Trends in prescribing antibiotics for children in Dutch general practice

Hanneke B. M. Otters1*, Johannes C. van der Wouden1, Francois G. Schellevis2, Lisette W. A. van Suijlekom-Smit3 and Bart W. Koes1

1Department of General Practice, Ff305, P.O. Box 1738, Erasmus MC, University Medical Center Rotterdam, 3000 DR Rotterdam; 2NIVEL, Netherlands Institute for Health Services Research; 3Department of Paediatrics, Erasmus MC, University Medical Center/Sophia Childrens Hospital, Rotterdam, The Netherlands

Received 15 August 2003; returned 13 October 2003; revised 6 November 2003; accepted 8 November 2003

Objective: To assess changes in antibiotic prescribing patterns for children between 1987 and 2001, and to identify general practice characteristics associated with higher antibiotic prescribing rates.

Methods: Cross-sectional national survey of Dutch general practice in 1987 and 2001. Data were used for all children aged 0–17 years; 86,577 children in 103 participating practices in 1987, and 76,010 children in 90 participating practices in 2001. Population-based, contact-based and disease-based antibiotic prescription rates were evaluated by age, gender and diagnosis. Practice characteristics associated with inappropriate broad-spectrum antibiotic prescription were identified.

Results: Population-based prescription rates decreased from 300/1000 children (95% CI, 292–307) in 1987 to 232/1000 children in 2001 (95% CI, 228–235). In 1987, the contact-based prescription rate was 108/1000 contacts (95% CI, 106–111) and this was somewhat similar in 2001: 103/1000 contacts (95% CI, 101–105). In 2001, increased disease-based prescription rates were observed for acute otitis media, acute bronchitis, acute upper airway infections, acute tonsillitis and cough. Overall, non-recommended broad-spectrum antibiotics were prescribed more often in 2001 than in 1987 (87% in 1987 versus 90% in 2001, P < 0.001). Adjusted for other practice characteristics, general practitioners in single-handed practices prescribed 58% more broad-spectrum antibiotics inappropriately for upper airway infections than general practitioners in group practices.

Conclusion: Antibiotic prescribing in children is still relatively low in the Netherlands. However, the prescription of broad-spectrum antibiotics for inappropriate diagnoses has increased, an unfavourable trend given the emerging bacterial resistance. Single-handed practices should especially be targeted to improve antibiotic prescribing in children.

Keywords: antibiotic prescription, children, general practice, cross-sectional study

Introduction

In general practice, antibiotic drug use is highest among children and approximately 70% of all antibiotics in children are prescribed for upper respiratory tract infections.1,2 As in other developed countries, the most frequent type of misuse is prescribing antimicrobial agents for infections which are commonly caused by a virus.3–5 Although non-hospital antimicrobial drug use in the Netherlands is the lowest in the European Union,6,7 several nationwide studies have reported inappropriate high antibiotic prescribing.4–10 Moreover, there seems to be a large variation between physicians in antibiotic prescribing.11,12 In view of the emerging worldwide threat of bacterial antibiotic resistance, there is an increasing need to identify determinants and patterns of antibiotic prescribing to identify where clinical practice can be improved.2,13–15

Detailed information on antibiotic drug prescribing in general practice is scarce. Results from the first Dutch national survey in general practice in 1987, showed that 20% of all antibiotics for children were prescribed by 5% of the general practitioners.10 Since the first national survey was carried out, evidence-based guidelines rationalizing antibiotic prescription have been developed by the Dutch College of General Practitioners. These guidelines in general recommend restrictive antibiotic prescription and favour narrow-spectrum antibiotics; for example, antibiotics are recommended only for patients with severe tonsillitis, penethicillin being the antibiotic of first choice. A new guideline is always published in the Dutch...
We carried out this study to obtain insight into the antibiotic prescribing patterns in 2001 and to compare these with those in 1987.

The objectives of this study are to examine antibiotic drug prescribing for children in primary care, by diagnosis, age and gender, to evaluate changes in antibiotic prescribing since 1987, and to assess whether practice characteristics are associated with higher prescription rates.

