TRENDS IN ANTIMICROBIAL PRESCRIBING RATES FOR ALASKA NATIVE AND AMERICAN INDIAN PERSONS <18 YEARS OF AGE RESIDING IN THE ANCHORAGE REGION

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ABSTRACT

Objectives. In the U.S., the total number of antimicrobials prescribed in ambulatory care declined between 1989 and 2000; however, antimicrobial resistance increased among many pathogens. We evaluated antimicrobial prescribing patterns from 1992 to 2004 in Alaska Native/American Indian (AI/AN) persons <18 years old, residing in the Anchorage region who received care through the AI/AN health system.

Study design. Retrospective study based on medical records.

Methods. Medical records were used to obtain data on oral antibiotics prescribed for ambulatory and emergency-room visits. Antimicrobial prescribing rates were calculated per population and per ambulatory-clinic visit.

Results. The total number of antimicrobial courses prescribed increased 94% from 4,929 (1992) to 9,561 (2004). However, the total number of ambulatory-clinic visits also increased (79%) from 49,008 (1992) to 87,486 (2004), while the population of AI/AN persons <18 in Anchorage region rose 14%. The population-based rate of antimicrobial prescriptions (per 1,000 persons) rose from 309 (1992) to 524 (2004) (p<0.001). The visit-based annual rate (per 1,000 visits) remained stable from 101 (1992) to 109 (2004) (p=0.651). Overall, visit-based prescription rates in AI/AN persons were lower than previously reported among children in the U.S. (range 250–340). Penicillins comprised >50% of antimicrobials prescribed from 1992 to 2004. Visit-based prescribing rates from 1992 to 2004 changed: penicillin, +27% (p=0.210); cephalosporins, +33% (p=0.023); trimethoprim-sulfamethoxazole, −48% (p<0.001).
Conclusions. Visit-based antimicrobial prescribing rates in the Anchorage region for AI/AN children receiving care in the AI/AN health system have been stable over a 13-year period. Although a trend in decreased antibiotic prescribing has been seen in the general U.S. population, visit-based prescribing rates in the Anchorage region for AI/AN children have remained below those in previous studies in the U.S. (Int J Circumpolar Health 2009; 68(4):337-346)

Keywords: antimicrobial prescribing, Alaska Native children, antibiotic, prescription rates, AI/AN

INTRODUCTION

The growing trend of antimicrobial resistance among bacteria is of major public health concern (1,2). Prescription of antimicrobials for viral infections, use of broad-spectrum antimicrobials when targeted therapy is appropriate and general over-prescribing of antimicrobials can lead to the development of antimicrobial resistance (3). In Alaska, high rates of antimicrobial resistance have been documented among Staphylococcus aureus, Streptococcus pneumoniae, Helicobacter pylori (H. pylori) and other bacterial infections (4–9).

Data collected in the U.S. between 1980 and 1992 via the National Ambulatory Medical Care Survey (NAMCS) revealed that the antimicrobial prescribing rate for children by office-based physicians rose 48% from 1980 to 1992, and distribution among antimicrobial classes shifted from prescribing of older agents such as penicillin (specifically ampicillin) to prescribing of newer agents such as amoxicillin and the cephalosporins (10). The more recent data collected by McCaig et al. between 1992 and 2000 via the NAMCS and National Hospital Ambulatory Medical Care Survey demonstrated a decline in the annual population- and visit-based rates of antimicrobial prescribing by 23% and 25%, respectively. However, while prescribing of amoxicillin and ampicillin, cephalosporins and erythromycins declined, prescribing of the newer, more expensive, broad-spectrum agents increased. Increases occurred for azithromycin, clarithromycin and the quinolones in patients >15 years of age, and in amoxicillin-clavulanate in patients <15 years of age (11,12).

