Herausgeber, Druck und Verlag
Hallwag AG, CH-3000 Bern 1, Nordring 4

Schweiz. Rundschau Med. (PRAXIS) *71*
Nr. 36, 1385–1389 (1982)

Schweizerische Rundschau für Medizin
Revue suisse PRAXIS de médecine

Prevention of Upper Respiratory Tract Infections in Preschool Children: A Clinical Study

Klinischer Versuch zur Prophylaxe von Infekten der oberen Luftwege beim Kind im Vorschulalter

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Summary

Upper respiratory tract infections (U. R. T. I.) are the most common motivation for consultations in paediatric practice. In an investigation conducted during the winters of 1978—79 and 1979—80 in 156 children of preschool age sheltered in crèches, day nurseries, or nursery schools we made the following observations.

Taking nasal discharge, clear or purulent, as an indicator, we found that these children were suffering from U. R. T. I. during about a third of the winter. The close contact in which children in these institutions mix with each other during several hours a day makes prevention of spread of infection by droplets of saliva exceedingly difficult.

A placebo-controlled double-blind crossover trial, conducted during the winter of 1978—79, of a syrup containing a yeast extract disclosed no statistically significant difference in the incidence of U. R. T. I. between the yeast extract period and the placebo period.

In a placebo-controlled double-blind trial during the winter of 1979—80, Broncho-Vaxom, a lyophilised bacterial lysate possessing the property of stimulating cellular and humoral immunity, exerted a preventive and curative action statistically superior to that of the placebo, in preschool children susceptible to recurring U. R. T. I.

Broncho-Vaxom should be recommended for preschool children during the early winter months.

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Zusammenfassung

Infektionen der oberen Atmungswege sind die häufigste Ursache pädiatrischer Konsultationen.

In einer während der Winterperioden 1978/79 und 1979/80 an 156 Kindern im Vorschulalter (die meisten davon in Kinder- oder Säuglingskrippen lebend) durchgeführten Doppelblindstudie machten wir folgende Beobachtungen:

1. *Nimmt man den klaren und den eitrigen Nasenausfluss als Kriterium, leiden Kinder im Vorschulalter durchschnittlich während eines Drittels des Winter an Infektionen der oberen Atmungswege.*
2. *Infolge des engen Kontaktes unter den Kindern während mehrerer Stunden täglich ist es sehr schwierig, eine Übertragung der Infektion durch Speicheltröpfchen zu verhindern.*

   Eine erste Doppelblindstudie mit «cross-over» im Winter 1978/79 wurde mit einem Hefeextrakt-Sirup durchgeführt. Dabei wurde kein statistisch signifikanter Unterschied zur Plazebo-Gruppe in bezug auf die Häufigkeit der Infektionen der Atmungswege festgestellt.
3. *Durch die präventive und die kurative Verabreichung eines Bakterienlysates, welches die zelluläre und die humorale Abwehr stimuliert, wurde bei den Kindern im Vorschulalter, welche zu rezidivierenden Infektionen der oberen Atmungswege neigen, eine im Vergleich zum Plazebo statistisch signifikante Wirkung erzielt. Die Verabreichung von Broncho-Vaxom während der ersten Wintermonate kann somit empfohlen werden.*

Résumé

Les infections des voies respiratoires supérieures sont la cause la plus fréquente des consultations en pédiatrie. Une étude en double aveugle, poursuivie pendant les hivers 1978—1979 et 1979—1980 chez 156 enfants de l'âge préscolaire vivant pour la moyenne en crèche ou en pouponnière, nous a permis d'observer les faits suivants:

