PREVALENCE OF *STREPTOCOCCUS PNEUMONIAE* SEROTYPES OF THE HEPTAVALENT CONJUGATED VACCINE IN PEDIATRIC INFECTIONS

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Abstract: Severe evolution of pneumococcal infections with multiresistant strains in children under 2 years of age determined the introduction, in some countries, of the heptavalent vaccine, which includes the most frequent capsular serotypes. The knowledge of serotypes circulating in our area is crucial for the introduction of such a vaccine in our country. We studied 202 pneumococcal strains; out of these, serologic identification of 172 strains established classification in 23 serotypes/15 serogroups; 24 strains were non-typable. 66,3% of isolates belong to serotypes 23F/23B, 6B/6A and 19F/19A. Only 54% of the serotypes isolated from children under 2 years of age are included in the heptavalent vaccine. Pneumococcal strains with high level resistance to beta-lactams and multiresistant to other antibiotics belong to the 2 most frequently isolated serotypes, 19A and 23B. Vaccinal serotypes 4 and 18C were not identified in our study.

INTRODUCTION

The incidence of Penicillin resistant pneumococci has dramatically risen worldwide, especially in the 1990s.

This situation is made worst by the recent emergence of the high level resistance to third generation extended-spectrum cephalosporins used in treating severe pneumococcal infections (Coman, 2003; Charpentier, Tuomanen 2000).

In this context, the 23-valent antipneumococcal vaccine gave good results in the prophilaxy of invasive infections in adults and children over two years old that present risk factors (Jackson, Neuzil, Yu, 2003).

The heptavalent vaccine has been recently introduced in the USA and then in other countries with recommended administration in the first two years of life, but possible to five years of life, including the most frequent isolated serotypes in pneumococcal infections at this age with the most important resistance to antibiotics. It is a powerful immunogene vaccine that proved to be efficient both in the prophilaxy of pneumococcal infections and in reducing the rate of nasopharyngeal portage (Appelbaum, 2002; Whitney and coll., 2003).

MATERIAL AND METHODS

We studied 202 *Streptococcus pneumoniae* strains isolated from children hospitalized in the Emergency pediatric hospital “Sf. Maria” from Iaşi, Romania during January 2001-December 2003; They were isolated as follows: lower respiratory tract infections (92), otitis media (57), ocular infections (33) and invasive infections (20) (pleurisy: 4, bacteremia: 8, meningitis: 3 and peritonitis: 2).

The biological probes from which the *Streptococcus pneumoniae* strains were isolated, have been bacteriologically treated according to the algoritm specific to each product.

Preliminary identification of the species was based on the aspect of the colonies, on sheep blood agar and the susceptibility to optochin and confirmed by the positive slide agglutination test. Serotypes were identified by means of the quellung reaction using antisera provided by Statens Serum Institut (Copenhagen).

Susceptibility to penicillin, erythromycin, clyndamicin, chloramphenicol and trimethoprim-sulfamethoxazole followed NCCLS 2003 recommendations. Strains exhibiting an inhibition zone of < 20 mm to 1 µg oxacillin were tested for susceptibility to penicillin and cephotaxim (CTX) by means of „E-test” (AB-Biodisk, Solna Sweden), following the same interpreting criteria. In order to check the working conditions, S.pneumoniae ATCC 49619 was used.

RESULTS AND DISCUSSIONS

The 202 studied strains were collected from 115 boys (56.9%) and 87 girls (43,1%), aged as follows (fig1):

< 2 years : 65.3 %

2-5 years : 21.8%

>5 years : 12.9%

The serologic identification with available sera in 172 strains established classification in 23 serotypes/15 serogroups; 24 strains were nontypeable.