Materials and methods

Data were analysed from the first and second Dutch national surveys of general practice, which were carried out by the Netherlands Institute for Health Services Research (NIVEL) in 1987 and 2001, respectively. For this study, data from both surveys for children aged 0–17 years were analysed. In the Netherlands, general practices have a fixed list size, meaning that all non-institutionalized inhabitants are listed in a general practice.

First Dutch National Survey 1987

A non-proportionally stratified sample of 161 general practitioners was selected randomly to participate in the survey. The general practitioners were divided into four groups and each group registered all contacts between patient and practice on registration forms during one of the four consecutive 3 month periods during 1987. The registration periods were distributed evenly among the four seasons to correct for seasonal variability of morbidity. Data recorded from each consultation included patient characteristics (age, gender, reason for encounter, diagnosis and prescription of drugs). Diagnoses made by the general practitioner were coded afterwards by specially trained workers using the International Classification of Primary Care (ICPC). Other demographic patient characteristics were obtained by questionnaire. Because of an under-representation of deprived areas, the population was weighted to the Dutch population of 1987.

Second National Survey 2001

The second national survey was carried out in 2001 and has been described in detail elsewhere. In short, 195 general practitioners in 104 practices registered all physician–patient contacts during 12 months. General practitioners registered all health problems presented within a consultation and diagnoses were coded using the ICPC. Also, all prescriptions made by the general practitioner were registered. Characteristics of participating practices such as pharmacy holding, the type of practice (single-handed/group practice), settlement in rural or urban area and list size were obtained by mailed questionnaire. Patient characteristics such as age and gender were derived from the general practitioners’ computerized patient files.

For this analysis, data from 14 of the 104 practices were excluded for various reasons: 10 practices with inadequate registration of patient contacts or drug prescription were excluded after quality control. Four other practices were excluded because they appeared not to have registered morbidity or prescription data because of software problems.

Episodes of disease

Both surveys are episode orientated, meaning that different consultations concerning the same health problem are linked to one episode. The last diagnosis made by the general practitioner is considered the diagnosis of the episode of care.

Prescription measures

Prescriptions are coded according to the ATC classification. All prescriptions of antibiotics for systemic use (Anatomic Therapeutical Chemical group J01) are analysed from both surveys. In addition, from the survey of 1987, antibiotics of ATC groups J03A, J03B and G04A are analysed as well, because in 2001 these ATC groups no longer exist and the antibiotics with these codes are incorporated in the J01 category. (e.g. 1987: ATC code J03A: sulphonamides, ATC code J03B: trimethoprim in combination with sulphonamides, G04A: antibiotics for urinary tract). Antibiotics are analysed by age group, gender and diagnosis for which the prescription was made. Narrow-spectrum antibiotics are defined as antibiotics with ATC codes J01CE and J01CF (phenoxymethylpenicillin, penethicillin, fluocoxacillin and benzylpenicillin). Prescriptions are evaluated and compared by 1000 person years. To take into account differences in consultation rates and the number of health problems encountered in general practice, prescription rates are also examined per 1000 patient contacts (a contact-based prescription rate) and by disease-specific episodes (a disease-based prescription rate). The latter is a measure of the likelihood of antibiotic prescription for a certain health problem. For example, if a certain health problem has 20 prescriptions per 100 episodes, it can be interpreted that 20% of episodes of that disease are treated with antibiotics.

To assess whether certain practices in the survey of 2001 were associated with antibiotic prescribing, a measure of inappropriate antibiotic prescription was computed in order to identify general practices in which improvement of judicious antibiotic prescription is most needed. The measure calculated for each participating practice is the number of broad-spectrum antibiotic prescriptions for the diagnoses with ICPC code R05 (cough), R74 (acute upper airway infection) and R78 (acute bronchitis) per full-time-equivalent general practitioner. For these diagnoses, antibiotics are generally considered inappropriate and this is supported by overwhelming evidence. Prescription of broad-spectrum antibiotics for these diagnoses is considered even more inappropriate.

Analysis

The 95% confidence intervals were calculated around prescription rates, and differences in proportions of types of prescribed antibiotics in both surveys were tested with $\chi^2$ tests. To identify characteristics of general practices associated with inappropriate antibiotic prescribing, a Poisson regression model was used. As dependent variable, the number of broad-spectrum antibiotic prescriptions for diagnoses R05 (cough), R74 (acute upper airway infection) and R78 (acute bronchitis) per full-time-equivalent general practitioner was used. Independent practice characteristics entered in the model were: the type of practice organization (single-handed versus group practice); the number of children listed in the practice; the proportion of children in the practice as a proxy of experience with childhood conditions, pharmacy holding and degree of urbanization.