1. ***Si l'on tient compte des jetages nasaux clairs et purulents, les enfants d'âge préscolaire souffrirent en moyenne pendant le tiers de l'hiver d'infections des voies respiratoires supérieures.***
2. ***Etant donné la promiscuité des enfants qui vivent en contact étroit pendant plusieurs heures de la journée, il est très difficile de prévenir les infections transmises par gouttelettes de salive. Une première étude a été faite en double aveugle avec un sirop contenant un complexe à base de levures. Aucune différence statistique avec le groupe placebo en ce qui concerne le nombre d'infections des voies respiratoires des enfants traités en cross-over durant l'hiver 1978—1979.***
3. ***L'administration préventive et curative d'un lysat bactérien capable de stimuler l'immunité cellulaire et humorale a permis de montrer chez des enfants de l'âge préscolaire enclins aux infections récidivantes des voies respiratoires supérieures, traités durant l'hiver 1979—1980, une action statistiquement significative par rapport à un groupe placebo. On peut donc recommander le Broncho-Vaxom pendant les premiers mois de l'hiver.***

Introduction

Upper respiratory tract infections (U.R.T.I.) in children of preschool age are the most frequent cause of absenteeism in crèches and day nurseries (1, 3, 7, 10, 12). Parents, mothers especially, send their children to these institutions so as to be free to go out to work, but the presence of a sick child at home makes this impossible.
Contagion is common in these institutions because of the intimate conditions under which the children associate with one another. It is hardly possible to prevent a child with coryza from passing it on to his companions. A mother may find it difficult to understand why her child should be turned away just because of a cold, yet the cold and its accompanying pharyngitis are due to viral or bacterial infection which spreads easily in droplets of saliva or in the ambient air.
These considerations explain the interest of any means for enhancing children's resistance to upper respiratory tract infections.

Patients and methods

The protective properties of two preparations – a yeast extract believed to increase the body's resistance to infection, and an immunobiotherapeutic agent, Broncho-Vaxom®* – have been evaluated by us in 156 children of preschool age in double-blind studies carried out during the winters of 1978-79 and 1979-80.

1. First study (winter 1978/79)

Our first trial included 86 children aged 10 months to 5 years (mean 2.8 years) cared for during the day in a crèche or a day nursery at Geneva. About 25 % of them also spent the night there and went home at the weekends. They were allocated in equal numbers by a random method to receiving three teaspoonfuls daily for two months (December 1978 and January 1979) of either a syrup containing the yeast extract or a syrup containing a placebo. During February and March 1979 the group which had received the yeast extract received the placebo, and *vice versa*.

2. Second study (winter 1979/80)

This trial concerned 70 children, also aged 10 months to 5 years (mean 2.5 years), of whom 41 spent their days at a crèche or a day nursery and their nights at home and 29, recruited in our private practice, were either permanently at home or spent part of each day at a nursery school. Thirty-six children were given on empty stomach in the morning one capsule of Broncho-Vaxom *Children* containing 3.5 mg of a lyophilised bacterial lysate made up of *Haemophilus influenzae; Diplococcus pneumoniae; Klebsiella pneumoniae et ozaenae; Staphylococcus aureus; Streptococcus pyogenes et viridans; Neisseria catarrhalis*. According to the recommended dosage schedule, the capsules were given on 10 consecutive days per month for three consecutive months. In this case mid-November 1979 to mid-February 1980.
The remaining 34 children were given 3 packages of 10 capsules of a placebo according to the same time schedule.
The capsules were opened and their contents, mixed with food for ease of administration, were administered by the head nurse at the crèche or by the parents to 29 children of our private practice. Observation was for four months – the three treatment months and one month of follow-up.

Criteria of selection

There were no special criteria of selection for the children in institutions except that their parents should agree to their taking part in the investigation. The private practice children were chosen because of their high susceptibility to upper respiratory tract infections.

Distribution of cases

Allocation to the product and placebo groups was by

** We thank OM Laboratories, Meyrin/Geneva, Switzerland, for kindly supplying the Broncho-Vaxom Children capsules used in this study.*

randomisation and the code was not broken until the trial was completed.

Surveillance

1. Children treated in the crèche or day nursery

The nurse in charge made a record every morning of each child's general condition, noting any nasal discharge (if present, whether clear or purulent), cough, or fever, and whether the child was having an antibiotic. We checked these entries and examined the children at the institutions twice a month.

