Original Article

Antimicrobial Resistance of *S. pneumoniae* and *H. influenzae* at Hat Yai Hospital

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Abstract **From February 1993 to January 1994, nasopharyngeal swabs were collected from 228 patients aged under five years old who presented with acute respiratory infection (ARI) at Hat Yai Hospital to determine the presence and susceptibility of *S. pneumoniae* and *H. influenzae*. ARI was further classified as upper respiratory tract infection (URI) in 111 cases and pneumonia in 117 cases. Positive isolation was found in 144 patients. *S. pneumoniae* was isolated from 53 cases of URI (47.7%) and 34 cases with pneumonia (29.1%) and the isolation rates were significantly different (P = 0.005). However, the isolation rates of *H. influenzae* were similar which revealed 45.9 percent from cases with URI and 41.9 percent with pneumonia. Susceptibility testing disclosed that both micro-organisms were still sensitive to penicillin, chloramphenicol and cotrimoxazole. Thus the choice of empiric antibiotic for treatment of ARI remains the same as previously recommended in the national ARIC program.** *(J Infect Dis Antimicrob Agents 1998;15:5-8.)*

INTRODUCTION

Acute respiratory infection in children (ARIC), including pneumonia, is a major cause of children's morbidity and mortality in developing countries (1-3). Two common treatable micro-organisms that cause fatal pneumonia in ARIC are *S. pneumoniae* and *H. influenzae* (4). To reduce the morbidity and mortality, an ARIC control program was designed for developing countries by World Health Organization (WHO). In patient management protocols, WHO recommends that children with cough alone, should not receive antibiotics. Children with cough, difficult breathing and tachypnea, without chest indrawing or other danger signs, are to be treated as out-patients with an antimicrobial agents. Children with cough and chest indrawing should be admitted and treated with parenteral penicillin. However, children with very severe disease should be treated with chloramphenicol (5). It can be seen that, for children aged younger than 5 years with pneumonia, the recommended antimicrobials must be active against the two micro-organisms.

In Thailand, national ARIC program has been established in 1990 by Ministry of Public Health (MOPH) (6-8). This program recommended amoxycillin and ampicillin as the empiric drugs of choice to be administered to pneumonia cases in any health centers while oral cotrimoxazole is an alternative for non-severe pneumonia (7). However, recent studies revealed a worldwide rising trend of antimicrobial resistance of *S. pneumoniae* and *H. influenzae* (9-16). This phenomenon is of great concern since it is likely to influence the outcome of standard case management of ARIC program. To reassure that the antimicrobials used in the control program for ARIC in Thailand were still applicable to current situation, a multi-site surveillance of antimicrobial resistance of *S. pneumoniae* and *H. influenzae* with assistance of WHO was introduced. It was carried out in 1992 and 1994 in six zonal ARIC training centers in Thailand. These centers also act as models to implement standard case management, train local doctors and supervise the running of other small health centers in their zones. Hat Yai Hospital is designated as one zonal ARIC training center located in southern region of the country. In this communi-

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cation, the isolation rate of *S. pneumoniae* and *H. influenzae* in the nasopharynx of children with acute respiratory tract infection at Hat Yai Hospital was reported together with their susceptibility patterns to the antimicrobials as recommended in the national ARIC program.

MATERIAL AND METHOD

From February 1993 to January 1994, nasopharyngeal swabs were collected and cultured to determine the presence of *S. pneumoniae* and *H. influenzae* in the throats of children aged under five years old who presented with acute respiratory infection (ARI) at Hat Yai Hospital. The diagnosis of ARI was standardized by pediatricians who had completed an ARI training course. ARI was further classified as upper respiratory tract infection (URI) and pneumonia. Nasopharyngeal culture was performed with the use of a swab with flexible wire shaft by a trained collection team. Laboratory personnels were trained and technique of isolation and susceptibility testing were standardized by WHO consultants. Blood and cerebrospinal fluid (CSF) cultures were also done in severe pneumonia or meningitis to determine the presence and susceptibility of *S. pneumoniae* and *H. influenzae.* Antimicrobial susceptibility was done by disc diffusion (Kirby Baur) method and minimal inhibitory concentration (MIC) by agar dilution method. Serotyping of *H. influenzae* was performed by Denmark and Australia reference laboratories and detection of beta-lactamase by rapid acidometric method.

RESULTS

During February 1993 and January 1994, nasopharyngeal swabs were collected from 228 patients aged under five years old who presented with ARI at Hat Yai Hospital. Of these, URI was diagnosed in 111 cases and pneumonia in 117 cases. One hundred and forty-four patients (63.2%) had positive nasopharyngeal isolation of either *S. pneumoniae* or *H. influenzae* or both. The former was isolated in 44 (19.3%) and the latter in 57 cases (25.0%) and both micro-organisms in 43 (18.9%) cases respectively. For each diagnosis, *S. pneumoniae* was isolated from 53 cases of URI (47.7%) and 34 cases with pneumonia (29.1%) and the difference in the isolation rates for both diagnoses which was higher in URI, was statistically significant (P = 0.005; 95% CI = 1.17-2.32). However, the isolation rates of *H. influenzae* in URI and pneumonia were similar which revealed the positive isolations in 51 cases (45.9%) with URI and 49 cases (41.9%) with pneumonia (P = 0.627; 95% CI of the difference of isolation rate = 0.82-1.47). Serotyping of *H. influenzae* disclosed the prevalence ratio of type B to non-type B in both URI and pneumonia were almost similar which were 21.7 in the former and 30.6 in the latter (P = 0.454; 95% CI of difference of the prevalence ratio = 0.36-1.42).