Inappropriate antimicrobial prescribing has been an important issue in the U.S. and other countries over the past two decades. In 1992, based on NAMCS data, the U.S. Centers for Disease Control and Prevention (CDC) estimated that >40% of antibiotics prescribed in doctors’ offices were inappropriate (13). The reasons for this are likely multifactorial; however, some pediatricians have commented that parental pressure plays a role (14). As noted in publications by McCaig et al. (11,15), there has been a dramatic decline in the prescribing of antimicrobials in the U.S. outpatient setting overall, and specifically to both children and adolescents in doctors’ offices. In Alaska, scant data are available on antimicrobial prescribing rates; however, previous studies have documented that education can substantially decrease overall antibiotic prescribing.
in the treatment of respiratory infections (16). While high rates of antimicrobial resistance have been documented in Alaska and other Arctic countries, very few studies have looked at antimicrobial prescribing rates in this region. The objectives of this study were to determine the total number of antimicrobials prescribed to Alaska Native/American Indian (AI/AN) persons <18 years of age at the Alaska Native Medical Center (ANMC) and its outpatient clinics located in the Anchorage region from 1992 to 2004, to calculate the population- and visit-based prescribing rates for AI/AN persons, to evaluate the population- and visit-based rates by antimicrobial class and to compare these data with national trends.

MATERIAL AND METHODS

We collected data on outpatient visits and antibiotics dispensed at the Alaska Native Medical Center to AI/AN persons via an electronic data system known as the Resource Patient Management System (RPMS). ANMC is a 150-bed referral hospital for AI/AN persons living throughout the state. It also has a primary care centre which provides over 500,000 clinic visits per year. Health care services are pre-paid based on a compact with the U.S. federal government for AI/AN persons. The Alaska Native population encompasses 229 tribes, which are culturally and ethnically diverse. In Anchorage, 9.7% (26,932 of 277,498 people) of the population is represented by AI/AN persons.

This project is one of 3 identical quality assurance projects going on at 3 different hospitals in Alaska; the Alaska Area IRB had reviewed this type of quality assurance project and determined that no IRB review was needed. Prior to the manuscript being sent to the IJCH, the Alaska Native Tribal Health Consortium’s Health Research Review Committee and ANMC’s Abstract Manuscripts, and Protocol Committee reviewed and approved the manuscript for submission.

We reviewed data from AI/AN persons less than 18 years of age who were prescribed oral antibiotics at ANMC’s ambulatory care clinics and who resided in the Anchorage region from 1992 to 2004. The “Anchorage region” comprises all of south-central Alaska and a portion of the Aleutian Islands and is equivalent to the Indian Health Service (IHS) designation of the Anchorage Service Unit. Data on topical and parenteral antibiotics were not obtained.

The following data were collected: patient identification number; age at visit; gender; community of residence (town/village); region of residence; date of visit; facility where service was performed; and type of antimicrobials prescribed (up to 2 recorded per visit).

Antimicrobial drugs were grouped into the following categories: azithromycin/clarithromycin, cephalosporins, erythromycin, penicillins, fluoroquinolones, tetracyclines, sulfamethoxazole-trimethoprim (SMX-TMP) and other. The “other” category included clindamycin, furazolidone, methenamine, metronidazole, neomycin, nitrofurantoin and vancomycin.

We calculated both population-based and visit-based antimicrobial drug prescribing rates in this study. The population-based rate was defined as the annual number of antimicrobial prescriptions recorded in the ambulatory care setting at ANMC for AI/AN persons less than 18 years of age residing in
the Anchorage region divided by the AI/AN population less than 18 years of age residing in the Anchorage region. Population denominators were based on data obtained from the Alaska Department of Labor and Workforce Development website (www.labor.state.ak.us, accessed 8/3/08). Rates are presented per 1,000 persons per year. The visit-based rate was defined as the annual number of antimicrobial prescriptions recorded in the ambulatory care setting at ANMC for AI/AN persons less than 18 years of age residing in the Anchorage region divided by the annual number of ambulatory care visits at ANMC for AI/AN persons less than 18 years of age residing in the Anchorage region.