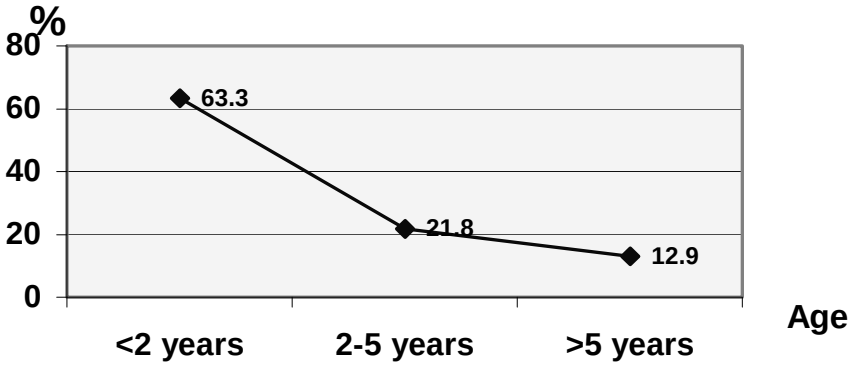

Fig. 1. Frequencies of *S. pneumoniae* strains at different ages

Globally, the higher proportion of 66.3% belonged to the serogroups and serotypes 23F/23B, 6B/6A, 19F/19A from the isolated ones, whereas the other serotypes were found in a significantly lower proportion of less than 10% each (fig. 2).

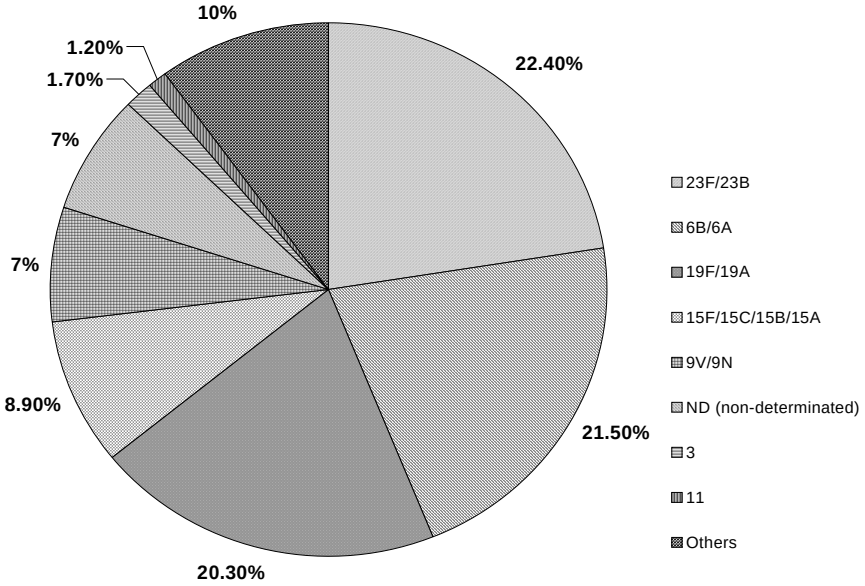

Fig. 2. Frequencies of various capsular serogroups and serotypes *S. pneumoniae* isolated from pediatric infections

Their distribution according to the infection type does not vary much except the isolated strains from purulent conjunctivitis in which half of the nontypeable strains or strains belonging to the serogroup 23F/23B are registered. Comparing the isolated serotypes with the ones included in the heptavalent vaccine (4,6B, 9V, 14, 18C, 19F, 23F), it results that only 54% of these have a vaccine as correspondent for children under two years of age. If we take into account the immune cross-reactions to the serotypes from the same serological group, the proportion is 77.9%. It is important to mention that the serotypes 4 and 18C have not been identified in our study (fig3).

