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Recent changes in nasopharyngeal flora of children in Japan

Hayashi T, Yoshizaki T, Ohara K, Yoshida S, Kumai T, Harabuchi Y

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Author: Tatsuya Hayashi, Tomoki Yoshizaki, Kenzo Ohara, Saeko Yoshida

Takumi Kumai, Yasuaki Harabuchi

Institute: Department of Otolaryngology- Head and Neck Surgery, Asahikawa Medical University, Japan

Short title: Nasopharyngeal flora of children

Full address:

Department of Otolaryngology- Head and Neck Surgery, Asahikawa Medical University

Midorigaoka Higashi 2-1-1-1, Asahikawa, Hokkaido 078-8510, Japan

Phone: +81-166-68-2554 Fax: +81-166-68-2559

email: thayashi@asahikawa-med.ac.jp

Abstract

We investigated the relationship between nasopharyngeal flora of pediatric patients and antibiotic consumption in a local community in Japan between 2000 and 2009 retrospectively. There was a clear relationship between the lower annual consumption rate of cephalosporins and the lower annual prevalence of non-susceptible strains of *Streptococcus pneumoniae* (SP). High prevalence of BLNAR (ß-lactamase non-producing ampicillin resistant *Haemophilus influenzae*) has been one of the bacteriological features of Japan.

Backgrounds

Surveillance of nasopharyngeal bacterial pathogens of acute otitis media (AOM) in Japan showed an increase in prevalence of non-susceptible strains of SP and *Haemophilus influenzae* (HI) reached over 70% and 50%, respectively around 2000 in Japan. Another feature of bacteriological profile in Japan is that about 90 percent of non-susceptible strains of HI are those of BLNAR (ß-lactamase non-producing ampicillin resistant HI). Excessive usage of cephalosporins has considered a main cause of the increase. In order to spread appropriate uses of antibacterial agents, the guideline for pediatric patients with AOM issued in 2006 and revised in 2009 in Japan. This guideline recommends wait-and-see policy for first 3 days in mild cases and amoxicillin as the first line antibiotic [1].

We have treated children with AOM by almost the same treatment manner as the guideline since 2001 at Nemuro Municipal Hospital before the guideline was published.

Purpose of this study is to clarify the recent changes in the prevalence of non-susceptible strains of AOM pathogens obtained from nasopharynx along with changes in antibiotic choice before introduction of heptavalent conjugate pneumococcal vaccine (PCV7) to Japan.

Material and Methods

1. Consumption of ß-lactams

Gross weight of each prescribed antibiotic for children that was provided as a form of granule and/or syrup was obtained from the pharmacy database. Defined daily dose system was used to compare annual consumption of each ß-lactam [2].

2. Nasopharyngeal bacteriology

A retrospective study of nasopharyngeal flora from pediatric patients with upper and/or lower respiratory tract infections treated at Nemuro Municipal Hospital between 2000 and 2009 was performed. Strains of SP with MIC to penicillin G being 0.06 μg/mL or under was defined as PSSP, between 0.12 and 1.0 μg/mL as PISP, and 2 μg/mL or over as PRSP, respectively. Strains of HI without producing ß-lactamase with MIC to ampicilin (ABPC) being 4 μg/mL or over were defined as BLNAR, 2 μg/mL as low BLNAR, and 1 μg/mL or under as BLNAS

(ß-lactamase non producing ABPC susceptible). ß-lactamase producing strains of HI were classified as BLPAR (ß-lactamase producing ABPC resistant).

Results

1. Annual consumption of ß-lactams for children

After pediatricians and otolaryngologists at Nemuro Municipal Hospital decided to use AMPC as the first line in 2001, the proportion of annual consumption of cephalosporins in all ß-lactams for children has decreased from 79% in 1999 to 28% in 2009.

2. Annual changes in prevalence of non-susceptible strains (Table)

In 2001, only 25% (90strains) of 362 SP strains were PSSP, 59% and 17% were PISP and PRSP, respectively. After we changed the way to choose antibiotics, the prevalence of PSSP increased up to 53% of all isolated SP, and that of PRSP decreased by 16.5%.

The prevalence of BLNAS had been decreasing in all strains of HI, and that of low BLNAR+BLNAR had been increasing until 2007 from 62 to 30% and 38 to 70%, respectively. However, the prevalence of BLNAR decreased a little in 2008 and 2009.

Discussion

Before the Japanese version of AOM guideline was issued, we started using the similar treatment algorithm to the guideline and succeeded in reducing the prevalence of

non-susceptible strains of SP by about 30%. Though the key to success was AMPC as the first-line antibiotic, another factor might have been that Nemuro is a geographically isolated community with 32,000 residents and the limited number of clinicians who prescribed antibiotics for children.

On the other hand, we still have a continued problem about the high prevalence of BLNAR. The reason why the proportion of BLNAR has not shown an obvious decrease might be that antibiotics we use, such as cefditoren pivoxil (CDTR-PI), do not have sufficient efficacy to kill them and/or may select BLNAR in nasopharynx in spite of showing the best MIC value to BLNAR of all oral antibiotics available in Japan [3]. In addition, we do not think the decrease in the prevalence of non-susceptible strains of SP has reached the sufficient level.

In 2010, PCV7 has become available in Japan over 10 years after the US or other developed countries. We are expecting the efficacy of this vaccine in Japan. However we have already known the use of vaccine led to an increase in the rate of AOM due to non-vaccine serotypes [4]. Therefore, there must be no change in the importance of an appropriate use of antibiotics even in the multivalent vaccine era.

Reference

1. Japan Otological Society, Japan Society for Pediatric ORL, Japan Soceity of Infectious

Diseases in Otolaryngology: Clinical practice guideline for pediatric acute otitis media (in Japanese). Otol Jpn 2006; 16: 1-34.

2. WHO. ATC/DDD index 2010. In: http://www.whocc.no/atc_ddd_index/.

3. Takahata S, Kato Y, Sanbongi Y, Maebashi K, Ida T: Comparison of the efficacies of oral beta-lactams in selection of Haemophilus influenzae transformants with mutated ftsI genes. Antimicrob Agents Chemother ; 52: 1880-1883.

4. Eskola J, Kilpi T, Palmu A, Jokinen J, Haapakoski J, Herva E, Takala A, Kayhty H, Karma P, Kohberger R, Siber G, Makela PH: Efficacy of a pneumococcal conjugate vaccine against acute otitis media. N Engl J Med 344: 403-409, 2001.

Table: Changes in prevalence of susceptible and non-susceptible strains of *S. pneumoniae* and *H. influenzae*

	2001	**2007**	**2009**
S. pneumoniae			
PSSP	90 (25%)		411(53%)
PISP	212 (59%)		358 (46%)
PRSP	60 (17%)		4 (0.5%)
H.influenzae			
BLNAS	330 (62%)	223(30%)	320 (41%)
low BLNAR	85 (16%)	167 (22%)	135 (17%)
BLNAR	114 (22%)	359 (48%)	303 (39%)
BLPAR	0 (0%)	0 (0%)	17 (2%)