Statistical analyses were performed using STATA 5.0. Trends in population-based antimicrobial drug prescribing rates were assessed using a weighted linear regression, while trends in visit-based antimicrobial drug prescribing rates were assessed with a weighted least squares logistic model. All p-values are 2-sided and those <0.05 are considered statistically significant.

RESULTS

Over the study period, the total annual number of oral antimicrobials prescribed at ANMC to AI/AN persons <18 years old in the Anchorage region increased 94% from 4,929 to 9,561 (Fig. 1). This increase in prescribing was more pronounced among children aged 5–17 than in those <5. Penicillins represented over 50% of the antimicrobials dispensed each year; SMX-TMP and the cephalosporins represented approximately 25% of antimicrobials dispensed each year (Fig. 1). While the total number of ambulatory care visits rose 79% from 49,008 to 87,486, it should also be noted that the population of Alaska Native children <18 years of age in the Anchorage region rose 14% from 15,945 to 18,236 over the 13-year study period.

![Figure 1. Categories of antimicrobials prescribed annually among AI/AN persons <18 years of age in Anchorage, Alaska.](image-url)
Population-Based Prescribing Rates

Children <18 years of age

The annual population-based rate of antimicrobial prescribing increased 70% from 309 to 524 antimicrobial prescriptions per 1,000 persons over the study period (p<0.001) (Table I). Population-based prescribing rates per 1,000 children <18 years of age have risen significantly from 1992 to 2004 in the following classes: cephalosporins (+114% from 36 to 77; p=0.001), penicillins (+98% from 158 to 313; p<0.001) and tetracyclines (+114% from 7 to 15; p=0.002). The population-based prescribing rates per 1,000 children <18 years of age has dramatically declined for erythromycin (−73% from 40 to 11; p<0.001) and slightly declined for SMX-TMP (−16% from 64 to 54; p=0.007) (Fig. 2). Rates for azithromycin/clarithromycin have not changed significantly since first prescribed in 1996 (+120% from 15 to 33; p=0.820).

Table 1. Population and visit-based prescribing rates AN/Al children <18 yrs of age in Anchorage, Alaska.

| Year | Population-based prescribing rates (per 1,000 persons) | Visit-based prescribing rates (per 1,000 patient-based visits) |
|------|-------------------------------------------------------|-------------------------------------------------------------|
| 1992 | 309                                                   | 101                                                         |
| 1993 | 400                                                   | 126                                                         |
| 1994 | 409                                                   | 122                                                         |
| 1995 | 443                                                   | 123                                                         |
| 1996 | 403                                                   | 120                                                         |
| 1997 | 441                                                   | 115                                                         |
| 1998 | 523                                                   | 118                                                         |
| 1999 | 577                                                   | 135                                                         |
| 2000 | 618                                                   | 130                                                         |
| 2001 | 606                                                   | 114                                                         |
| 2002 | 605                                                   | 146                                                         |
| 2003 | 560                                                   | 119                                                         |
| 2004 | 524                                                   | 109                                                         |
| Trend | p<0.001                                              | p=0.651                                                     |

Figure 2. Population-based prescribing rate for AI/AN persons <18 years of age by antibiotic class, Anchorage, Alaska.
Children <5 years of age
The annual population-based rate of antimicrobial prescribing increased 48% from 687 to 1,015 antimicrobial prescriptions per 1,000 persons (p=0.005) over the 13-year study period. The population-based prescribing rates per 1,000 children <5 years of age have increased for cephalosporins (+93% from 71 to 137; p=0.003) and penicillins (+129% from 302 to 693; p<0.001). Use of azithromycin/clarithromycin has not changed significantly since first prescribed in 1996 (+70% from 27 to 46; p=0.750). Prescribing rates have declined for erythromycin (−92% from 101 to 8; p<0.001) and SMX-TMP (−47% from 211 to 111; p<0.001). There was minimal use of the fluoroquinolones and tetracyclines in the <5 year age group.

