Incidence of antibiotic prescribing in dental practice in Norway and its contribution to national consumption

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Objectives: To assess dentistry-based utilization of the 11 antibiotics prescribed by dentists in Norway and its relative contribution to national outpatient consumption and to determine the relationship between numbers of prescriptions and the consumption of these antibiotics.

Methods: Data on national antibiotic prescriptions by dentists in 2004 and 2005 were used. Consumption of the antibiotics was expressed using WHO defined daily doses (DDDs), DDDs per 1000 inhabitants per day (DIDs) and numbers of prescriptions per 1000 inhabitants (PIDs).

Results: Analysis of 268,834 prescriptions issued by 4765 dentists showed that the dentists’ prescriptions contributed 8% of the total national consumption of the 11 antibiotics and 13.5%, 2.8% and 1.2% of the national β-lactam penicillins, macrolides and lincosamides and tetracyclines utilization, respectively. The dentists’ contributions to the national phenoxymethylpenicillin, spiramycin and metronidazole consumptions were considerably higher (≥13.2%) than for the other prescribed antibiotics (<8.6%). There was a strong positive correlation between numbers of DDDs and numbers of prescriptions and between DIDs and numbers of PIDs.

Conclusions: Reliance of Norwegian dentists on phenoxymethylpenicillin as their first choice suggests a low prevalence of antibiotic resistance among oral bacteria in Norway. Norwegian dentists prefer to prescribe narrow-spectrum antibiotics; their prescribing is conservative and relatively low compared with that of physicians.

Keywords: antibiotics, dentists, prescriptions, utilization

Introduction

Bacterial resistance to antimicrobials has been an ongoing challenge for clinicians ever since the discovery of antimicrobial agents because bacteria have succeeded in developing resistance to all antibacterial agents shortly after they had been marketed. Evolution of bacteria towards resistance to antibacterials, including multidrug resistance, seems unavoidable because it represents a particular aspect of the general evolution of bacteria that is genetically determined and confers a survival advantage. There is sufficient evidence for a significant relationship between increase in antimicrobial resistance and antimicrobial utilization with higher resistance levels in bacteria from areas with high antibiotic utilization than in bacteria from areas with low antibiotic utilization. Therefore, one strategy that has been widely adopted to curtail the rapid emergence and subsequent dissemination of resistance genes is to restrain the use of antibacterial drugs.

Inappropriate prescribing and use have been identified as major factors in the emergence of antibiotic resistance. Consequently, modification and surveillance of prescribing attitudes have become crucial. On 1 January 2004, the Norwegian Prescription Database (NorPD) was established at the Norwegian Institute of Public Health, Department of Pharmacoepidemiology. The magnitude of antibiotic prescribing can be determined by analysis of available national consumption data. The NorPD is one of the seven Norwegian central health registers and it contains information about delivery of medicines from pharmacies in Norway. Among the 38 NorPD registration variables are demographics of the prescribers as well as the type of and various information about the prescribed drugs. This database is used for pharmacoepidemiological research and pharmaceutical statistics. The statistical

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material is organized in the database according to the Anatomical Therapeutic Chemical (ATC) classification, and a technical unit called the defined daily dose (DDD) is used as the unit of drug consumption measurement that is independent of different drug preparations. The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults and does not reflect the recommended or prescribed daily dose. The ATC classification for veterinary medicinal products, ATCVet, is based on the same main principles as the ATC system for medicines for human usage.

In Norway, physicians, dentists and veterinarians have the right to prescribe antibiotics. The WHO Collaborating Centre for Drug Statistics Methodology, also located at the Norwegian Institute of Public Health, Department of Pharmacoepidemiology, is responsible for the development and maintenance of the ATC/DDD system. One purpose of this system is to serve as a tool for drug utilization research in order to improve quality of drug use. One component of this is the presentation and comparison of drug consumption statistics at national and international levels. Another purpose is to maintain stable ATC codes and DDDs over time in order to allow trends in drug consumption to be studied without the complication of frequent changes to the system. The extent of antibiotic use by outpatients has been expressed as number of DDDs per 1000 inhabitants per (DID).

