Practice variation among Dutch paediatricians in palivizumab prescription rates: the importance of parental counselling approach

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ABSTRACT

Aim: To investigate differences in palivizumab prescription rates between Dutch paediatricians, and the role of parent counselling in this practice variation.

Methods: A retrospective chart review of premature infants <32 weeks of gestation, aged less than six months at the start of the winter season, born between January 2012 and July 2014, in three secondary hospital-based paediatric practices in the Netherlands.

Results: We included 208 patients, 133 (64%) of whom received palivizumab. Prescription rates varied considerably between the three hospitals: 8% (6/64), 89% (32/36) and 99% (97/98). A noticeable difference in the way parents were counselled about palivizumab was the use of the number needed to treat (NNT). In the hospital with the lowest prescription rate (8%), an NNT of 20 to prevent one hospitalisation was explicitly discussed with parents. Bronchiolitis-related hospital admissions occurred in 11.3% of patients receiving palivizumab compared to 20.0% in nonimmunised infants (p = 0.086).

Conclusion: Considerable practice variation exists among Dutch paediatricians regarding palivizumab prescription rates. The counselling method seems to play an important role. Presenting palivizumab prophylaxis as a preference-sensitive decision, combined with the explicit use and explanation of an NNT, leads many parents to refrain from respiratory syncytial virus immunisation.

INTRODUCTION

Viral bronchiolitis occurs in annual epidemics affecting approximately one-third of all children less than two years of age (1). 7–10% of infected infants are hospitalised, of whom 5–10% are admitted to a paediatric intensive care unit for mechanical ventilation (2). Respiratory syncytial virus (RSV) is the most important cause of bronchiolitis and can be detected in about 40–80% of patients (1). Palivizumab, a passive immunisation against RSV, has been available since 1998. It is administered intramuscularly every month during the winter season. On account of its high costs (€1054 per month or >€5000 per season) (3), health insurance companies in the Netherlands restrict reimbursement of palivizumab to certain groups of patients at high risk of severe bronchiolitis, such as premature infants with a gestational age of <32 weeks and less than six months of age at the start of the winter season, children <12 months of age with congenital lung disease, cystic fibrosis or severe immunodeficiency, and children less than two years of age with hemodynamically significant congenital heart disease (3). The use of palivizumab in such high-risk groups reduces RSV-related hospitalisations from 10.1% to 4.9% (4). The number needed to treat (NNT) to prevent one RSV-related hospital admission is 20 and 56 to prevent an intensive care admission (4).

Practice variation in the treatment of bronchiolitis is large (5); however, specific data on the variation in palivizumab prescriptions are sparse. Guidelines regarding the recommendation for the prescription of palivizumab differ per country. In 2014, the American Academy of Paediatrics restricted its use for only premature infants <29 weeks of gestation or premature infants with chronic lung or heart disease.
PATIENTS AND METHODS
We performed a retrospective chart review in three secondary hospital-based paediatric practices in the Netherlands (Hospital A: Martini Hospital in Groningen (2315 paediatric admissions and 3909 outpatients in 2014), Hospital B: Deventer Hospital in Deventer (2282 paediatric admissions and 3909 outpatients in 2014) and Hospital C: Isala in Zwolle (3722 paediatric admissions and 6920 outpatients in 2014). All premature infants born between January 2012 and July 2014 at <32 weeks of gestation and less than six months of age at the start of the winter season (September) were included. In the electronic patient files of included patients, all bronchiolitis-related hospital admissions during the winter season (September–April) were documented. Bronchiolitis was defined as signs of upper airway (rhinorrhoea, blocked nose) and lower airway infection (cough, tachypnoea, dyspnoea, increased work of breathing, crackles or wheeze on auscultation) in the winter season (September–April) (1). According to Dutch national bronchiolitis guidelines, indications for hospital admission were: agitation/decreased consciousness, tachypnoea >50/min in combination with other risk factors; need for oxygen (transcutaneous oxygen saturation 92%) or transcutaneous oxygen saturation 93–94% in combination with moderately severe dyspnoea or alarming social circumstances; dehydration or inadequate intake (<50%); or risk of apnoea in infants less than one to two months (10). We also collected results of viral respiratory diagnostics to distinguish RSV-positive from RSV-negative bronchiolitis. This was done by rapid RSV antigen testing in hospitals A and B and by real-time multiplex PCR in Hospital C (11).

