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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 (\geq 13.2%) than for the other prescribed antibiotics (\leq 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.¹ 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.² 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 anti-bacterial drugs. $^{3,4}\,$

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.⁵ 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.⁶ 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.⁶ 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.⁶ 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 to allow trends in drug consumption to be studied without the complication of frequent changes to the system.⁶ The extent of antibiotic use by outpatients has been expressed as number of DDDs per 1000 inhabitants per (DID).⁷

There is a reason for concern in general dental practice regarding bacterial antibiotic resistance.^{8,9} 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.¹⁰ Consequently, dental professionals have been provided with information about antibiotic resistance and advice on the clinical use of antibiotics in dentistry.¹¹⁻¹³ Although it has been stated that the current situation clearly requires judicious and prudent consideration before antibiotic therapy is administered, ¹² 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.¹⁴ 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 J01AA02; 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.⁵ 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.^{5,15}

The extent of antibiotic use related to dentistry-based prescribing was calculated as the corresponding number of DDDs per 1000 inhabitants per day (DID) and as the corresponding number of prescriptions per 1000 inhabitants per day (PID) for each antibiotic.¹⁶ 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 total national 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 31 December 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 veterinarian antibiotic consumption was in the range 108-123 518 DDDs. Phenoxymethylpenicillin and metronidazole were the two most frequently prescribed antibiotics by dentists and accounted for 75% and 6.3%, respectively, in 2004 versus 73% and 6.9%, respectively, in 2005 of all the dentists' antibiotic prescriptions. The prescription of metronidazole (ATC code J01XD01) was zero. The relative contributions of the 11 antibiotics prescribed by dentists to the total national consumption ranged from 15.7% to 0.2% and could be subgrouped follows:>13.2% (phenoxymethylpenicillin>spiramycin> as metronidazole), <13.2% to 1% (clindamycin>amoxicillin> erythromycin>doxycycline>azithromycin>tetracycline) and <1% (oxytetracycline>clarithromycin). Contributions by the dentists in 2004 and 2005 to the total national outpatient consumptions of phenoxymethylpenicillin, spiramycin and metronidazole (15.7%, 15% and 13.2% in 2004 versus 15.2%, 15.5% and 16.2% in 2005) were considerably higher than for the other eight antibiotics. Consumption by dentists in Norway contributed by ~8% to the total consumption of the 11 drugs.

Antibiotic consumption in dental practice

[able 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

Dentists'

Dentists' Dentists' Dentists' Dentists <thdentists< th=""> Dentists Dentists</thdentists<>	Dentists' DDDs consumption 004 2005 1296 1 011 397	Physicians' DDDs consumption 2004 200 5 092 218 5 535	DDDs	Veterinaria							
ibiotics 2004 2005 yl penicillin 98.387 101.624 9 8.276 9502 6.400 6030	10	2004 5 092 218		consumption	consumption	Total DDDs consumption	consumption	DDDs consumption	Ds 1ption	contributed by dentists	ited by ists
yl penicillin 98.387 101 624 9 8276 9502 6401 6030	1 (5 092 218	2005	2004	2005	2004	2005	2004	2005	2004	2005
8276 9502 6401 6030			5 535 464	87 040	81 038	6 148 554	6 627 899	15.7	15.2	0.5789	0.6018
6/01 6030		241 795	227 884	7416	8343	287 247	281 990	13.2	16.2	0.0227	0.0272
	49 236 52 858	1 586 972	1 747 500	2454	3141	1 638 662	1 803 499	3.0	2.9	0.0294	0.0314
Amoxicillin 6090 6523 64.6		1 251 329	$1 \ 396 \ 343$	60 849	59 589	1 376 823	1 527 770	4.7	4.7	0.0386	0.0427
Clindamycin 4862 6130 20 9		$214\ 809$	267 449	17 299	17 022	253 099	311 435	8.3	8.6	0.0125	0.0160
Doxycycline 3034 3160 38.9	38 904 40 408	2 593 476	2 725 700	123 518	119 380	2 755 898	2 885 488	1.4	1.4	0.0232	0.0240
Azithromycin 1581 1593 83	8386 8559	448 633	512 483	787	740	457 806	521 782	1.8	1.6	0.0050	0.0050
Spiramycin 990 956 35.	3543 3436	19 320	18 153	626	446	23 489	22 035	15.0	15.5	0.0021	0.0020
Tetracycline 944 786 11 6	1 629 10 103	1 006 176	$1 \ 049 \ 873$	1604	1897	$1 \ 019 \ 409$	$1\ 061\ 873$	1.1	0.9	0.0069	0.0060
Oxytetracycline 355 365 31	3115 3394	296 243	296 544	40 061	35869	339 419	335 807	0.9	1.0	0.0018	0.0020
Clarithromycin 118 128 15	1579 1241	587 759	612 337	108	141	589 446	613 719	0.2	0.2	0.0009	0.0007

