Distribution of pathogens causing nosocomial infection in patients with bronchial asthma

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ABSTRACT. This study aimed to analyze nosocomial respiratory infection (NRI) in patients with bronchial asthma. Among the clinical data of 575 asthmatic patients that was collected and analyzed, 52 were diagnosed with NRI. The most common gram-positive bacterial species was Streptococcus pneumoniae, which was detected in 8 patients, whereas the predominant Gram-negative bacteria included Haemophilus influenzae (11 patients), Moraxella catarrhalis (8 patients), and Escherichia coli (7 patients). The simultaneous detection of all strains was predominant in patients older than 65 years of age, whereas the detection rates of S. pneumoniae, H. influenzae, E. coli, and M. catarrhalis were predominant in patients younger than 65 years old. The differences in the detection rates were not significant between the male and female groups. From this study, we can conclude that S. pneumoniae, H. influenzae, E. coli, and M. catarrhalis are common NRI-causing pathogens, and bacterial infection is the main risk factor for NRI in asthmatic patients.

Key words: Bronchial asthma; Distribution of pathogens; Nosocomial infection
INTRODUCTION

Bacterial infection is considered the main risk factor for nosocomial respiratory infection (NRI) in asthmatic patients (Eder et al., 2006; Bisgaard et al., 2007; Hauk et al., 2008; Marra et al., 2009; Bisgaard et al., 2010) but its mechanism remains unclear. Otero et al. (2013) reported that bacterial infection may elicit the imbalanced expression of T helper cells types 1 and 2 (Koch et al., 2007). Peroni et al. (2010) analyzed the pathogen distribution in elderly asthmatic patients and revealed that asthma was induced by the ecological imbalance of pathogenic microbes, which was confirmed by an animal experiment study by Piacentini et al. (2010). Current research has revealed that bacterial infection-induced asthma involves bacterial heat shock proteins, which may compromise the human immune system and induce asthma. This conclusion has been corroborated by the results of subsequent experiments involving antimicrobial treatments. In addition, bacterial infection induces inflammation and cytokines produced by T helper cells, which can induce airway hyperresponsiveness and asthma. Other studies (Ortiz-Stern et al., 2011; Okamoto et al., 2012) have demonstrated that bacterial lipopolysaccharides can promote the growth of mucosal dendritic cells that are important to the immune response. Furthermore, several research centers in the United States have found that *Chlamydia* or *Mycoplasma pneumoniae* can induce asthma; however, these data warrant further confirmation (Grayston et al., 1990; Emre et al., 1995; Von Hertzen et al., 1996). Therefore, the treatment of asthma should be conducted concomitantly with the control and prevention of NRI.

Material and methods

General data

A total of 575 patients with acute asthma, including 309 men and 266 women between the ages of 42 and 85 years, were recruited from the Department of Respiratory Medicine in Huzhou Central Hospital (China) between January 2008 and January 2011. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Huzhou Central Hospital, and written informed consent was obtained from all participants.

Sample collection and bacterial identification

Oropharyngeal and nasopharyngeal secretions of patients were collected, and a disposable sputum suction tube was inserted into the lower respiratory tract to collect sputum for future bacterial identification. The bacterial strains were cultured on Müller-Hinton agar; susceptibility paper disks and petri dishes were purchased from Oxoid (United Kingdom). Bacterial strains were isolated and identified according to conventional microbiological tests using a VITEK 32 automatic analyzer from Bio-Merieux (France). The colonies of the unidentified bacterial strains were stained after isolation and examined under an optical microscope. Oxidase and catalase tests were performed on gram-negative and gram-positive bacteria, respectively.

Statistical analysis

Data were analyzed with the SPSS16.0 (IBM, Chicago, IL, USA) software. Comparison between groups was performed using the chi-square test, and the significance level was set at $P < 0.05$. 
RESULTS

Pathogen distribution

Among the 52 pathogen strains identified, 12 bacterial strains (23.07%) were gram-positive and 38 bacterial strains (73.07%) were gram-negative. In addition, 2 fungal strains were identified, representing 3.8% of the pathogenic strains (Table 1).

Table 1. Constituent ratios (%) of the pathogens causing NRI in asthmatic patients.

