p<0.001$, χ^2-test). In the N.P.R.D. group there were few postoperative respiratory infections, and the differ-

* OM Laboratories Ltd., Meyrin/Geneva, Switzerland.

ence between the *Broncho-Vaxom®* and the placebo patients was not significant (Table 1).

Whereas among the *Broncho-Vaxom®* patients there was no statistically significant difference in the incidence of postoperative respiratory infections between the P.R.D. and N.P.R.D. groups, such a difference was present in the placebo patients (50 % and 12.5 % respectively ; $p<0.05$, χ^2-test). This indicates that patients with and without previous respiratory disease respond similarly to *Broncho-Vaxom®*.

no placebo patients in the N.P.R.D. group has this operation. The resulting values were 4.05 days for the *Broncho-Vaxom®* patients and 4.81 days for the placebo patients.

Tolerance

Tolerance was excellent in all the patients treated, whether with the active or the placebo preparations.

Table 1: Postoperative respiratory infections in 80 patients treated pre-operatively with Broncho-Vaxom® (42) and with placebo (38)

	P.R.D.				*N.P.R.D.*			
	Broncho-Vaxom		*placebo*		*Broncho-Vaxom*		*placebo*	
	No. p.	No. inf.	No. p.	No. inf.	No. p.	No. inf.	No. p.	No. inf.
Biliary passages	6	1	7	4	8	0	7	1
Stomach and duodenum	4	1	4	2	4	0	2	0
Hiatus hernia	1	0	2	1	2	0	0	0
Parietal hernia	5	0	5	1	8	1	7	1
Colon	4	1	4	3	0	0	0	0
Total	20	3	22	11	22	1	16	2
Percentage	15%		50%		4,5%		12,5%	

P.R.D. = previous respiratory disease
N.P.R.D. = no previous respiratory disease
p. = patients
inf. = infections

The mean duration of stay in hospital, determined for each category of operation (Table 2) and analysed by Student's t test, was significantly different in the *Broncho-Vaxom®* and placebo patients when the numbers of patients who inderwent the different operations were great enough to permit statistical analysis.

The mean duration of hospitalisation was 5.57 days for the 42 *Broncho-Vaxom®* patients and 6.84 days for the 38 placebo patients, a reduction in bed occupancy thanks to *Broncho-Vaxom®* of 1.27 days (19 %).

In the P.R.D. group the mean duration of hospitalisation was 6.45 days for the *Broncho-Vaxom®* patients and 8.31 days for the placebo patients. In the N.P.R.D. group comparison of the *Broncho-Vaxom®* and placebo patients in this respect required exclusion of the values for hiatus hernia, since

Conclusion

Preventive administration of *Broncho-Vaxom®* reduced the incidence of respiratory infections during the postoperative period, especially in the patients of the P.R.D. group. The reduction was statistically significant. The use of *Broncho-Vaxom®* also substantially reduced the duration of hospital stay, a reduction which amounted to almost two days in the case of the patients with P.R.D.

In the total series, the economy in bed occupancy was more than a day per patient. Whereas the mean duration of hospitalisation was only 5.57 days in the *Broncho-Vaxom®* patients it was 6.84 in the placebo patients.

Table 2: Mean duration in days of postoperative stay in hospital in 80 patients treated pre-operatively with Broncho-Vaxom® (42) and with placebo (38)

Type of operation	P.R.D.			N.P.R.D.		
	Broncho-Vaxom	*placebo*	*stat.*	Broncho-Vaxom	*placebo*	*stat.*
Biliary passages	5,66	9,42	**	5,00	5,57	**
Stomach and duodenum	7,00	8,00	*	6,00	6,00	–
Hiatus hernia	7,00	8,50	–	7,00	–	–
Parietal hernia	3,00	4,20	*	3,37	3,71	**
Colon	11,25	13,75	n.s.	–	–	–
Mean	6,45	8,31		4,77	4,81	

P.R.D. = Previous respiratory disease
N.P.R.D. = no previous respiratory disease
* $p<0.01$
** $p<0.05$
– too few cases for statistical analysis
n.s. Not significant

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