Cost-effectiveness of Palivizumab in Prevention against RSV Hospitalizations in Risk Groups

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Abstract

Objective: This study aims to evaluate the cost-effectiveness of Palivizumab in preventing Respiratory Syncytial Virus (RSV) infection among risk groups.

Methods: Patients enrolled correspond to children aged <2 years admitted in pediatric units of Hotel-Dieu university Hospital (HDF) between January 2014 and January 2016 for RSV infection. We ended up with 32 cases of RSV infection that respond to immunization recommendations and did not receive the prophylaxis. We divided them into 4 groups: Premature babies, those who have congenital heart disease (CHD), those with bronchopulmonary dysplasia (BPD) and those who had more than 2 risk factors. For each group, we compared hospitalization cost to the estimated immune-prophylaxis cost, and we analyzed RSV morbidity in each group.

Results: RSV hospitalization among premature babies is the most frequent, hospitalization cost is the highest in babies with pulmonary disease and the group with heart disease is associated to the highest risk of pediatric intensive care unit (PICU) admission. There was no significant statistical difference between hospitalization cost and immunization cost added to consequent presumed hospitalization.

Conclusion: For a neutral cost-effectiveness of Palivizumab, immunoprophylaxis reduces RSV hospitalization rate, decreases hospitalization stay, need of oxygen, and PICU transfer along with parental anxiety and work abstention. Palivizumab may be cost-effective in subgroups: prematurity <32 week gestation or cardiac and chronic pulmonary diseases aged less than one year at epidemic RSV season.

Keywords: Infants; RSV; Infections; Emergency; Immunoprophylaxis; Vaccination

Introduction

RSV is the most common agent found in low respiratory tract infections in infants and young children, affecting almost every child aged less than two years old. Many studies demonstrate the prevalence of RSV and the associated high morbidity and cost. Studies along different states of America show that RSV infections account 21/1000 emergency consultation, which 51.7% will require a hospitalization [1]. The estimated cost of annual hospitalization for RSV infection in USA goes up to 3 to 4 million USD. In England, a cohort study was done over 3 years and estimates a hospitalization rate at 4.4% of RSV infections, a PICU admission at 2.7%, need of oxygen in 1.5% of cases, and a mortality rate at 0.2%; with an estimated hospitalization cost at 542,203 Euros [2]. In Australia, every year up to 7000 infants are admitted due to RSV infection, with an annual cost of about 37 million USD [3]. Canada represents the highest rate of RSV hospitalization estimated to 168 hospitalizations/1000 newborns. In the Middle-East region, there are few studies conducted to study the burden of the disease. At 2006, Jordan conducted one of the largest series of young hospitalized children in the Middle East for acute respiratory infections. Described risk factors associated with RSV hospitalization include male sex, young age, birth in the first half of the RSV season, day care attendance, lack of breastfeeding, smoke exposure, and household crowding or siblings. RSV-positive children were more likely to require oxygen, had a longer hospital stay and hospital charges were 25% higher than RSV-negative children. Therefore, one RSV hospitalization consumes a substantial proportion of the entire annual allocation of healthcare resources per child in Jordan. Beside the direct cost of hospitalization, some adds the cost of consultation into emergencies department, the number of days parents took off, the recurrence risk and long-term asthma. Palivizumab,
the only agent available for immune-prophylaxis against RSV, has demonstrated its efficacy in reducing hospitalizations. The impact study is the largest study that proved Palivizumab efficiency by reducing hospitalization rate by 55%, hospitalization length by 45%, need of oxygen by 40% and PICU admission by 57%. These findings are the most representative among risk groups: Premature babies <32 week gestation and infants with bronchopulmonary dysplasia [4]. The usage of Palivizumab remains restraint due to its cost, since 5 doses are required during the epidemic season with a cost reaching a total of 5600 USD. Therefore, many countries have analyzed the cost-effectiveness of Palivizumab to adjust the recommendations of its use. The results were controversial, depending on each country’s economic policy and on the risk groups studied.

In Canada, Palivizumab was cost-effective when studies incriminated indirect cost of RSV hospitalization [5]. In England, cost-effectiveness analysis shows an incremental cost effectiveness ratio (ICER) significant if Palivizumab is used in premature babies <32 week gestation, cardiac patients and those with pulmonary dysplasia [6]. In Florida, studies showed a neutral cost-effectiveness of Palivizumab [7]. The AAP still recommends usage of Palivizumab in: premature babies <32 week gestation, cardiac patients and those with pulmonary dysplasia aged less than 2 years, infants having congenital heart disease or bronchopulmonary dysplasia aged less than two years.

Cost-effectiveness analysis

The statistical analysis was done by PASW software, using multiple statistical tests: Kruskal-Wallis, Wilcoxon Signed Rank and Student test.

Results

91% of RSV hospitalizations occur between November and February. The mean age of hospitalization is 3.5 months, all risk factors combined. 75% of admitted cases have sibling aged less than 5 years at home, and 25% go to nurseries. Hospitalization rate is the highest among premature infants (44%) (Figure 1).

Methods

Patients

We conducted our study in Hotel Dieu de France University Medical Center, over two years (Jan 2014-2016). Among 115 hospitalizations in pediatric units for bronchiolitis, we enrolled 32 cases of children aged less than 2 years old, who did not receive immunization despite a risk factor (Premature <35 GA aged <6 months, bronchopulmonary dysplasia, congenital heart disease aged less than 2 years or those with more than 2 factors combined).

