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ORIGINAL ARTICLE

High Rates of Prescribing Antimicrobials for Prophylaxis in Children and Neonates: Results From the Antibiotic Resistance and Prescribing in European Children Point Prevalence Survey

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Background. This study was conducted to assess the variation in prescription practices for systemic antimicrobial agents used for prophylaxis among pediatric patients hospitalized in 41 countries worldwide.

Methods. Using the standardized Antibiotic Resistance and Prescribing in European Children Point Prevalence Survey protocol, a cross-sectional point-prevalence survey was conducted at 226 pediatric hospitals in 41 countries from October 1 to November 30, 2012.

Results. Overall, 17 693 pediatric patients were surveyed and 36.7% of them received antibiotics (n = 6499). Of 6818 inpatient children, 2242 (32.9%) received at least 1 antimicrobial for prophylactic use. Of 11 899 prescriptions for antimicrobials, 3400 (28.6%) were provided for prophylactic use. Prophylaxis for medical diseases was the indication in 73.4% of cases (2495 of 3400), whereas 26.6% of prescriptions were for surgical diseases (905 of 3400). In approximately half the cases (48.7% [1656 of 3400]), a combination of 2 or more antimicrobials was prescribed. The use of broad-spectrum antibiotics (BSAs), which included tetracyclines, macrolides, lincosamides, and sulfonamides/trimethoprim, was high (51.8% [1761 of 3400]). Broad-spectrum antibiotic use for medical prophylaxis was more common in Asia (risk ratio [RR], 1.322; 95% confidence interval [CI], 1.202–1.653) and more restricted in Australia (RR, 0.619; 95% CI, 0.521–0.736). Prescription of BSA for surgical prophylaxis also varied according to United Nations region. Finally, a high percentage of surgical patients (79.7% [721 of 905]) received their prophylaxis for longer than 1 day.

Conclusions. A high proportion of hospitalized children received prophylactic BSAs. This represents a clear target for quality improvement. Collectively speaking, it is critical to reduce total prophylactic prescribing, BSA use, and prolonged prescription.

Key Words: antimicrobials; inpatients; pediatrics; point-prevalence survey; prophylactic prescribing.

Antimicrobial agents are among the most commonly prescribed medications, especially for children and neonates. Although the appropriate selection and administration of antibiotics certainly saves lives, their widespread overuse—especially of broad-spectrum antibiotics—has also contributed to significant increases in antimicrobial resistance [1, 2]. Therefore, pediatric-specific antibiotic stewardship programs are urgently needed [3]. These programs must specifically address the substantial differences that exist between children and adults [4].

Prophylactic use of antibiotics to prevent infections is contentious. National guidelines emphasizing short duration and focused use already exist for surgical prophylaxis [5, 6]. Because pediatric-specific surgical prophylaxis data are sparse, pediatric recommendations have been extrapolated from adult data [5, 6]. Guidelines for medical antibiotic prophylaxis can only be found for a few specific medical conditions, such as congenital heart anomalies, vesicoureteral reflux, acute rheumatic fever, asplenia and sickle cell disease, meningococcal and pertussis exposure, *Pneumocystis* pneumonia prophylaxis, and latent tuberculosis infection [7]. To date, data on which children receive antimicrobial prophylaxis and why they do have not been available. Cross-sectional point-prevalence surveys (PPS) are a validated method for analyzing data on antimicrobial usage and for determining quality indicators [8, 9]. We analyzed data on prophylactic antibiotic prescribing from the Antibiotic Resistance and Prescribing in European Children (ARPEC) project [8], a multicenter, cross-sectional study investigating prescription variations for systemic antimicrobial agents at 226 pediatric hospitals in 41 countries worldwide [10].

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METHODS

Data Source and Study Population

Data were extracted from the global ARPEC internet-based PPS, which was performed between October 1 and November 30, 2012, at 226 pediatric hospitals in 41 countries worldwide [10]. The study included all children who were hospitalized and received at least 1 antimicrobial for prophylactic indications on the day of the survey.