Extra Poisson dispersion was taken into account. For analysis, SPSS version 11.0 and SAS version 8.2 were used.

Results

Antibiotic prescription rates, by age and gender

During the survey of 1987, 86,777 children had 59,855 encounters in general practice resulting in 50,829 episodes of disease. A total of
Paediatric antibiotic prescription in Dutch general practice

5648 patients received 6487 antibiotic prescriptions resulting in an overall antibiotic prescription rate of 300 per 1000 person years (95% CI, 292–307) and 108 per 1000 GP contacts. In the survey of 2001, a total of 76 010 children aged 0–17 years presented 152 282 episodes of disease during 17 272 contacts with general practice. A total of 17 636 antibiotic prescriptions were issued to 12 231 patients, which gives a significantly lower overall prescription rate of 232 per 1000 person years (95% CI, 228–235) (Table 1). The distribution of prescriptions by ICPC chapter is shown in Table 2. Taking into account the differences in consultation rates in both surveys, the contact-based prescription rate of 1987 is 108 per 1000 encounters in 1987 (95% CI, 106–111), compared to 103 per 1000 encounters in 2001 (95% CI, 101–105); this difference between surveys is just significant. Overall, girls received somewhat more antibiotics than boys, but the 0- to 4-year-old boys received most antibiotic prescriptions: 500 per 1000 person years in 1987 and 444 per 1000 person years in 2001.

Antibiotic prescriptions per ICPC category

The health problems, for which antibiotics were prescribed, are distributed among the ICPC chapters. Antibiotic prescriptions are not only presented per 1000 person years, but also per 100 ICPC chapter-specific episodes. The overall antibiotic prescription rate per 100 episodes in the second survey was 11.6 (95% CI, 11.4–11.8); this can be interpreted as, 11.6% of all episodes of disease were treated with antibiotics. In 1987, this episode-based prescription rate was 12.7 per 100 episodes (95% CI, 12.4–13.0). In 2001, 45% of the antibiotics were prescribed for respiratory problems, compared with 66% in 1987. In 2001, 25% of these respiratory episodes were treated with antibiotics.

Table 1. Numbers of antibiotic prescriptions by age category and gender: comparison of national surveys 1987 and 2001

<table>
<thead>
<tr>
<th>Age Category</th>
<th>National Survey 1987</th>
<th>National Survey 2001</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of prescriptions</td>
<td>no. per 1000 pys</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>6487</td>
<td>300</td>
</tr>
<tr>
<td>Boys</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–4</td>
<td>1485</td>
<td>500</td>
</tr>
<tr>
<td>5–9</td>
<td>902</td>
<td>302</td>
</tr>
<tr>
<td>10–14</td>
<td>401</td>
<td>137</td>
</tr>
<tr>
<td>15–17</td>
<td>441</td>
<td>191</td>
</tr>
<tr>
<td>total</td>
<td>3229</td>
<td>289</td>
</tr>
<tr>
<td>Girls</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–4</td>
<td>1283</td>
<td>460</td>
</tr>
<tr>
<td>5–9</td>
<td>907</td>
<td>324</td>
</tr>
<tr>
<td>10–14</td>
<td>465</td>
<td>163</td>
</tr>
<tr>
<td>15–17</td>
<td>603</td>
<td>292</td>
</tr>
<tr>
<td>total</td>
<td>3258</td>
<td>311</td>
</tr>
</tbody>
</table>

*Total number of antibiotic prescriptions, per 1000 person years (pys) and per 1000 GP contacts in each age category (including all patient contacts).