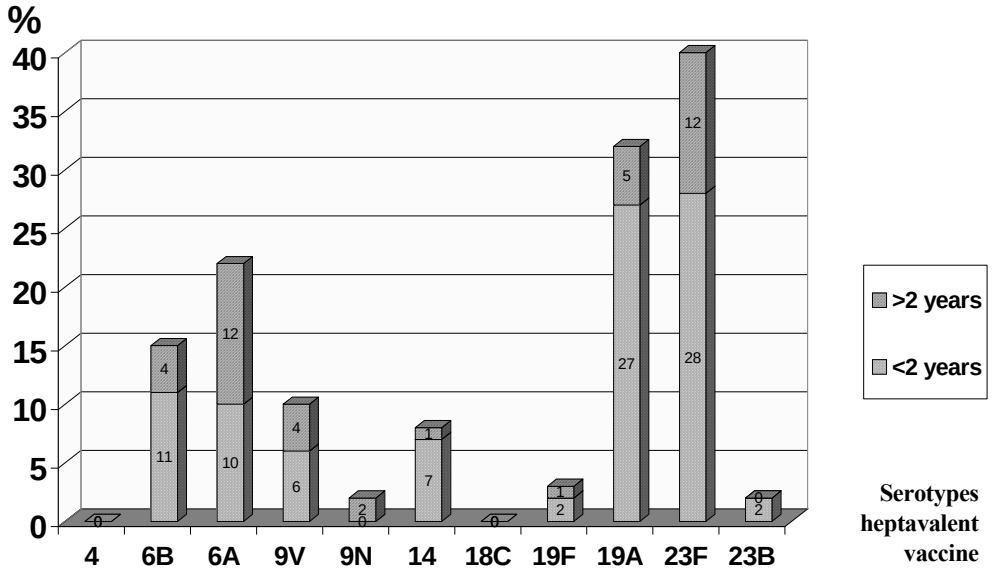

Fig. 3. Serotypes /serogroups *S. pneumoniae* isolated from pediatric infections which have a correspondent in the heptavalent vaccine

The intermediate penicillin-resistant strains are widely spread according to the circulating serotypes belonging to 14 serotypes from the 23 identified ones.

The highly penicillin-resistant strains were identified in serotypes 19A, 23F, 6B, 9V, 14 and in 3 nontypeable strains (Table1)

Table 1. The relationship between the *Streptococcus pneumoniae* serotypes and their resistance to β-lactamins.

Serotypes	Penicillin			Cephotaxim		
	S	I	R	S	I	R
19F	1	2	-	3	–	-
19A	1	5	26	18	7	7
23F	4	16	20	32	6	2
23B	2	-	-	2	-	-
6B	1	12	2	14	1	-
6A	4	18	-	22	-	-
9V	2	4	4	10	-	-

Serotypes	Penicillin			Cephotaxim		
	S	I	R	S	I	R
9N	2	-	-	2	-	-
14	1	5	2	8	-	-
15B	-	7	-	7	-	-
15C	1	3	-	4	-	-
15A	1	1	-	2	-	-
15F	1	-	-	1	-	-
11D	1	-	-	1	-	-
11A	1	-	-	1	-	-
16F	1	-	-	1	-	-
17F	2	-	-	2	-	-
1	1	-	-	1	-	-
2	1	-	-	1	-	-
3	3	-	-	3	-	-
22F	-	1	-	1	-	-
35F	-	1	-	1	-	-
ND	4	5	3	10	-	2

S – Susceptible I – Intermediate R – Resistant

The highly-cephotaxim resistant strains belonged to serotypes 19A and 23F.

The antibiotics-multiresistant strains belonged to a limited number of capsular serotypes generally stable in time and different in teritory. In these conditions, the specific prophilaxy measures could be a solution to this problem. As in our casuistic, the most numerous and severe infections evolve in children under two years of age, the category for which the antipenumococcal vaccine with 23 serotypes does not operate.

USA introduced the heptavalent vaccine in 2000 in order to diminish infant morbidity caused by pneumococcal infections and limit the multiresistant serotypes to antibiotics from spreading (Appelbaum 2003, Whitney 2003). The use of this type of vaccine in other countries is conditioned by the knowledge of the circulating serotypes in the respective area. Recent studies have shown that the heptavalent vaccine is effective for 67% of children under two years of age in Canada (Jette, 2001). The heptavalent vaccine is less effiective in Asia as only 23% of the isolated strains from meningitis have its vaccinal correspondent.

In our casuistics, only 54% of the serotypes (respectively 77,9% of the serogroups) are represented in the heptavalent vaccine. This relatively small number of studied strains does not contribute to a real appreciation of the prevalence of other serotypes. Developping a long term national or regional programme on this topic is considered an option.

CONCLUSIONS

There is a relationship between the resistance to antibiotics and their attachment to certain serotypes as most highly penicillin-resistant strains and the cephotaxim-resistant strains belong to serotypes 19A and 23F.

Determining the capsular serotypes of circulating strains in a specific geographical area offers the possibility of appreciating the efficiency of some vaccines, commercialised by prestigious

enterprises at present. Knowledge of the vaccines capacity to cover the circulant serotypes is required before use.

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