For 82 isolates of *S. pneumoniae,* resistance to penicillin, chloramphenicol and cotrimoxazole was found in 14, 9 and 11 isolates respectively. For susceptibility testing among *H. influenzae,* 94 isolates were evaluable by the time of the test. Resistance to ampicillin, chloramphenicol and cotrimoxazole in *H. influenzae* was detected in 2, 3 and 3 isolates of *H. influenzae* type B and 9, 13 and 12 isolates of non-type B *H. influenzae* respectively. The details of resistance rates of *S. pneumoniae* and *H. influenzae* to these antimicrobials were showed in Table 2. Beta-lactamase was detected in 10 isolates of *H. influenzae* which showed complete resistance to ampicillin. One isolate of non-betalactamase producing *H. influenzae* was intermediately resistant to ampicillin while the other 83 non-betalactamase producing isolates were

Table 1. Numbers and prevalence rate (%) of the isolation of *S. pneumoniae* and *H. influenzae* by diagnosis.

Organisms isolated	Pneumonia (n = 117)	URI (n = 111)	Total isolates
S. pneumoniae	34 (29.1%)	53 (47.7%)	87
*H. influenzae**	49 (41.9%)	51 (45.9%)	100
– type b	15	10	25
– non-type b	34	35	69

* Six isolates from patients with URI were missing during serotyping.

Table 2. Antimicrobial resistance of *S. pneumoniae* and *H. influenzae*.

Micro-organisms	Complete resistance (%)	Intermediate resistance (%)	Sensitive (%)
S. pneumoniae (82)			
Penicillin	1 (1.2)	13 (15.9)	68 (82.9)
Chloramphenicol	0	9 (11.0)	73 (89.0)
Cotrimoxazole	11 (13.4)	0	71 (86.6)
H. influenzae (94)			
Ampicillin	10 (10.6)	1 (1.1)	83 (88.3)
Chloramphenicol	16 (17.0)	0	78 (83.0)
Cotrimoxazole	10 (10.6)	5 (5.4)	79 (84.0)

fully susceptible. Thus, susceptibility testing disclosed that the majority of both micro-organisms were still sensitive to penicillin, chloramphenicol and cotrimoxazole.

DISCUSSION

Periodic surveillance of drug susceptibility to antimicrobials among bacteria which cause common and serious infections is mandatory especially for the antimicrobials that are recommended as empirical therapy in children. This is particularly true when considering infections occurring during the childhood when the immunity is not fully developed and organ damage has a negative impact in growth and development. In addition, sequele of the mismanaged infection can cause permanent organ damage and subsequent disability such as deafness and cerebral palsy both of which can be avoided. Under these circumstances, the choice of appropriate antimicrobial for therapy of the infections is critical and needs reassessment frequently.

Nasopharyngeal isolation of those common micro-organisms and their susceptibility patterns were illustrated in the study. The colonization of nasopharyngeal micro-organisms changes with time and is influenced by the child's environment, being particularly in children in day care centers. Clinical resistance to penicillin in *S. pneumoniae* was first reported in Boston in 1965, in Australia in 1967, and subsequence around the world (13,17-19). In south Africa, penicillin- and chloramphenicol-resistant as well as multiresistant strains have been isolated (13), and emerged as a worldwide problem. The value of nasopharyngeal culture in patients with ARI including pneumonia has been recently investigated by a report (21). In the study, the proportion of nasopharyngeal isolation of *S. pneumoniae* and *H. influenzae* which were resistant to penicillin, chloramphenicol and cotrimoxazole, were similar to that of resistant blood isolates to the same drugs. However, we need a bigger amounts of the isolates to confirm that susceptibility pattern of nasopharyngeal isolates of the studied micro-organism can be used as representatives of the blood isolates. The susceptibility pattern of nasopharyngeal isolates could not be compared with those isolated from cerebrospinal fluid or true sputum since very few or none was isolated from the specimens. At Ramathibodi Hospital which is a university hospital, only one (20) of cases with pneumonia, were the pathogens simultaneously isolated from blood and cerebrospinal fluid and eight percent at Children Hospital. In this study, no organism was isolated from blood. It may be explained by the drug marketting in Thailand where antimicrobials can be bought freely from any drugstores without prescription. Fortunately, the drug resistance rates did not rapidly emerge in the microorganisms studied. As we know, a process of continuous selection of resistance strains is presumed, that may be uncountabled if drugs are freely distributed and used. Several studies, however implicated certain risk factors in the development of penicillin resistance among *S. pneumoniae* and *H. infuenzae* infections. Resistance of *H. infuenzae* to ampicillin is well studied and known to be due to a plasmid responsible for betalactamase (penicillinase) production. Thus it was not surprising to find out that all strains of our isolate that production of betalactamase was detectable, were resistant to penicillin and ampicillin. Resistance to chloramphenicol is less well understood, but for multiresistant strain, the mechanism may be due to plasmid-mediated production of an acetyl transferase (9).