Children 5–17 years of age
The annual population-based rate of antimicrobial prescribing increased 97% from 183 to 361 antimicrobial prescriptions per 1,000 persons (p<0.001) over the 13-year study period. The population-based prescribing rates per 1,000 children 5–17 years of age have increased in the following classes: cephalosporins (+138% from 24 to 57; p<0.001), penicillins (+69% from 110 to 186; p<0.001), tetracyclines (+122% from 9 to 20; p=0.002) and SMX-TMP (+133% from 15 to 35; p=0.017). Rates declined for erythromycin (−37% from 19 to 12; p=0.043). Rates of azithromycin/clarithromycin prescription have not changed significantly (+164% from 11 to 29; p=0.296 since 1996). There was minimal use of the fluoroquinolones and tetracyclines in this age group.

Visit-based prescribing rates
Children <18 years of age
The annual visit-based rate of antimicrobial prescribing remained relatively constant over the study period (p=0.651) over the study period (Table I). Visit-based prescribing rates per 1,000 visits for children <18 years of age have increased in the following classes from 1992 to 2004: fluoroquinolones (>500% from 0.02 to 1.25; p<0.001), cephalosporins (+33% from 12 to 16; p=0.023) and tetracyclines (+41% from 2.2 to 3.1; p=0.043). Rates for prescribing of penicillins (+27% from 51 to 65, p=0.210) and azithromycin/clarithromycin since 1996 (+55% from 4.4 to 6.8; p=0.343) have risen, but not significantly. A decrease in visit-based prescribing rates has occurred in the following classes: erythromycin (−82% from 12.9 to 2.3; p<0.001) and SMX-TMP (−48% from 21 to 11; p<0.001) (Fig. 3).

Children <5 years of age
The annual visit-based rate of antimicrobial prescribing remained relatively constant over the study period (p=0.100). The visit-based prescribing patterns in children <5 years of age are similar to those for children <18 years of age, with the exception of much lower fluoroquinolone and tetracycline use (Fig. 4). Visit-based prescribing rates per 1,000 visits for children <5 years of age have shown non-significant increases in the following classes from 1992 to 2004: cephalosporins (+17% from 10.2 to 11.9; p=0.071), penicillins (+38% from 43.3 to 59.7; p=0.124) and azithromycin/clarithromycin (+13% from 3.52 to 3.99; p=0.156 since 1996). A decrease in visit-based prescribing rates has occurred in the following classes: erythromycin (−96% from 14.5 to 0.6; p<0.001) and SMX-TMP (−68% from 30.2 to 9.6; p<0.001). There was minimal use of fluoroquinolones and tetracyclines in this group.
**Children 5–17 years of age**

The annual visit-based rate of antimicrobial prescribing per 1,000 visits has increased in the following classes: cephalosporins (+64% from 13.7 to 22.5; \(p=0.009\)), fluoroquinolones (>500% from 0.05 to 1.89; \(p<0.001\)) and tetracyclines (+51% from 5.13 to 7.75; \(p=0.030\)). Rates of prescribing of azithromycin/clarithromycin since 1996 (95% from 5.7 to 11.1; \(p=0.911\)), penicillins (+17% from 61.8 to 72.6; \(p=0.390\)) and SMX-TMP (+64% from 8.4 to 13.8; \(p=0.816\)) did not show significant changes. A decrease in visit-based prescribing rates has occurred with erythromycin (~56% from 10.8 to 4.7; \(p<0.001\)).
**DISCUSSION**

In this study, we determined that from 1992 to 2004, the annual number of antimicrobials prescribed in outpatient clinics at ANMC doubled and population-based prescribing rates rose; however, visit-based prescribing rates remained constant. We also observed that while penicillins remained the most widely used class of antimicrobials in the outpatient setting, visit-based antimicrobial prescribing rates over the study period increased for fluoroquinolones, tetracyclines and cephalosporins (with increasing use of second and third generation cephalosporins) while prescribing rates for erythromycin and SMX-TMP declined.