Table 2. Distribution of prescriptions by the ICPC chapters

<table>
<thead>
<tr>
<th>ICPC Chapter</th>
<th>National Survey 1987</th>
<th>National Survey 2001</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. (%))</td>
<td>no. per 1000 pys</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A General/ unspecified</td>
<td>185 (2.9%)</td>
<td>8.5</td>
</tr>
<tr>
<td>H Ear</td>
<td>890 (13.7%)</td>
<td>41.1</td>
</tr>
<tr>
<td>R Respiratory tract</td>
<td>4303 (66.3%)</td>
<td>198.8</td>
</tr>
<tr>
<td>U Urinary tract</td>
<td>433 (6.7%)</td>
<td>20.0</td>
</tr>
<tr>
<td>Other ICPC chapters</td>
<td>673 (10.4%)</td>
<td>30.9</td>
</tr>
<tr>
<td>Unknown</td>
<td>6487 (100%)</td>
<td>299.7</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>17 636 (100%)</td>
</tr>
</tbody>
</table>

*Total number, prescription per 1000 person years (pys) and per 100 chapter specific episodes of disease.
compared with 33% in 1987 (difference: 8% \( P < 0.001 \)). In 2001, 29% of the ear problems were treated with antibiotics; in 1987 this proportion was 23% (\( P < 0.001 \)).

Diagnoses for the most frequently prescribed antibiotics

Table 3 shows the top 15 diagnoses for which antibiotics were given. In 1987 and 2001 these health problems accounted for 82% and 75% of all antibiotic prescriptions, respectively. In 2001, acute otitis media was the most important diagnosis for which antibiotics were prescribed, followed by acute bronchitis (the number one reason in 1987) and urinary tract infection. The likelihood of receiving an antibiotic prescription for these diagnoses in 2001 increased significantly. On average, all episodes of urinary tract infection were prescribed at least one antibiotic prescription in 2001; during a few episodes more than one antibiotic prescription was made. Antibiotic prescription for episodes of asthma decreased from 27.9% in 1987 to 7.3% in 2001.

The distribution of the different kinds of antibiotics is illustrated in Figure 1. The proportion of narrow-spectrum antibiotics decreased from 13% in 1987 to 10% in 2001 (\( P < 0.001 \)). In 2001, the proportion of macrolides had increased from 8% to 16% (\( P < 0.001 \)).
Paediatric antibiotic prescription in Dutch general practice

prescribed for respiratory tract infections. Tetracyclines were prescribed less frequently in 2001.

Practice characteristics associated with inappropriate prescription

Table 4 shows the relationship between practice characteristics and prescription rates of broad-spectrum antibiotics for diagnoses R05 (cough), R74 (acute upper airway infection) and R78 (acute bronchitis) in 2001. After adjustment for the number of children listed in the practice and other practice characteristics, the type of practice is significantly associated with an inappropriate prescription rate: single-handed practices prescribe 58% (rate ratio 1.58; 95% CI, 1.07–2.35) more broad-spectrum antibiotics for inappropriate diagnoses compared with group practices. Having a high proportion of children listed in the practice is associated with a 55% higher inappropriate antibiotic prescribing than practices with a normal or low proportion of children (rate ratio 1.55; 95% CI, 1.08–2.23). The location of the practice (rural/urban) and whether or not the general practice is pharmacy holding are not associated with these prescriptions.

Discussion

The overall antibiotic prescription rate per 1000 children in general practice has decreased from 300 in the survey of 1987 to 232 in the survey of 2001 (Table 1). This implies a declining prescription rate of antibiotics in children. However, if differences in consultation rate are accounted for, reflected in the contact-based prescription rate, it becomes clear that prescription rates by general practitioners have remained almost the same since 1987 (Table 2). Possibly, this difference in population-based and contact-based prescription rate reflects a higher threshold of contacting the general practitioner in 2001. For example, nowadays parents may have become increasingly aware of the viral origin of infectious respiratory diseases and the lack of efficacy of antibiotics in these infections. Therefore they may visit their general practitioner less often, or only when disease is more severe. Indeed, the finding that fewer antibiotics were prescribed for respiratory tract infections in 2001 is consistent with this hypothesis. Moreover, the results of a recent study by McCaig et al. support our findings.18 They also found a greater decrease in population-based antibiotic prescription rates than in visit-based prescription rates. They found a decrease in visit-based prescription rates over time; however, they did not account for telephone consultations. In our study all contacts with general practice were included in both the numerator and denominator.