Data Collection

The cross-sectional, hospital-based PPS used the standardized ARPEC-PPS protocol, which consisted of 2 sets of data collection forms: one for patients on pediatric wards and a second for infants on neonatal wards [8, 10]. Participating hospitals were asked to conduct a 1-day PPS during a regular working day during October–November 2012. To capture meaningful information about antimicrobial prophylaxis from the previous 24-hour period, pediatric surgical wards were not audited on Mondays. This included all children under 18 years old who had been admitted before midnight the previous day and were still present in hospital at 8:00 AM on the day of the survey. The surveillance mainly focused on systemic antimicrobial agents, but it also included antibiotics and other antimicrobials used as intestinal anti-infectives (following the Anatomical Therapeutic Chemical classification system) [11]. This included antibacterials for systemic use, antibiotics used for treatment of tuberculosis or leprosy, antibiotics used as intestinal anti-infectives, nitroimidazole derivates, antifungals, antivirals for systemic use, and antimalarials [10]. The following antibiotics were arbitrarily classified as broad-spectrum: tetracyclines, penicillins with extended spectrum (eg, piperacillin ± tazobactam, ticarcillin + clavulanic acid); second-, third-, and fourth-generation cephalosporins; carbapenems; sulfonamides and trimethoprim; macrolides; lincosamides; aminoglycosides; and fluoroquinolones and polymixins. We classified carbapenems, fluoroquinolones, and glycopeptides as reserve antibiotics. In addition to the antimicrobial agents (name, application route, dose per administration, number of doses per day), the following information was collected: patient age, gender, current weight, underlying diagnoses, and type of prophylaxis. Two types of prophylaxes were distinguished: surgical and medical. In addition, the duration of surgical prophylaxis was categorized as single dose, equal to 24 hours or else greater than 24 hours. All data were collected anonymously [8]. Countries were classified according to the United Nations Standard Country and Area Codes [12].

Data Analysis

Anonymous patient data were collected on paper forms, and then all data were mandatorily entered using a web-based system for data collection, validation, and reporting. For statistical analysis, GraphPad Prism version 6 (GraphPad Software, La Jolla, CA) was used. A patient-level analysis focused on the use of prophylactic antimicrobials. Results were expressed as a percentage of the total number of patients treated. Proportional differences were compared using either a χ^2 test or a Fisher's exact test, as appropriate. Prophylactic prescribing in Europe was used as the comparison point. All statistical tests were 2-tailed and considered significant if the P value was <.05. Data regarding prophylactic prescriptions in African and Eastern European hospitals were excluded from statistical analysis, either because the number of prescriptions was too low to provide for meaningful data interpretation (Africa) or because data on prophylactic prescribing were not reported (Eastern Europe).

RESULTS

Study Population and Antimicrobial Rate

Prophylactic antimicrobial prescribing practices were evaluated for 17 693 surveyed children and infants hospitalized at 226 hospitals (H) in 41 countries (C) worldwide, including Europe (172H; 24C), Africa (6H; 4C), Asia (25H; 8C), Australia (6H), Latin America (11H; 3C), and North America (4H; 1C [all from the United States]) [10]. In Europe, there was overrepresentation (ie, >50%) of hospitals and patients from the United Kingdom (65H) [10]. Overall, 6818 hospitalized children and neonates received 11 899 antimicrobial prescriptions, among whom 2242 patients (32.9%) received at least 1 antimicrobial for prophylactic use. Rates for prophylactic antimicrobial prescribing in children ≥30 days of age were 70.4% for medical prophylaxis (corresponding to 19.9% of all antimicrobial prescriptions) and 29.6% (or 8.3% of all antimicrobials) for surgical prophylaxis. In neonates <30 days of age, the rates were 83.5% (or 24.9% of all antimicrobials) and 16.5% (or 4.9% of all antimicrobials) (Table 1). Systemic antibiotics were prescribed in 36.7% of all patients surveyed (6499 of 17 693) [10].

Therapeutic Versus Prophylactic Antimicrobial Use

Antimicrobials were provided for therapeutic use in 70.7% of prescriptions (8408 of 11 899), whereas 28.6% (3400 of 11 899) were for prophylactic use and 0.8% of indications were reported to be unknown (n = 91). Of the 3400 prescriptions for prophylactic use, 2482 were given to children ≥30 days of age and 918 were given to neonates <30 days of age. Prophylaxis for medical diseases was the indication in 73.4% of cases (2495 of 3400), whereas one quarter of prescriptions were for surgical diseases (26.6% [905 of 3400]; Table 1). Prescribing for medical prophylaxis was significantly higher in infants <30 days of age. In addition, children from Western Europe, Australia, and North America received more antimicrobials for medical prophylaxis compared with children from northern Europe, southern Europe, Asia, and Latin America (Table 1). Except for patients in Africa, in over 90% of cases, the antimicrobial selection was empiric.