The overall population-based prescribing rate increased 70% over the 13-year study period. The population-based prescribing rate, which indicates the number of antimicrobials prescribed per AI/AN child in the Anchorage region at ANMC, is likely an underestimation, since not all AI/AN persons receive care at ANMC and the denominator represents the entire AI/AN population in the Anchorage region. Elevated population-based prescribing rates may in part be explained by the fact that a new ANMC facility (including outpatient clinics) opened in 1997. Prior to 1997, ANMC was located in a much smaller facility in Anchorage. This may have resulted in an increase in the total number of antimicrobials prescribed as the number of clinic visits rose from 1998 onward, while the AI/AN population of the Anchorage region remained fairly stable over the same time period. Because of these limitations, we believe that visit-based rates are a better measure to monitor trends in prescribing behaviour over time.

The spike in visit-based rates in 2002 is primarily a function of a decrease in the reported denominator of visits from that year, rather than an increase in antibiotic prescriptions. When comparing the visit-based antimicrobial prescribing rate for AI/AN persons residing in the Anchorage region receiving care at ANMC (range 101–146) to the U.S. rate (range 250–340), we see the U.S. rate declining while the Anchorage region rate for AI/AN persons receiving care at ANMC remains constant. Comparing the magnitude of the rates between AI/AN persons residing in the Anchorage region receiving care at ANMC and the rest of the U.S. may be difficult due to some differences in methodology. In our study, we included a greater number of categories under the term “ambulatory clinic” than did the U.S. study. In addition, the number of ambulatory care visits for AI/AN persons (denominator for visit-based rates for Alaska Native persons) may be high relative to the number of ambulatory care visits for children in the U.S. (denominator for U.S. visit-based rates). AI/AN patients may seek health care more often, because health care services are pre-paid based on a compact with the U.S. federal government.

In our study, we found that the majority of the antimicrobials being dispensed were penicillins, followed by cephalosporins and SMX-TMP. When comparing the antimicrobial classes individually, we see that the penicillin population-based and visit-based rates are far higher than the other classes; however, among children <18 years of age, the only antimicrobials that demonstrated statistically significant increases in regards to visit-based prescribing rates were the fluoroquinolones, cephalosporins (with increasing use of second
and third generation cephalosporins) and tetracyclines. This is consistent with recent studies performed in pediatric populations that demonstrate significant increases in the use of penicillins (amoxicillin-clavulanate) and second- and third-generation cephalosporins (17).

There were several limitations to the study. Data were only reviewed from one hospital facility in Alaska and therefore may not be generalized to the rest of the state. AI/AN patients who chose to receive their care at other hospitals outside of ANMC were not included. Diagnosis codes were unavailable; therefore, we were unable both to determine rates of antimicrobial prescriptions for specific diagnoses and to look at the type of antimicrobial class used for specific diagnoses. When comparing our data to the U.S. data, we evaluated different age groups (<15 for U.S. vs. <18 years of age for Alaska), different clinic categories and different visiting rates (17). In addition, no more than 2 antibiotics could be reviewed per patient per visit.

Antimicrobial resistance is now a global public health problem. It is promoted by antimicrobial use and the greater the usage, the greater the selective pressure for the emergence of resistant bacteria (18). In this study, we documented visit-based antibiotic prescribing rates for AI/AN children <18 years of age residing in the Anchorage region receiving care at ANMC and determined these rates have been stable over a 13-year period. Although a trend in decreased antibiotic prescribing has been seen in the general U.S. population, prescribing rates in our area have not decreased but remained below those of the overall U.S. rate. This study represents the use of administrative data for prescrip-

**Conflict of interest**

Anne Marie Bott, PharmD, BCPS is employed by the Alaska Native Medical Center. Michael G Bruce, MD, MPH, Thomas W Hennessy, MD, MPH and Lisa Bulkow, MS are employed by the Centers for Disease Control and Prevention. John Coleman, PharmD is employed by the Indian Health Service. In-kind financial support from the Centers for Disease Control and Prevention has been provided.

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