In 2001, the 0- to 4-year-old boys received most antibiotics and this was also found in the UK.1

Antibiotics were prescribed more often for diseases of the ear in 2001. In fact, the likelihood of antibiotic prescription for acute otitis media has increased by about 65% (Table 3). The likelihood of antibiotic prescription has also increased, to a lesser extent, for acute tonsillitis (R76). This increase in antibiotic prescriptions for these infections is surprisingly high and unexpected, because published guidelines for acute otitis media and acute tonsillitis rationalized judicious use of antibiotics. Particularly for these health problems we expected a decrease in antibiotic prescriptions. It is possible that parents contact general practice with more severely ill children. In that case, general practitioners are not more inclined to prescribe antibiotics for these infections but are contacted by a patient population with more severe disease. Unfortunately, we have no information on the severity of disease.

Non-recommended, broad-spectrum antibiotics have gained ground during the past decade, and the recommended small-spectrum antibiotics are prescribed less often (Figure 1). In particular, the newer broad-spectrum macrolides are prescribed more often. This has also been found by others, for example a recent study by Resi et al. showed that macrolides were prescribed most often in children over 6 years of age.25 This trend is disturbing because the use of these antibiotics especially gives rise to the increasing problem of bacterial resistance.26-28 We identified general practices in 2001 that were associated with inappropriate antibiotic prescribing. It appeared that, adjusted for other practice characteristics, single-handed general practices prescribe 58% more inappropriate antibiotics for inappropriate diagnoses than their colleagues in group practices. Single-handed practices should be targeted in order to prevent inappropriate prescribing in order to enhance judicious antibiotic prescription. To our knowledge, this predictor of inappropriate antibiotic prescribing has not been found by others and opens opportunities to improve antibiotic prescription. For example, intervention studies to prevent inappropriate antibiotic prescription for these diagnoses could be carried out by targeting these practices. Unexpectedly, in this survey, practices with a large proportion of children more often prescribe antibiotics inappropriately. Apparently, experience with children and childhood diseases does not necessarily improve antibiotic prescribing patterns.

These data provide good insight into non-hospital antibiotic drug use in children, because antibiotics are not available over-the-counter in the Netherlands. However, this study does have some limitations. In the survey of 1987, diagnosis coding with the ICPC was carried out afterwards by specially trained clerks, whereas during the second survey, general practitioners coded the diagnosis themselves. This could explain the difference in the proportion of prescriptions not accounted for in the survey of 2001 (0.06% in 1987 and 12.6% in 2001). This could affect the comparability of the disease-specific and episode-based prescription rates, in particular if the missing diagnoses are not randomly distributed among the ICPC chapters and

Table 4. Characteristics of general practices associated with the number of prescriptions of broad-spectrum antibiotics for diagnoses of R05 (cough), R74 (acute upper airway infection) and R78 (acute bronchitis), survey 2001

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Rate ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single handed&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.58</td>
<td>1.07–2.35</td>
<td>0.02</td>
</tr>
<tr>
<td>High proportion of children in practice&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.55</td>
<td>1.08–2.23</td>
<td>0.02</td>
</tr>
<tr>
<td>Pharmacy holding</td>
<td>1.26</td>
<td>0.78–2.03</td>
<td>0.35</td>
</tr>
<tr>
<td>Urban&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.72</td>
<td>0.49–1.06</td>
<td>0.10</td>
</tr>
<tr>
<td>Semirural&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.73</td>
<td>0.46–1.17</td>
<td>0.19</td>
</tr>
</tbody>
</table>

<sup>a</sup>Adjusted for the number of children listed in the practice and the other practice characteristics.
<sup>b</sup>Reference: group practice.
<sup>c</sup>Reference: low/normal proportion of children in practice (≤20%).
<sup>d</sup>Reference: practices in rural area.
diagnoses. However, this does not influence the population-based, contact-based and total episode-based prescription rates.

Although antimicrobial drug use is low in the Netherlands compared with other countries, clearly inappropriate indications such as upper respiratory tract infections and acute otitis media still account for a large fraction of antibiotic use, and inappropriate prescribing of broad-spectrum antibiotics has increased. Antibiotic resistance caused by improper antibiotic use is a threatening problem and in the past decades much effort has been made to rationalize and change antibiotic prescribing. The results of this study show that challenges remain to improve clinical practice in primary care. In particular, single-handed practices could be targeted to reduce broad-spectrum prescriptions for inappropriate diagnoses.

References