There is a reason for concern in general dental practice regarding bacterial antibiotic resistance. Penicillin resistance in Fusobacterium nucleatum has been on the rise, roughly 25% of strains of the genera Prevotella and Porphyromonas are penicillin-resistant, and these microbes are likely to be present in mature dental infections. Consequently, dental professionals have been provided with information about antibiotic resistance and advice on the clinical use of antibiotics in dentistry. Although it has been stated that the current situation clearly requires judicious and prudent consideration before antibiotic therapy is administered, there is scant information in the literature regarding the contribution of antibiotics used in dentistry to the total consumption of antibiotics and to antimicrobial resistance. A surveillance system for antimicrobial resistance, including identification of antimicrobial resistance and antimicrobial usage, has been recommended for dentistry. The contribution from dental practice to the national outpatient consumption of antibiotics is therefore of interest.

The objective of our study was to assess the utilization of antibiotics in Norwegian dental practice and its relative contribution to the total national antibiotic consumption by outpatients, and any correlation between the number of antibiotic prescriptions and extent of antibiotic use.

**Materials and methods**

Aggregated data on all prescriptions in 2004 and 2005 of 11 antibiotics (phenoxymethylpenicillin, ATC code J01CE02; amoxicillin, ATC code J01CA04; erythromycin, ATC code J01FA01; doxycycline, ATC code J01AX02; metronidazole, ATC codes P01AB01 and J01XD01; clindamycin, ATC code J01FF01; tetracycline, ATC code J01AA07; spiramycin, ATC code J01FA02; oxytetracycline, ATC code J01AA06; clarithromycin, ATC code J01FA09; azithromycin, ATC code J01FA10) in the 19 counties of Norway were obtained from NorPD. These antibiotics were chosen because according to NorPD, they were the antimicrobial drugs prescribed by Norwegian dentists. The aggregated data contained the numbers of prescriptions issued by dentists, the number of dentists having prescribed the antibiotics and the total DDDs. The number of authorized dentists and the population size for each county in both years were obtained from the State Authorization of Healthcare Personnel and the Norwegian Institute of Public Health, respectively. The extent of antibiotic use related to dentistry-based prescribing was calculated as the corresponding number of DDDs per 1000 inhabitants per day (PID) and as the corresponding number of prescriptions per 1000 inhabitants per day (PDD) for each antibiotic. The retrieved prescription data and the sums (i.e. the combined consumption by dentists, physicians and veterinarians) of DDDs from the 19 counties were used and are referred to as the corresponding national total data. The relative contribution of each antibiotic prescribed by dentists to the total national outpatient consumption of the same antibiotics in both 2004 and 2005 was calculated by dividing each of the former DDDs by the corresponding total national ones.

The NorPD data were entered into an SPSS database (SPSS 13.0 for Windows, SPSS Inc., Chicago, IL, USA), and correlations between the numbers of DDDs and the numbers of prescriptions issued by dentists as well as between the numbers of DIDs and the numbers of PIDs for the 11 antibiotics in both 2004 and 2005 were measured with the two-tailed Spearman coefficient for non-parametric correlations.

**Results**

We analysed 131 128 prescriptions issued by 4355 dentists and 137 706 prescriptions issued by 4231 dentists in 2004 and 2005, respectively. The numbers of authorized dentists in Norway on 1 January 2005 and 2006 were 5939 and 6135, respectively. The population size in the country was 4 574 796 and 4 603 743 on 1 January 2004 and 2005, respectively. The 268 834 prescriptions were issued by 4765 different dentists working in all types of dental settings in Norway: public clinics, private offices, hospitals and teaching universities. This means that 73.3% and 70.0% of the authorized dentists in Norway issued antibiotic prescriptions in 2005 and 2006, respectively.