<table>
<thead>
<tr>
<th>Pathogen Strain</th>
<th>Constituent ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive bacteria</td>
<td>12 23.08</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>8 15.39</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>2 3.85</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>1 1.92</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>1 1.92</td>
</tr>
<tr>
<td>Gram-negative bacteria</td>
<td>38 73.07</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>11 21.15</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>8 15.39</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>7 13.46</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>6 11.54</td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td>3 5.76</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>2 3.85</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>1 1.92</td>
</tr>
<tr>
<td>Fungus</td>
<td>2 3.85</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>1 1.93</td>
</tr>
<tr>
<td>Candida krusei</td>
<td>1 1.92</td>
</tr>
<tr>
<td>Total</td>
<td>52 100.0</td>
</tr>
</tbody>
</table>

Association between pathogen distribution and patient age and sex

Among the 52 patients with NRI, 28 were men and 24 were women. Regarding age, 25 patients were younger than 65 and 27 patients were older than 65. The differences in the detection rates were not significant between the male and female groups; however, they reached statistical significance in patients older than 65 years of age ($\chi^2 = 7.519$, $P < 0.05$; Table 2).

Table 2. Constituent ratios of the pathogens in different genders of patients at various ages (%).

<table>
<thead>
<tr>
<th>Strain Constituent Ratio</th>
<th>Gram-positive bacteria (N = 12)</th>
<th>Gram-negative bacteria (N = 38)</th>
<th>Fungus (N = 2)</th>
<th>$\chi^2$ value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65</td>
<td>83.83 (10)</td>
<td>34.21 (13)</td>
<td>100.00 (2)</td>
<td>7.519</td>
<td>0.132</td>
</tr>
<tr>
<td>(years) ≤65</td>
<td>16.67 (2)</td>
<td>65.79 (25)</td>
<td>0.00 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender Male</td>
<td>58.33 (7)</td>
<td>52.63 (20)</td>
<td>50.00 (1)</td>
<td>0.132</td>
<td>0.936</td>
</tr>
<tr>
<td>Female</td>
<td>41.67 (5)</td>
<td>47.37 (18)</td>
<td>0.00 (1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

Recently, the association between bacterial infection and asthma has gained attention in the field of medicine. Many studies have confirmed that bacterial endotoxins can cause airway hyperresponsiveness and trigger asthma, likely due to bacterial endotoxins promoting an increase in the permeability of tracheal mucosal epithelial cells. Bacterial lipopolysaccharides can also stimulate the immune response as antigens disturb the balance between immune cell subtypes and induce asthma (Zhu et al., 2010). Moreover, it has been noted that the respiratory system of indi-
individuals with asthma contains more proteobacteria, and bacterial colonization occurs earlier than
that in non-asthmatics (Huffnagle, 2010; Marri et al., 2013). Some studies conducted early in the
twentieth century revealed that respiratory infection correlated with asthma, but most scholars dis-
agree with this conclusion. At present, the mechanism of asthma induced by bacterial infection is
contradicted both nationally and internationally. However, bacterial respiratory infections reportedly
allow pathogens and allergens to stimulate the production of specific antibodies, which can remain
attached to the respiratory mucosa, cause allergic reactions through the presence of allergens, and
induce asthma (Fernández-Benítez, 2001). In addition, bacterial respiratory infections can damage
airway epithelial cells and increase their permeability, with the subsequent release of inflammatory
mediators, and induce asthma (Talbot et al., 2005; Edwards et al., 2012; Habibzay et al., 2012).

In addition, some researchers observed that *C. pneumoniae* can induce asthma (Horvat et al.,
2010a, 2010b; Starkey et al., 2012). It has been reported (Jahnsen et al., 2006; Ahmed et al.,
2007; Goleva et al., 2008) that NRI-induced asthma may be associated with neural regulatory
mechanisms. The researchers define a bacterial infection to be when epithelial cells are injured
and the stimulated sensory receptors of damaged cells induce spasms and cough, thereby trigger-
ing airway hyperresponsiveness and asthma.

Fifty-two patients were diagnosed with NRI among 575 asthmatic patients (infection rate of
9.04%). Most NRI-causing bacteria in asthmatic patients were gram-negative, including 11 strains
of *Haemophilus influenzae*, 8 strains of *Moraxella catarrhalis*, and 7 strains of *Escherichia coli*.
The total detection rate was predominant in patients older than 65 years, whereas the detection
rates of *Streptococcus pneumoniae*, *H. influenzae*, *E. coli*, and *M. catarrhalis* were predominant in
patients younger than 65 years. The differences in the detection rates were not significant between
the male and female groups; however, these differences reached statistical significance in patients
older than 65 ($\chi^2 = 7.519, P = 0.023$). These results were similar to those obtained in the study by
Nagayama et al. (2001).

Therefore, we conclude that bacterial infection is the main risk factor for NRI in patients
with bronchial asthma (Eder et al., 2006; Bisgaard et al., 2007; Hauk et al., 2008; Marra et al.,
2009; Bisgaard et al., 2010). For this reason, the treatment of asthma should be conducted in as-
sociation with the control and prevention of NRI. Once NRI is detected, pathogenic strains should
be immediately identified and adequately controlled.

**Conflicts of interest**

The authors declare no conflict of interest.

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