The routine parent counselling method in each hospital was assessed by interviewing the paediatricians and nurse practitioners who counselled parents regarding palivizumab. We asked what they thought the method for counselling was in their hospital. In all three hospitals, this counselling could be done by several different paediatricians or other healthcare professionals, the vast majority of these counselling conversations were done by three to five members of the team, dedicated to the neonatal care.

Statistics
Nonparametric tests were used because of non-normal distributions. For categorical data, Pearson’s chi-square test was used, and when numbers were too small for the chi-square test, Fisher’s exact test was used. For continuous data, the Mann–Whitney U-test was used. Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 22 (IBM Corp, Armonk, NY, USA).

The study was approved by the local medical ethics review boards of all three hospitals.

RESULTS
Patients
A total of 208 infants were included, 133 (64%) of whom received palivizumab: 97/98 in the Hospital A (99%), 32/56 in Hospital B (89%) and 6/74 in Hospital C (8%, p < 0.001). There were no significant differences in characteristics of nonimmunised and immunised patients (Table 1).

Counselling methods
In all hospitals, parents of infants born <32 weeks of gestation and younger than six months of age at the start of the winter season received information about palivizumab prophylaxis. The exact procedure of counselling and the provided information varied (Table 2). Whilst palivizumab prophylaxis was recommended as a reasonable therapeutic option by the medical team in hospitals A and B, it was presented as a preference-sensitive decision (12) in Hospital C, with limited therapeutic benefit – the NNT of 20 was explicitly mentioned in each counselling session.

Bronchiolitis-related hospital admissions
Bronchiolitis-related hospital admissions (regardless of the causing virus) occurred in 11.3% of patients receiving palivizumab and in 20.0% of nonimmunised infants: (p = 0.086). Hospital A had 11.2% bronchiolitis-related hospital admissions, Hospital B 13.9% and Hospital C 18.9% (p = 0.156).

During the study period, three patients with bronchiolitis, all premature infants born at <29 weeks of gestation with congenital lung disease, were admitted to paediatric intensive care. There were no deaths.

The RSV status was known in 27 of 30 patients admitted with bronchiolitis; 13/27 children were RSV-positive. Fewer patients were hospitalised with RSV-positive bronchiolitis in the immunised group (2/133; 1.5%) than in the nonimmunised group (11/74; 14.9% p < 0.001). RSV-negative bronchiolitis occurred in 13/133, 9.8% of immunised infants, compared to 4/74; 5.4% of nonimmunised infants (p = 0.262).
This study shows large practice variation between Dutch paediatricians regarding palivizumab prescription rates in premature infants, with immunisations rates varying from 8% to 99% among three hospitals. Presenting palivizumab prophylaxis as a preference-sensitive decision, with limited therapeutic benefit as reflected by an NNT of 20, leads many parents to refrain from palivizumab prophylaxis, whilst presenting it as a reasonable treatment option by the medical team resulted in high uptake of palivizumab immunisation. Bronchiolitis-associated hospitalisations were found in 20.0% of nonimmunised children and in 11.3% of immunised children. Although not statistically significant, our findings are in agreement with current literature (13).

It appears likely that the differences in immunisation rates between the three hospitals are the result of differences in the parent counselling method. Palivizumab can reduce RSV-related bronchiolitis hospital admissions in high-risk infants, and since its use is reimbursed by health insurance, most paediatricians tend to propose palivizumab prophylaxis as a reasonable treatment option to infants from high-risk groups, as was the case in hospitals A and B. This advice could influence the patients’ decision (14). It can also be argued, however, that the relatively small magnitude of the benefit of palivizumab and the costs and burdens of the prophylactic regimen required to receive it (13), justify presenting it as a preference-sensitive decision, meaning it is a reasonable but not essential option in which preferences of both medical team and parents play a role (12,15). This was the approach chosen in Hospital C. The results of this study illustrate that the way in which treatment options are being presented to patients and their parents has a major impact on the clinical decision that is being taken. Currently available evidence suggests that if patients are being presented with quantitative information about benefits and risks of treatment in a decision aid, they