The 11 antibiotics ranked by the numbers of the dentists’ prescriptions, consumptions (DDDs) and extent of use (DIDs) are shown in Table 1. The table also shows that the magnitude of the corresponding numbers of PIDs for the 11 antibiotics in both 2004 and 2005 was calculated by

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Antibiotic consumption in dental practice

Table 1. Eleven antibiotics prescribed by dentists in Norway, number of prescriptions, DDDs prescribed by dentists, physicians and veterinarians and the total of these, the relative contributions of dentists’ DDDs to the total DDDs and dentists’ DIDs contributions in 2004 and 2005

<table>
<thead>
<tr>
<th>Prescribed antibiotics</th>
<th>2004 Dentists’ DDDs</th>
<th>2004 Physicians’ DDDs</th>
<th>2004 Veterinarians’ DDDs</th>
<th>Total DDDs</th>
<th>Dentists’ % contribution to total national consumption</th>
<th>Dentists’ DIDs contributed by prescriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenoxymethyl penicillin</td>
<td>98 387 101 624</td>
<td>241 296 611 397</td>
<td>218 509 2 535 464</td>
<td>3 535 464 87 040 81 038 6 148 554 6 627 899 15.7 15.2 0.5789 0.6018</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td>82 36 45 036</td>
<td>241 36 45 793</td>
<td>287 247 281 990</td>
<td>281 990 13.2 16.2 0.0227 0.0272</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>64 91 49 236</td>
<td>1 747 500 1 747 500</td>
<td>1 638 662 1 803 499</td>
<td>1 803 499 3.0 2.9 0.0294 0.0314</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>60 90 64 545</td>
<td>275 308 2 853 488</td>
<td>2 885 488 2 885 488</td>
<td>2 885 488 4.7 4.7 0.0386 0.0400</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>30 34 38 904</td>
<td>293 379 2 938 760</td>
<td>2 758 760 2 758 760</td>
<td>2 758 760 1.4 1.4 0.0160 0.0160</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>15 81 83 806</td>
<td>157 990 1 613 508</td>
<td>1 646 508 1 646 508</td>
<td>1 646 508 1.8 2.0 0.0060 0.0100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spiramycin</td>
<td>9 90 33 956</td>
<td>1 479 950 1 479 950</td>
<td>1 479 950 1 479 950</td>
<td>1 479 950 0.9 0.9 0.0018 0.0018</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetracycline</td>
<td>9 44 11 629</td>
<td>1 069 873 1 069 873</td>
<td>1 069 873 1 069 873</td>
<td>1 069 873 1.1 1.1 0.0060 0.0060</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxytetracycline</td>
<td>3 35 33 806</td>
<td>339 807 339 807</td>
<td>339 807 339 807</td>
<td>339 807 0.9 1.0 0.0018 0.0018</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>12 81 12 956</td>
<td>1 479 950 1 479 950</td>
<td>1 479 950 1 479 950</td>
<td>1 479 950 0.2 0.2 0.0009 0.0009</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dentists’ contributions to the national outpatient consumptions of β-lactam penicillins, macrolides and lincosamides and tetracyclines were 13.5%, 2.8% and 1.2%, respectively.

Table 2 shows the numbers of DDDs and the numbers of prescriptions by dentists as well as the numbers of DIDs and the numbers of PIDs for the 11 antibiotics in 2004 and 2005. The Spearman correlation coefficient between the numbers of DDDs and the numbers of prescriptions and between the numbers of DIDs and the numbers of prescriptions showed highly significant correlations (P values < 0.001).

Discussion

To the best of our knowledge, this study on 11 antibiotics prescribed by dentists in Norway in 2004 and 2005 is the first report using the WHO-defined drug measurement unit DDD, DIDs and PIDs to assess the consumption and the extent of antibiotic use in dental practice. Our results show that dentists in Norway prescribed the narrow-spectrum phenoxymethylpenicillin as their first choice; 75% and 73% of their total prescriptions in 2004 and 2005, respectively. Owing to increasing numbers of reports on oral bacterial resistance to narrow-spectrum penicillins, the broader spectrum antibiotic amoxicillin has been more frequently used. On the basis of a recent study in Norway on the resistance of 18 selected subgingival species to aminopenicillins and metronidazole, a low prevalence of resistance to the broad-spectrum ampicillin was found among the studied species. This finding could be in accordance with the reserved use of the broad-spectrum amoxicillin demonstrated in the present study. Compared with Norway, other countries do not prefer phenoxymethylpenicillin. For example, in England, 55.8% of prescriptions of penicillins were for amoxicillin, whereas phenoxymethylpenicillin prescriptions reached only 8.2%. Prescribing broad-spectrum instead of narrow-spectrum penicillins in cases with no supportive results from antibacterial resistance testing is not recommended, especially not when the treatment is based on empirical antibiotic therapy, as is the case for the management of most dental infections. The practice of using narrow-spectrum penicillins among Norwegians dentists is part of the country’s conservative prescription practice. In fact, in 2002, Norway was the first country in Europe with a trend to use phenoxymethylpenicillin.