DDDs, defined daily doses.⁶ DIDs, numbers of DDDs per 1000 inhabitants per day.⁷

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 PIDs 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.^{6,7} 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.⁹ 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.¹⁷ 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.^{18–21} For example, in England, 55.8% of prescriptions of penicillins were for amoxicillin, whereas phenoxymethylpenicillin prescriptions reached only 8.2%.¹⁸ 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.¹¹ 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.22

Metronidazole is the second most prescribed antibiotic in the present study and also was the second most prescribed by dentists elsewhere.^{18,19} 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.¹⁸ Dentists accounted for 45% of all metronidazole prescriptions in the UK.²³ 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.

	Numbers of DDDs		Numbers of dentists' prescriptions		Numbers of DDDs versus numbers of prescriptions ^a (P value)		PIDs		DIDs		PIDs versus DIDs ^a (P value)	
Prescribed antibiotics	2004	2005	2004	2005	2004	2005	2004	2005	2004	2005	2004	2005
Phenoxymethylpenicillin	969 296	1 011 397	98 387	101 624			0.0587	0.0604	0.5789	0.6018		
Amoxicillin	64 645	71 838	6090	6523			0.0036	0.0038	0.0386	0.0427		
Erythromycin	49 236	52 858	6491	6939			0.0038	0.0041	0.0294	0.0314		
Doxycycline	38 904	40 408	3034	3160			0.0018	0.0018	0.0232	0.0240		
Metronidazole	38 036	45 763	8276	9502			0.0049	0.0056	0.0227	0.0272		
					0.891	0.927					0.891	0.920
					(<0.001)	(<0.001)					(<0.001)	(<0.001)
Clindamycin	20 991	26 964	4862	6130			0.0029	0.0036	0.0125	0.0160		
Tetracycline	11 629	10 103	944	786			0.0005	0.0004	0.0069	0.0060		
Azithromycin	8386	8559	1581	1593			0.0009	0.0009	0.0050	0.0050		
Spiramycin	3543	3436	990	956			0.0005	0.0005	0.0021	0.0020		
Oxytetracycline	3115	3394	355	365			0.0002	0.0002	0.0018	0.0020		
Clarithromycin	1579	1241	118	128			0.0000	0.0000	0.0009	0.0020		

Table 2. Numbers of prescriptions issued by authorized dentists in Norway, corresponding numbers of DDDs, DIDs and PIDs and correlations between the numbers of DDDs and prescriptions for 11 antibiotics and between the numbers of DIDs and PIDs in 2004 and 2005

^aSpearman correlation coefficient.

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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.²⁴ 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.²⁵

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.^{23,26} 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.^{13,27,28} These conditions are in line with recommendations of two relevant textbooks published recently.^{10,29} 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.^{20,00,31}

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.¹⁶ The PIDs 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.¹⁶

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.⁷ 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.²²

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 system⁶ 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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