Conjugated Pneumococcal Vaccine for Children in Saudi Arabia: Following the Footsteps of Hib Vaccine

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ABSTRACT

This study was conducted to assess the impact of Hib vaccination on the Haemophilus influenzae type b incidence and occurrence of Streptococcus pneumoniae in the University Hospital of Riyadh, Saudi Arabia. The study also meant to consider the need for the introduction of routine conjugated pneumococcal vaccine for children. It was a retrospective study during the period of January 1996 to July 2007 reviewing all positive blood and CSF in children up to 18 years of age who were admitted to the hospital with a diagnosis of invasive disease with Haemophilus influenzae type b and Streptococcus pneumoniae. Eighty cases with invasive disease due to Haemophilus influenzae were admitted between 1996 and 2000. Hib conjugated vaccine has become routine in Saudi Arabia since the year 2000 and since then a significant steady drop of Haemophilus influenzae type b cases was observed with only 36 cases occurring between June 2001 and July 2007. On the other hand, no change was observed in the incidence of Streptococcus pneumoniae invasive disease. This study suggests that the prevention of invasive pneumococcal disease by immunization may be an attractive proposition. These results should initiate health authorities to encourage similar local and nationwide studies to support this suggestion.

Keywords: Conjugated Pneumococcal Vaccine (PCV), Streptococcus pneumoniae, Haemophilus Influenzae, Saudi Arabia, pneumonia, invasive disease.

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INTRODUCTION

Streptococcus pneumoniae, Haemophilus influenzae and Neisseria meningitides are the main causative agents of meningitis in children. These organisms cause more than 90% of all bacterial meningitis in children before the era of Haemophilus influenzae vaccination. Haemophilus influenzae type-b is a leading cause of invasive infection in children, affecting about 1 in 250 children up to 5 years of age. (1) Hib conjugated vaccine proved to be effective in reducing the incidence of all varieties of Hib disease including meningitis. (2) the use of Hib conjugate vaccine has become routine in Saudi Arabia since 2000. Streptococcus pneumoniae is still a leading cause of morbidity and mortality worldwide. (3) It causes a wide variety of disease ranging from severe invasive infections such as bacteremia and meningitis to relatively benign infections such as otitis media and sinusitis. Pneumococcal infections lead to the death of over one million children below 5 years of age annually. (4) Pneumococcal serotypes/serogroups prevalent invasive disease in Riyadh were studied before; (5) in that study 7-valent, 9-valent and 11-valent pneumococcal vaccine had coverage of 54%, 65% and 75% of the serogroups isolated respectively. Heptavalent pneumococcal vaccine (PCV 7) is recommended for universal use in children 23 months and younger. It is to be given concurrently with other recommended childhood vaccines at 2, 4, 6 and 12 and 15 months of age. (6)

The present study is designed to emphasize on the impact of Hib vaccination on the Haemophilus influenzae type b incidence. It is also intended to determine the occurrence of Streptococcus pneumonia in children admitted to the main University Hospital in Riyadh, Kingdom of
Saudi Arabia and to prove the need for the introduction of routine conjugated pneumococcal vaccine in children.

**MATERIAL AND METHODS**

This study was conducted in the Department of Pediatrics, College of Medicine, King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia during the period of September to December 2007.

The medical records of all children up to 18 years of age with a diagnosis of invasive disease due to *Haemophilus influenzae* and *Streptococcus Pneumoniae* admitted to King Khalid University Hospital during the period of January 1996 to July 2007 were reviewed. King Khalid University Hospital is a tertiary hospital with 850 beds facility situated in Riyadh, Saudi Arabia. It serves a wide variety of population, including nationals and expatriates from all different regions of Riyadh. All infants and children born in King Khalid University Hospital are followed in the primary care centers and are admitted to King Khalid University Hospital if acute illness develops. Patients were included in the study if they had a positive cerebrospinal fluid (CSF) or blood culture.

**Statistical analysis**

Data was entered and analyzed using MS Excel software. The Fischer exact test was applied to analyze the significance of differences between variables.
RESULTS

The total number of children with invasive disease due to *Haemophilus influenzae* indicated by blood stream infection and CSF infection was 80 between 1996 and 2000. The blood culture was positive in 62 (77.5%, table 1).

