Study of nasopharyngeal bacterial flora. Variations in nasopharyngeal bacterial flora in schoolchildren and adults when administered antimicrobial agents

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Abstract Changes in nasopharyngeal bacterial flora in adults with acute upper respiratory tract infection on administration of antimicrobial agents were investigated, and how these changes contrasted with those in children. Many patients with acute sinusitis due to allergies, and patients with malignancy and diabetes mellitus were included in the investigation. The detection rates of *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*, the major bacteria of acute otitis media (AOM), were 22%, 10%, and 7% respectively, which were significantly lower than those for children. Gram stain examination of nasopharyngeal swab samples showed a significant relation between leukocyte infiltration and the detection amount of *S. pneumoniae* (*P* = 0.0086). A significant relation (*P* = 0.0134) was also observed when *H. influenzae* was simultaneously detected. No significant change in the three major AOM bacteria present in nasopharyngeal bacterial flora after administration of antimicrobial agents was observed. However, all *S. pneumoniae* and *H. influenzae* detected after antimicrobial agent administration had the β-lactam-
resistance gene. It was observed that a significant improve-
ment in leukocyte infiltration occurred 6 to 10 days after
antimicrobial agent administration. In contrast, a significant
improvement in children was observed at 2 to 5 days. In the
adult subjects, this improvement was probably due to spon-
taneous remission rather than the effect of the antimicrobial
agents. Although investigation of the long-term administra-
tion of antimicrobial agents was also conducted, its benefits
for the patients were not elucidated.

Key words Acute upper respiratory tract infections · Acute
otitis media · Nasopharyngeal bacterial flora · Streptococcus
pneumoniae · Haemophilus influenzae · Antimicrobial
agents

Introduction

Accompanying the appearance of penicillin-resistant Streptococcus pneumoniae (PRSP), there have been increasing
numbers of reports worldwide concerning antimicrobial
treatment and infantile acute upper respiratory tract infec-
tions (AURTIs) and acute otitis media (AOM).1–3 Since
1993, we have conducted epidemiological studies in Japan
related to the drug resistance of Streptococcus pneumoniae
involved in upper respiratory tract infections.4–7 In addi-
tion to S. pneumoniae, these studies have also taken into
consideration Haemophilus influenzae. The reason for this
is that, in Japan, as well as PRSP, a tendency toward an
increase of β-lactamase-negative Ampicillin resistant H.
influenzae (BLNAR) has been observed.10–16 There have
been no reports of detailed examination of the two resistant
strains of PRSP and BLNAR that are involved in AURTI,
including AOM. This being the case, from 2002 through
2004, while focusing on the trends of PRSP and BLNAR
found in nasopharyngeal bacterial flora, we specifically
examined the nasopharyngeal bacterial flora of healthy
subjects, from infants to the elderly, and AURTI patients.
Some of the results of this research have already been
reported in the first report.11 In addition, the second report
part 116 and part 217 analyzed changes in nasopharyngeal
bacterial flora in infants aged 6 years or younger with
AURTI, including AOM, on administration of antimicro-
bial agents, while focusing on PRSP and BLNAR. In con-
trast to the second report part 116 and part 217, which cover
changes in the nasopharyngeal bacterial flora in infants,
this is a report of the results of a study of trends in the
nasopharyngeal bacterial flora of adults with AURTI on
administration of antimicrobial agents.

Methods

Subjects

The subjects of this study were 69 patients, aged from 7 years
to 80 years, chosen from 1544 cases gathered by the Study
Group for Upper Respiratory Tract Bacterial Flora.14 The
subjects were diagnosed by attending physicians as having
acute sinusitis, AOM, AURTI, acute exacerbation of chronic
sinusitis, or acute exacerbation of chronic otitis media, and
the nasopharyngeal bacterial flora of each of the subjects
were cultured and examined before and after administration
of antimicrobial agents. Taking into consideration the
number and age of the subjects as well as accompanying
physiological and social factors, the subjects were divided
into the age 7–15 group, age 16–39 group, age 40–59 group,
age 60–74 group, and age ≥ 79 group. The age 7–15 group
was included for analysis because, among the subjects there
were very few of this age, and the detection rates of S. pneu-
moniae and H. influenzae in children aged 6 years or lower
are significantly lower than the rates indicated in the second
report.16,17 Another reason is that, according to other
reports,19–22 resistance to S. pneumoniae and H. influenzae is
almost fully developed by the age of about 6 years.

Attending physicians investigated patient characteristics
to identity the presence of any underlying disease that could
influence the efficacy of the antimicrobial agent adminis-
tered, history of the same disease as the current disease,
antimicrobial agents already administered for the current
disease (previous administration of an antimicrobial agent),
and other factors. The type of antimicrobial agent adminis-
tered, dose, dose term, whether antimicrobial agent treat-
ment was continued after re-examination, and other factors
were also investigated. All of this information was obtained
with informed consent from the subjects or from a parent
or guardian of each subject.

Of the above subjects, 25 underwent repeated re-exami-
inations. The reason for this was to confirm the effectiveness
of the treatment and whether there was recurrence of infec-
tion or relapse. For some attending physicians, however,
this required making many judgments. Consequently, the
number of cases was insufficient for stratified analysis. As
a result, comparison of the nasopharyngeal bacterial flora
before and after doses of antimicrobial agents was con-
ducted by comparison with the overall results of the first
examinations. For these subjects, the dose term of oral anti-
microbial agents for many was 5 days, while for those
receiving intravenous doses it was from 3 to 4 days, after
which administration was continued orally. The term for
continued administration and re-administration of the pre-
scribed antimicrobial agent was about 5 days for many sub-
jects. As a result, the subjects were divided into the day 2–5
subgroup, for which the first nasopharyngeal bacterial flora
examination results were compared with the results of re-
examination conducted within 2 to 5 days after the initial
examination; the day 6–10 subgroup, for which the results
were compared with the results of re-examination con-
ducted 6 to 10 days after the initial examination; and the
day ≥ 11 subgroup, for which the results were compared
with the results of re-examination conducted 11 days or
more after the initial examination. Because of this, the
results of the re-examination repeated in the aforemen-
tioned 25 subjects were compared with the result of the first
examinations. Hereafter, the term of the re-examinations is
referred to as the re-examination term.

AURTI such as AOM in adults is almost always caused
by a virus. The bacteria inhabiting the nasopharynx of chil-