In conclusion, this study demonstrates that nasopharyngeal swab is another simple technique to detect or predict future resistance pattern of *S. pneumoniae*

and *H. influenzae*. However, resistance pattern of these microorganisms should be also compared with those isolated from appropriate specimens such as blood and cerebrospinal fluid. In the meantime the recommended drugs in the ARIC program are still valid until the next study will be performed.

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References

1. Monto AS. Acute respiratory infection in children of developing countries; challenge for the 1990s. Rev Infect Dis 1989;11:498-505.
2. Berman S. Epidemiology of acute respiratory infection in children of developing countries. Rev Infect Dis 1991;13 (Suppl. 6):454-62.
3. Timothy D. Use of nasopharyngeal isolates of *Streptococcus pneumoniae* and *Haemophilus influenzae* from children in Pakistan for surveillance for antimicrobial resistance. Pediatric Infect Dis J 1993;12:824-30.
4. Shann F. Etiology of severe pneumonia in children in developing countries. Pediatric Infect Dis 1988;86:247-52.
5. World Health Organization. Acute respiratory tract infection in children: care management in small hospital in developing countries. WHO/ARS/90.5. Geneva: World Health Organization, 1990.
6. Sunakorn P. Situation of Acute Respiratory Infection in Thailand. Publication of Tuberculosis Division, Department of Communicable Disease Control Ministry of Public Health, 1995.
7. Proceeding of Second National Seminar on Acute Respiratory Infection in Children, July 3-5, 1989, Bangkok, Thailand 1990. (ISBN 974-7953-88-9).
8. Sunakorn P, Chuchit L, Niltawat S, Wangweerawong M, Jacol RF. Epidemiology of acute respiratory infection in young children from Thailand. Pediatric Infect Dis J 1990;9:873-7.
9. Kenny JF, Isberg CD, Michaels RH. Meningitis due to *H. influenzae* type b resistance to both ampicillin and chloramphenicol. Pediatrics 1980;66:14-6.
10. Tremblay LD, L' Ecuyer J, et al. Susceptibility of *H. influenzae* to antimicrobial agents used in Canada. J Can Med Assoc 1990;143:895-901.
11. Appelbaum PC, Bhamjee A, Seragg JN, et al. *S. pneumoniae* resistant to penicillin and chloramphenicol. Lancet 1987;2:995-7.
12. Timothy D, Mastro AG, Nasnun KN, et al. Antimicrobial resistance of pneumococci in children with acute lower respiratory tract infection in Pakistan. Lancet 1991;337:156-9.
13. Appelbaum PC. Antimicrobial resistance in *S. pneumoniae*: an overview. Clin Infect Dis 1992;15:77-83.
14. Koomhaf HJ, Wasas A, Klugman K. Antimicrobial resistance in *S. pneumoniae*: a South African prospective. Clinical Infect Dis 1992;15:84-94.
15. Reichler MR, Allphin AA, Breimen RF, et al. The spread of multiply resistant *S. pneumoniae* at a day care center in Ohio. J Infect Dis 1992;166:1346-53.
16. Tan TQ, Mason EO, Kaplan LS, Penicillin-resistant systemic pneumococcal infections in children: a retrospective case-control study. Pediatrics 1993;92:761-7.
17. Hansman D, Glasglow H, Sturt J, et al. Increased resistance to penicillin of pneumococci isolated from man. N Engl J Med 1971;284:175-7.
18. Hansman D. Type distribution and antibiotics sensitivity of pneumococci from carriers in Kiriwina, Trobriand Island (New Guinea). Med J Aust 1972;2:771-3.
19. Hansman D, Devitte L, Miles H, Riley I. Pneumococci relatively insensitive to penicillin in Australia and Papua New Guinea. Med J Aust 1974;2:353-6.
20. Suwanjutha S. Etiology of acute respiratory infection in Thai children under 5 years old: a hospital based study. Natl Semian on ARIC, 1989.
21. Mastro TD, Ghafoor A, Nomani NK, et al. Antimicrobial resistance of pneumococci in children with acute lower respiratory tract infection in Pakistan. Lancet 1991;337:156.
22. Gray BM, Converse GM, Dillon HC. Epidemiologic study of *Streptococcus pneumoniae* in infants: acquistion, carriage and infection during the first 24 months of life. J Infect Dis 1980;142:23-33.
23. Trottier S, Stenberg K, Svanberg-Eden C. Turnover of nontypable *Haemophilus influenzae* in the nasopharynx of healthy children. J Clin Microbiol 1989;27:175-9.