Table (1): Pediatric Patients with Haemophilus Influenzae Type b Invasive Disease (1996 – 2000), King Khalid University Hospital

<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>7</td>
<td>17</td>
<td>11</td>
<td>14</td>
<td>13</td>
<td>62</td>
</tr>
<tr>
<td>CSF</td>
<td>2</td>
<td>5</td>
<td>7</td>
<td>3</td>
<td>1</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>23</td>
<td>18</td>
<td>17</td>
<td>14</td>
<td>80</td>
</tr>
</tbody>
</table>

Thirty six cases with invasive disease due to *H. influenzae* between January 2001 and July 2007 were reported (Table 2).

Table (2): Pediatric Patients with Haemophilus Influenzae type b Invasive Disease (2001 – 2007), King Khalid University Hospital

<table>
<thead>
<tr>
<th>Positive Culture</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>3</td>
<td>7</td>
<td>9</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td>CSF</td>
<td>2</td>
<td>2</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
<td>9</td>
<td>16</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>36</td>
</tr>
</tbody>
</table>
In 24 cases of these, the organism was isolated from blood culture and in 12 cases from CSF. Compared to the 1996-2000 period, there is clear drop of *H. Influenzae* cases after introduction of routine vaccination. During the first three years (2001-2003) there were 30 cases of *H. Influenzae* invasive disease compared to only 6 cases in the last three years (2004 - July 2007).

During the period of 1996 to 2000 *S. pneumoniae* was isolated from 65 pediatric patients (Table 3). The blood and CSF cultures were positive in 54 and 11 cases, respectively.

**Table (3): Pediatric Patients with Streptococcus Pneumoniae Invasive Disease (1996-2000) in the Main Teaching Hospital, Riyadh, Saudi Arabia.**

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>9</td>
<td>18</td>
<td>14</td>
<td>4</td>
<td>9</td>
<td>54</td>
</tr>
<tr>
<td>CSF</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>21</td>
<td>17</td>
<td>7</td>
<td>10</td>
<td>65</td>
</tr>
</tbody>
</table>

Table (4) shows the number of pediatric patients with invasive pneumococcal diseases, *S. pneumoniae* was isolated from blood culture in 58 and from CSF in 18 cases.

**Table (4): Pediatric Patients with Streptococcus Pneumoniae Invasive Disease (2001-2007) in the Main Teaching Hospital in Riyadh, KSA**

<table>
<thead>
<tr>
<th>Positive Culture</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>7</td>
<td>8</td>
<td>13</td>
<td>12</td>
<td>6</td>
<td>7</td>
<td>5</td>
<td>58</td>
</tr>
<tr>
<td>CSF</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>12</td>
<td>15</td>
<td>14</td>
<td>8</td>
<td>11</td>
<td>8</td>
<td>76</td>
</tr>
</tbody>
</table>
Comparing these results with previous ones showed no difference in prevalence of streptococcus pneumoniae infection between the periods of 1996 to 2000 and 2001 to 2007, (Figures 1 and 2). Figures 1 and 2 also demonstrate clearly the difference between the prevalence of H. influenzae invasive disease between these two periods of time.

Fig. (1): Yearly Statistics of Pediatric Patients Between the Periods of 1996 to 2000 and 2001 to 2007 (blood culture)
Fig. (2): Yearly Statistics of Pediatric Patients Between the Periods of 1996 to 2000 and 2001 to 2007 (CSF culture)

**DISCUSSION**

This study has demonstrated three main points; the first is the role of *H. influenzae* type b and *S. pneumoniae* as a cause of invasive disease of children in a major hospital in Saudi Arabia. The second is that implementation of Hib vaccine was effective in reducing *H. influenzae* invasive disease at least in the population served by the main teaching
hospital in Riyadh, Saudi Arabia. The third is the consistency of Pneumococcal invasive disease during the last 11 years in the same population. In Saudi Arabia, a number of retrospective studies on childhood bacterial meningitis from different provinces of the country have shown that Hib was the commonest cause of childhood meningitis.\(^{(7,8)}\) In the present study, we calculated the incidence of invasive disease caused by \textit{Haemophilus influenzae} type b and \textit{S. Pneumoniae} from 1996 to 2000 (Fig. 1 and 2). There were 80 children with \textit{H. Influenzae} and 65 with \textit{S. Pneumoniae} invasive disease in 5 years period (Tables 1, 3).