Metronidazole is the second most prescribed antibiotic in the present study and also was the second most prescribed by dentists elsewhere. This is not surprising because the antibiotic has good anti-anaerobe properties and should be dentists’ first choice when treating anaerobe infections using an antibacterial drug. The Norwegian dentists prescribed metronidazole in 6.3% and 6.9% of their prescriptions in 2004 and 2005, respectively, compared with 22.2% of the total number of prescriptions issued by 10% of the dentists working in England. Dentists accounted for 45% of all metronidazole prescriptions in the UK. It is worth mentioning here that metronidazole under the ATC classification has several codes. In our study, metronidazole consumption was recorded under two ATC codes, namely J01XD01 and P01AB01. The former code has only one preparation in Norway, which is for parenteral use, and tablets are one of the preparations available under the ATC code P01AB01. In Norway, dentists do not inject drugs, and consequently, there were no prescriptions issued by dentists under code J01XD01.
<table>
<thead>
<tr>
<th>Prescribed antibiotics</th>
<th>Numbers of DDDs</th>
<th>Numbers of dentists’ prescriptions</th>
<th>Numbers of DDDs versus numbers of prescriptions&lt;sup&gt;a&lt;/sup&gt; (P value)</th>
<th>PIDs</th>
<th>DIDs</th>
<th>PIDs versus DIDs&lt;sup&gt;a&lt;/sup&gt; (P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenoxymethylpenicillin</td>
<td>969 296</td>
<td>1 011 397</td>
<td>98 387 101 624</td>
<td>0.0587</td>
<td>0.0604</td>
<td>0.5789 0.6018</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>64 645</td>
<td>71 838</td>
<td>6090 6523</td>
<td>0.0036</td>
<td>0.0038</td>
<td>0.0386 0.0427</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>49 236</td>
<td>52 858</td>
<td>6491 6939</td>
<td>0.0038</td>
<td>0.0041</td>
<td>0.0294 0.0314</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>38 904</td>
<td>40 408</td>
<td>3034 3160</td>
<td>0.0018</td>
<td>0.0018</td>
<td>0.0232 0.0240</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>38 036</td>
<td>45 763</td>
<td>8276 9502</td>
<td>0.0049</td>
<td>0.0056</td>
<td>0.0227 0.0272</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.891 (&lt;0.001)</td>
<td>0.927 (&lt;0.001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>20 991</td>
<td>26 964</td>
<td>4862 6130</td>
<td>0.0029</td>
<td>0.0036</td>
<td>0.0125 0.0160</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>11 629</td>
<td>10 103</td>
<td>944 786</td>
<td>0.0005</td>
<td>0.0004</td>
<td>0.0069 0.0060</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>8386</td>
<td>8559</td>
<td>1581 1593</td>
<td>0.0009</td>
<td>0.0009</td>
<td>0.0050 0.0050</td>
</tr>
<tr>
<td>Spiramycin</td>
<td>3543</td>
<td>3436</td>
<td>990 956</td>
<td>0.0005</td>
<td>0.0005</td>
<td>0.0021 0.0020</td>
</tr>
<tr>
<td>Oxytetracycline</td>
<td>3115</td>
<td>3394</td>
<td>355 365</td>
<td>0.0002</td>
<td>0.0002</td>
<td>0.0018 0.0020</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>1579</td>
<td>1241</td>
<td>118 128</td>
<td>0.0000</td>
<td>0.0000</td>
<td>0.0009 0.0020</td>
</tr>
</tbody>
</table>