2. Children treated at home

The parents of the children treated at home noted the same particulars daily on a form provided, and brought the children to the consultation room twice a month for examination. At these visits we inspected, and if necessary completed, the parents' records.

3. Statistical analysis

The Student's t-test was used for statistical evaluation and was established as follows:
*** = $p<0.001$, ** = $p<0.01$, * = $p<0.05$, n. s. = not significant.

Results

1. Acceptance of drugs

The yeast extract syrup and the Broncho-Vaxom capsules both proved acceptable to the children, even the youngest.

2. Tolerance

No intolerance to either preparation was reported by nurses or parents.
Good patient acceptance and good tolerance make for good compliance.

3. Efficacy of the drugs

– 1st study (winter 1978/79)

The number of children with fever or those treated by antibiotics was negligible and we made an evaluation only on nasal discharge which can be easily objectivated. In general, a clear nasal discharge indicates a viral infection or an allergic condition, a purulent nasal discharge a bacterial infection. As it appears from Table 1, the yeast extract conferred no protection against upper respiratory tract infections in the preschool children cared for in crèches or day nurseries. The incidence of clear and purulent nasal discharge was the same during the yeast extract and the placebo periods alike.
It is of particular interest to note the similarity between the results recorded in both groups. Out of a total of 4177 surveillance days, the 86 children had a clear nasal discharge on 576 days (14 %) and a purulent nasal discharge on 662 days (16 %) when receiving the yeast extract. When the same children were taking the placebo (4114 surveillance days) they had clear nasal discharge on 615 days (15 %) and purulent nasal discharge on 634 days (15 %).

– 2nd study (winter 1979/80)

As in the above study, the incidence of nasal discharge, both the clear and the purulent, was noted in the treated and the placebo group (Table 2).

Study in a crèche and a day nursery

It was noted that the incidence of clear nasal discharge in the children treated with Broncho-Vaxom was on the average 18 % of the total surveillance days and the figures for the purulent discharge were 8 %. In the placebo groups the incidence of both the clear and the purulent nasal discharge was 22 % and 13 % respectively, which is comparable to the first study.
It seems therefore, that the Broncho-Vaxom-treated children suffered less frequently from purulent discharge ($p<0.05$) than those of the placebo group. The difference was statistically significant. With regard to the clear discharge indicating a viral infection, the difference was statistically significant only during the 2nd and 3rd months.

Study in private practice

a) Children treated with Broncho-Vaxom

The incidence of both the clear and purulent nasal discharge remained constant throughout the winter amounting to 23 % and 6 % respectively of the surveillance days.

Table 1. Nasal discharge in children in a crèche or a day nursery treated with a yeast extract or a placebo in a crossover study.

Preparation	Mean age (years)	No. of children	No. of surveillance days	Nasal discharge Clear days	%	Purulent days	%
Yeast extract	2.8	86	4177	576	14	662	16
Placebo	2.8	86	4114	615	15	634	15
Student's t-test				n. s.		n. s.	

Table 2. Comparison of the efficacy of Broncho-Vaxom and a placebo in preventing upper respiratory tract infections in pre-school children.

Crèche and day nursery

Clear nasal discharge

Preparation	No. of children	Mean age (years)	1st month		2nd and 3rd months		4th month		Total		No. of surveillance days
			days	%	days	%	days	%	days	%	
Broncho-Vaxom	20	2.5	108	19	145	15	124	22	377	18	2100
Placebo	21	2.5	141	24	225	25	114	19	480	22	2210
Student's t-test			n. s.		*		n. s.		n. s.		