Collected data

A questionnaire was done to establish morbidity among each risk group: hospital stay length, PICU admission, mortality, need of oxygen, number of days off took by parents, and to evaluate co-factors: going to nursery and having siblings at home. The financial unit of HDF provided us the hospitalization cost of each of these cases, and then we calculated the presumed cost of immune-prophylaxis according to age and weight of each patient. Knowing that Palivizumab reduces hospitalization rate without total annulation, we estimated the cost of hospitalization after prophylaxis added to the cost of Palivizumab. We presumed that Palivizumab reduces hospitalization rate by 76% in premature babies, 45% in patient with CHD, 39% in patients with BPD and 55% in combined groups.

Table 1: 4 groups.

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<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Premature &lt;35 week</td>
<td>14</td>
<td>43.8%</td>
</tr>
<tr>
<td>CHD</td>
<td>11</td>
<td>34.4%</td>
</tr>
<tr>
<td>BPD</td>
<td>4</td>
<td>12.5%</td>
</tr>
<tr>
<td>Combined factors</td>
<td>3</td>
<td>9.4%</td>
</tr>
</tbody>
</table>

The mean hospitalization length stay is 4 days, PICU admission is found in 37.5% cases, one death is reported in PICU admissions with a child having a severe CHD. 80% of children need oxygen during their stay, while 6 cases required assisted ventilation (Table 1).

The PICU admission was highly associated to age <3 months and the median length stay in PICU is 3 days, with a median cost of 2681.6 USD (Figure 2).

Hospitalization cost varied between 1098.15 and 5495 USD, with a median cost of 2411 USD. The group having BPD is associated to the highest cost.

Figure 1: RSV hospitalizations between November and February.

This article is available from: http://pediatrics.imedpub.com/archive.php
Figure 2: PICU admissions with a child having a severe CHD.

The mean number of abstention days is 3 days, with no significant difference between the 4 groups (Table 2).

Table 2: Hospital cost vs. abstention days.

<table>
<thead>
<tr>
<th></th>
<th>Premature</th>
<th>CHD</th>
<th>BDP</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Cost</td>
<td>1526.2</td>
<td>2505</td>
<td>3800</td>
<td>2495.2</td>
</tr>
<tr>
<td>SD</td>
<td>1259.8</td>
<td>926.7</td>
<td>209.6</td>
<td>843.2</td>
</tr>
<tr>
<td>Abstention days</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>SD</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Vaccination cost is estimated, knowing that each dose is 15 mg/kg and available doses are 50 and 100 mg costing each 557 USD and 967 USD. The median cost is 1114 USD with a maximal cost at 3458 USD. Comparison between Hospitalization and prophylaxis cost is shown here in this Figure 3.

While comparing the 4 sub-groups, we couldn’t analyze mortality rate due to the small number. There was no significant difference in abstention days, as mentioned before (Table 3).

Table 3: Comparison of mortality rate between 4 sub-groups.

<table>
<thead>
<tr>
<th></th>
<th>Premature</th>
<th>CHD</th>
<th>BDP</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>PICU admission</td>
<td>35.7%</td>
<td>45.5%</td>
<td>25.0%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

However cost-hospitalization was significantly different, the final tests analyze the difference between hospitalization cost and immune-prophylaxis cost adjusted to presumed hospitalization. The greater gain is found in premature babies where 21,862 USD could’ve been saved: Wilcoxon signed rank and student tests are used next (Figures 4 and 5).

Figure 3: Comparison between hospitalization and prophylaxis cost.

Figure 4: Cost-hospitalization.

Figure 5: Difference between hospitalization cost and immune-prophylaxis.

Table 4: Mean values.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization cost</td>
<td>2542</td>
<td>1133</td>
<td>0.323†</td>
</tr>
<tr>
<td>Prophylaxis cost</td>
<td>2381</td>
<td>1129</td>
<td></td>
</tr>
<tr>
<td>Premature Hospitalization cost</td>
<td>2091</td>
<td>1259</td>
<td>0.363‡</td>
</tr>
<tr>
<td>Prophylaxis cost</td>
<td>1758</td>
<td>824</td>
<td></td>
</tr>
</tbody>
</table>
### Conclusion

Our study shows the high morbidity of respiratory infections due to RSV among children with high risk factors. The hospitalization rate is high with a median cost of 2411 USD. The mean length stay is 4 days, and 3 days in PICU. The need of oxygen is found in 80% of cases. Having a young sibling in home seems to be a major factor for RSV infection and should be included in prophylaxis recommendations. Those findings come close to the regional characteristics established in the Jordan Study. Beside the direct cost of hospitalization, the economic burden includes parental abstention from work estimated to 3 days/hospitalization. Prematurity is associated with the highest rate of hospitalization. PICU admission is highly associated to young age and BDP. Mortality may increase in CHD patients with instability. Palivizumab median cost (after adding presumed later-on hospitalization) is 1114 USD letting us save almost 22,000 USD in premature babies and groups with combined risk factors. There is no statistical difference between the two strategies, however at a neutral cost-effectiveness, Palivizumab reduces hospitalization rate and associated morbidities. A cost-effectiveness may be found if prophylaxis is saved for premature babies <32 GA or BDP and CHD aged less than one year old at the epidemic season of RSV (Table 4).

### References