This study showed the impact of vaccination on the number of cases with \textit{H. Influenzae} invasive disease in one of the three largest hospitals in Riyadh. This decrease is likely due to implementation of the routine Hib vaccination in the year 2000. In the beginning, from 2001 to 2003 (Table 2), the decrease was not optimal as the number of susceptible children in the community who were not vaccinated remained high and continued to serve as a reservoir for the organism in the community at large but from 2004 to July 2007 (Table 2), the total cases dropped to only 6 cases. Our study agrees with Almuneef et al.,\(^{(9)}\) who reported the significant reduction of Hib meningitis in Saudi children after the introduction of routine Hib vaccine. The efficacy of Hib vaccines against \textit{Haemophilus influenzae} invasive disease is now proven, the use of conjugate vaccines for the prevention of \textit{Haemophilus influenzae} type b (Hib) disease in children has substantially decreased the burden of disease in developed and developing countries.\(^{(10,11)}\)

In the present study, we found 65 children who suffered from invasive disease due to \textit{S. pneumoniae} between 1996 and 2000 (Table 3) and 76 children between 2001 and July 2007 (Table 4). The incidence of invasive
disease due to *S. pneumoniae* remains constant over the last 11 years. The importance of the study came from the fact that (KKUH) is one of the three largest hospitals in Riyadh. It serves a huge population representing all social strata of people. The results of this study may therefore represent the situation in Riyadh. As shown in a previous study (Al-Mazrou et al), the conjugate vaccine cover most of *S. pneumoniae* isolates from invasive disease in this city.

Numerous epidemiological surveillance reports published in North America, Europe, Asia and Africa refer to the distribution of the capsular type of *Streptococcus Pneumoniae* isolated from invasive infections. Al-Mazrou et al studied the distribution of serotypes/serogroups causing invasive disease in Saudi Arabia, they found 88% of the isolates belonged to only 10 serotypes / serogroups, namely, 6 and 9, 1 an 15, 14 and 23, 7, 18 and 22 in descending order of frequency. Potential coverage of the 7-valent, 9-valent and 11-valent conjugate vaccine for these serotype/serogroups was 54%, 65% and 73%, respectively. The serotypes were different from that shown in an earlier report from the Kingdom, when clinical isolates of *S. pneumoniae* were serotyped as serotype 14 was found to be the most prevalent, followed by 7, 1, 3 and 2. Many of the epidemiological surveillance reports published which stated the substantial disease burden and the availability of pneumococcal conjugate vaccines (PCVs) gave the introduction of a universal childhood pneumococcal conjugate vaccination program a potential prominent place on the health policy agenda in many countries. The seven-valent pneumococcal conjugate vaccine (PCV7) is currently licensed in Australia, North America, most part of Europe and Central and South America. It is also part of the universal infant vaccination program in the US, since 2000;
Australia 2005; Canada 2005; UK and Norway 2006; as well as the Netherlands 2006.(15) Previous studies reveal that the use of PCV7 has significantly reduced the burden of pneumococcal disease in young children. (16-18) Pneumococcal vaccines have a good record of eradicating carriage as well as protecting against invasive disease.(10,19) We reviewed the recommendations for use of the heptavalent pneumococcal conjugate vaccine by the American Academy of Pediatrics,(20) and other revised recommendations and supporting data for the use of pneumococcal vaccines.(6, 21)

**CONCLUSION**

The results of this present study suggest that the prevention of invasive pneumococcal disease by immunization is an attractive proposition. These results coupled with previous reported studies in this country should encourage cost effective material studies in this field before health authorities consider the implementation of routine conjugate pneumococcal vaccine in childhood immunization schedule.

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REFERENCES