Purulent nasal discharge

Preparation	No. of children	Mean age (years)	1st month		2nd and 3rd months		4th month		Total		No. of surveillance days
			days	%	days	%	days	%	days	%	
Broncho-Vaxom	20	2.5	30	5	78	9	63	12	171	8	2100
Placebo	21	2.5	74	13	126	13	87	14	287	13	2210
Student's t-test			**		*		**		*		

Private practice

Clear nasal discharge

Preparation	No. of children	Mean age (years)	1st month		2nd and 3rd months		4th month		Total		No. of surveillance days
			days	%	days	%	days	%	days	%	
Broncho-Vaxom (at 4th month 6)	16	2.7	96	24	226	25	35	19	357	23	1560
Placebo (at 4th month 7)	13	3.0	103	26	231	32	69	33	403	31	1320
Student's t-test			*		n. s.		n. s.		n. s.		

Purulent nasal discharge

Preparation	No. of children	Mean age (years)	1th month		2nd and 3rd months		4th month		Total		No. of surveillance days
			days	%	days	%	days	%	days	%	
Broncho-Vaxom (at 4th month 6)	16	2.7	30	6	54	6	10	6	94	6	1560
Placebo (at 4th month 7)	13	3.0	79	20	156	20	47	25	282	21	1320
Student's t-test			***		**		n. s.		**		

b) Children treated with a placebo

As for the Broncho-Vaxom-treated children, the incidence of clear nasal discharge in the placebo group was high, reaching an average of 31 % of the surveillance days. However, contrary to the subjects treated with Broncho-Vaxom, the placebo subjects showed 3 times higher incidence of purulent nasal discharge, a difference of high statistical significance ($p < 0.01$). The different efficacy of Broncho-Vaxom in the crèche and day nursery children and in the private practice children is probably due to the fact that the latter were selected among cases with high susceptibility to upper respiratory tract infections, a criterion not applied to the former. This is demonstrated by the figures of days with purulent discharge for the placebo subjects, which are 13 % for the children in the crèches and 21 % in the private practice.

Discussion

1. Study during the winter 1978/79

This study on 86 children sheltered in crèches or day nurseries for a total of over 8000 days showed that during 15 % of that time (over 1000 days) they had non-purulent rhinopharyngitis, and purulent rhinopharyngitis during 16 % (almost 1300 days). These children were thus suffering from rhinopharyngitis during a third of the time spent in institutions. The implications of these figures become fully apparent when we recall that the age range of children admitted to these institutions is 10 months to 5 years (mean 2.8 years) and that when a child of this age is at home because of illness the mother is obliged to interrupt her work. This study revealed no statistical difference between the children treated with the yeast extract and the same children when given a placebo.

2. Study during the winter 1979/80

In this winter, the incidence of purulent upper respiratory tract infections in the crèche or day nursery children was comparable to that in the preceding winter reaching 13 % of surveillance days in the placebo group. In our private practice children, on the other hand, with their high susceptibility to infection, it was on the average 21 %.

Broncho-Vaxom reduced the incidence of purulent upper respiratory tract infections in the children in the crèche and day nurseries reaching 8 % of the surveillance days against 13 % in the placebo group. The effect of Broncho-Vaxom was even more marked in the private practice children with their high susceptibility to infections with the incidence reaching 6 % against 21 % in the placebo group. It is interesting to note that the effect of Broncho-Vaxom was evident already during the first month of its administration. At the fourth month the number of cases was not any more sufficient for statistical significance.

The immunostimulant activity of Broncho-Vaxom has been demonstrated *in vitro* by other authors. They showed a significant increase in the lymphocyte counts and a very important enhancement of non-specific lymphocyte responses to PHA and PWM mitogens in Broncho-Vaxom-treated patients with serum IgA deficiency and diminished lymphocyte populations (2).

Potentiation of the lymphocyte response to mitogens (4) and sustained increase in concentrations of secretory IgA in the saliva and of IgG and IgM in the serum (9) have also been found in healthy subjects, that is, individuals with efficiently functioning immune systems, who have taken Broncho-Vaxom. Our results confirm the findings of other clinical studies with Broncho-Vaxom (5, 6, 11).

In conclusion, Broncho-Vaxom, easy to administer and well tolerated even by the very young, may be recommended with confidence for children who are susceptible to upper respiratory tract infections.

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