<sup>a</sup>Spearman correlation coefficient.
A surprise to the authors was that spiramycin consumption by dentists contributed relatively more to the total national consumption of this drug than did any of the other antibiotics. The explanation for this finding is the relative low number of spiramycin prescriptions issued by physicians and veterinarians and that the Felleskatalogen (the Norwegian Pharmaceutical Product Compendium) recommends spiramycin as an adjunct for treatment of periodontal disease when antimicrobial therapy is indicated. Furthermore, spiramycin has a unique property of reaching concentration levels in the gingival crevicular fluid exceeding levels in serum. It has a good activity against both anaerobic and aerobic oral bacteria, and it has been suggested that an extended activity of this drug is obtained for combination therapy, mainly with metronidazole.

On average, consumption by dentists in Norway contributed by ~8% to the total consumption of the 11 drugs. The only data published from other countries are related to prescriptions rather than actual consumption and showed that in England, dentists’ prescriptions accounted for ~7%, in the period 1993–96, and in the USA for almost 9%, in the period 1995–97, of the most commonly used antimicrobials in western countries. Our study is the first one informing about dentists’ contribution to the total national consumption of 11 antibiotics commonly prescribed in dental practice.

In dental practice, antibiotic prescribing is considerably less than that in medical practice, as also demonstrated in the present study. The conditions for prescribing antimicrobials in dentistry are: (i) therapeutic, to aid surgical treatment of an acute or chronic infection; (ii) therapeutic, to treat active infectious disease, e.g. acute ulcerative gingivitis; and (iii) prophylactic, to prevent metastatic infection, e.g. bacterial endocarditis. These conditions are in line with recommendations of two relevant textbooks published recently. However, dentists’ prescription practices and knowledge are not always optimal and non-clinical factors might influence their decision to prescribe. Studies conducted to assess the prescription knowledge of dentists revealed a lack of uniformity in prescription and sometimes the appropriate rationale for prescribing.

The figures in Table 1 show the relative contribution of the dentists’ antibiotic consumptions to the total consumptions of these antibiotics in Norway. For some of the 11 antibiotics, veterinarians have their own preparations (i.e. doxycycline, ATC code QJ01AA02; oxytetracycline, ATC codes QJ01AA06 and QG01AA07; amoxicillin, ATC codes QJ01CA04 and QJ01CR02 and QJ51RV01; clindamycin, ATC code QJ01FF01). They do, however, in some cases prescribe human preparations to animals. Therefore, the total national consumptions presented in Table 1 includes consumption related to human antibiotic preparations prescribed by veterinarians to animals.

The strong correlation between the numbers of DDDs and antimicrobial prescriptions demonstrated in our study is in accordance with a previous study. The PID numbers indicate the antimicrobial prescription rate, and there was a strong correlation with the numbers of DIDs (Table 2), which has also been found by others.

Limitations of the current study are use of DDDs, which assumes every individual to have a bodyweight of 70 kg and all patients to receive daily the same amount of prescribed drug, as well as lack of information on doses used, frequency of administration, duration of treatment, reasons for individual prescriptions and combined antibiotic therapy. Unfortunately, NorPD does not provide these missing data. DDDs give an estimate of consumption and trends but not an exact picture of actual use. However, DDD is the unit used in drug consumption measurements for estimation of trends in drug use over time and to compare drug use with best practice. Antibiotic consumption measurement is increasingly being recognized as an important factor for monitoring emerging resistance, and differences in antibiotic consumption may be responsible for differences in antibiotic resistance.

In conclusion, reliance of dentists in Norway on phenoxymethylpenicillin as their first choice indicates low prevalence of antibiotic resistance among oral bacteria in Norway and shows the conservative antibiotic practice of dentists in Norway. The data also indicate that the selective pressure on bacterial populations in Norway due to antibiotic prescriptions by dentists is probably low. Our investigation showed for the first time, to the best of our knowledge, the exact consumption figures of 11 antibiotics used in dentistry. We used the ATC/DDD system and calculated DID and PID values that allow our data to be compared directly with data of similar future studies in other countries.

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Transparency declarations

None to declare.

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