### Table 1: Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Palivizumab; n = 133</th>
<th>No Palivizumab; n = 75</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age, median [p25-p75]</td>
<td>29 + 5 [27 + 5 – 31 + 0]</td>
<td>30+0 [28+2 – 31+0]</td>
<td>0.526*</td>
</tr>
<tr>
<td>&lt;29 weeks of gestation, n (%)</td>
<td>57 (42.9%)</td>
<td>23 (30.7%)</td>
<td>0.083†</td>
</tr>
<tr>
<td>Congenital lung disease, n (%)</td>
<td>19 (14.3%)</td>
<td>6 (8.0%)</td>
<td>0.181†</td>
</tr>
<tr>
<td>Age in months when admitted because of bronchiolitis, median [p25-p75]</td>
<td>5.2 [4 – 8]</td>
<td>4.75 [2.5 – 8.5]</td>
<td>0.838*</td>
</tr>
<tr>
<td>Length of hospital stay in days, median [p25-p75]</td>
<td>5 [2.5 – 6]</td>
<td>6 [4 – 14]</td>
<td>0.506*</td>
</tr>
<tr>
<td>Paediatric intensive care admission, n (%)</td>
<td>2 (1.5%)</td>
<td>1 (1.3%)</td>
<td>1.00‡</td>
</tr>
</tbody>
</table>

*Mann-Whitney U-test.
†Pearson’s chi-square test.
‡Fisher’s exact test.

### Table 2: Procedure of counselling in the different Hospitals

<table>
<thead>
<tr>
<th></th>
<th>Hospital A</th>
<th>Hospital B</th>
<th>Hospital C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moment of counselling</td>
<td>At neonatology department before discharge</td>
<td>A few weeks before winter season</td>
<td>At neonatology department or after discharge</td>
</tr>
<tr>
<td>Face to face or phone</td>
<td>Face to face</td>
<td>Face to face</td>
<td>Face to face</td>
</tr>
<tr>
<td>Counselling by</td>
<td>Paediatrician</td>
<td>Paediatrician</td>
<td>Nurse practitioner, resident or paediatrician</td>
</tr>
<tr>
<td>Informed consent: Explaining pros and cons* of palivizumab</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Palivizumab prophylaxis presented as a reasonable therapeutic option, recommended by medical team</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Palivizumab prophylaxis presented as a preference-sensitive decision with limited therapeutic benefit (NNT 20)</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Written patient information</td>
<td>Provided by manufacturer†; sent home after consent is given by parents</td>
<td>Provided by manufacturer†; sent home a month before start winter season</td>
<td>Provided by hospital†, given at neonatology ward</td>
</tr>
</tbody>
</table>

*Pros: reduces hospitalisation rates for RSV bronchiolitis, is covered by health insurance; cons: requires five monthly injections, can cause pain and rash at injection site.
†The information provided by the manufacturer can be found at the website of Synagis (https://www.synagis.com/) and the information provided by the hospital can be found at the website of Hospital C (http://www.isala.nl/patienten/folders/5523-rs-virus).
are more likely to refrain from invasive or aggressive therapies (16,17). The role of discussing an NNT in this process is unclear. Whilst some authors argue that patients are unable to fully understand the concept of the NNT (18,19), others have reported improved patients’ understanding and satisfaction, when the numbers are explained explicitly or when using visual aids such as icon arrays and bar graphs (16,19–22).

Although RSV-related bronchiolitis occurred less commonly in palivizumab-immunised patients, this effect is diminished for overall bronchiolitis hospitalisation rates. In agreement with one other study (23), we even observed a trend towards more bronchiolitis-related hospitalisations caused by other viruses in the immunised group: preventing RSV bronchiolitis by palivizumab will not protect infants from developing bronchiolitis related to other viruses. This may help to explain the limited beneficial effect of palivizumab in preventing bronchiolitis-related hospital admissions.

Limitations of our study include the relatively small study sample and the retrospective design. This limited our ability to directly observe and compare the parent counselling regarding palivizumab in the different hospitals. Although the retrospective nature of our study precludes causal inference, there were no other apparent differences between the three hospitals that were likely to account for the striking difference in palivizumab prescription rates. However, apart from the counselling method used in the hospitals, the physician’s attitude might also have played a role. One could argue that perhaps the general attitude towards prescribing palivizumab in Hospital C was less favourable than in the other two hospitals. Although our study did not include a thorough investigation of the physicians’ attitude, the representative paediatricians certainly did not have the impression that these attitudes differed consistently between the hospitals. We suggest prospective studies regarding to further elaborate on the use of the NNT during patient counselling.

CONCLUSION
Practice variation among Dutch paediatricians regarding palivizumab prescription in premature infants is considerable. The results of this study suggest that the way of counselling and in which scientific information is being presented to parents affects the decision being made regarding palivizumab immunisation among Dutch paediatric practices. Presenting palivizumab prophylaxis as a preference-sensitive decision, combined with the explicit use and explanation of an NNT, leads many parents to refrain from RSV immunisation.

FUNDING
None.

CONFLICT OF INTEREST
The authors have no conflict of interest.

References