The administration route for antimicrobial prophylaxis was parenteral in 46.6% of prescriptions (1583 of 3400) and oral in 52.6% (1790 of 3400). A single antimicrobial agent was given

Table 1. Prophylactic Antimicrobial Prescriptions by Indication, Type of Treatment, and UN Region

	Antimicrobial Prescription	Prophylactic Use									
	All	Medical		RR (χ^2)	Surgical		RR (χ^2)	Empiric		Targeted	
Region	No.	No.	%	(95% CI)	No.	%	(95% CI)	No.	%	No.	%
Europe	7142	1562	21.9	**1.000**	528	7.4	**1.000**	1960	93.8	130	6.2
Eastern Europe	150	24	16.0	n.s.	0	0	n.d.	24	100	0	0
Northern Europe	2802	537	19.2	0.812 (0.739–0891)	150	5.4	0.615 (0.512–0.738)	639	93.0	48	7.0
Southern Europe	2306	438	19.0	0.817 (0.740–0.902)	261	11.3	2.050 (1.741–2.414)	670	95.6	29	4.1
Western Europe	1884	563	29.9	1.573 (1.439–1.719)	117	6.2	0.795 (0.651–0.969)	627	92.2	53	7.8
Africa	900	55	6.1	n.d.	9	1.0	n.d.	28	43.8	36	56.3
Asia	1635	298	18.2	0.833 (0.745–0.932)	196	12.0	1.622 (1.389–1.893)	447	90.5	47	9.5
Australia	839	278	33.1	1.515 (1.363–1.684)	66	7.9	n.s.	340	98.8	4	1.2
Latin America	74	115	15.5	0.707 (0.594–0.841)	52	7.0	n.s.	155	92.8	12	7.2
North America	639	187	29.3	1.338 (1.177–1.521)	54	8.5	n.s.	235	97.5	6	2.5
Children ≥30 days of age	9327	1854	19.9	**1.000**	778	8.3	**1.000**	2446	92.9	186	7.1
Infants <30 days of age	2572	641	24.9	1.254 (1.159–1.356)	127	4.9	0.592 (0.493–0.711)	719	93.6	49	6.4
Grand Total	**11 899**	**2495**	**21.0**		**905**	**7.6**		**3165**	**93.1**	**235**	**6.9**

Abbreviations: CI, confidence interval; n.d., not done; n.s., nonsignificant; RR, risk ratio (comparison point in bold); UN, United Nations.

for prophylactic purposes in 63.3% of patients (1420 of 2242), a combination of 2 antimicrobials in 25.7% (576 of 2242), and 3 or more agents in 11.0% (246 of 2242). A combination of 2 or more antimicrobials was more commonly prescribed in medical prophylaxis (38.9% [615 of 1582]) than in surgical prophylaxis (28.8% [183 of 636]; risk ratio [RR], 1.391; 95% confidence interval [CI], 1.199–1.613).

Indications and Types of Antimicrobial Prophylaxis

Our survey did not specifically collect data regarding the reason for medical prophylaxis. However, it did gather information about patients' underlying diseases.

For children ≥30 days of age receiving a prophylactic prescription, the most common underlying disease was oncological (33.0% [536 of 1623]), surgical (19.5% [316 of 1623]), and/or related to a chronic heart condition (6.6% [107 of 1623]). In 12.5% (203 of 1623) of children ≥30 days of age, there was no underlying disease. The 2 most common indications for antimicrobial prophylaxis in children ≥30 days of age were prophylaxis for medical problems (910 of 1623 [56.1%]) and prophylaxis for surgical disease (466 of 1623 [28.7%]).

In infants <30 days of age, the 3 most common underlying conditions were respiratory distress (22.3% [138 of 619]), premature rupture of membranes (17.8% [110 of 619]), and surgical disease (12.0% [74 of 619]). In 14.2% (88 of 619) of infants <30 days of age, no underlying disease was present. Four indications accounted for >80% of antimicrobial prophylaxis in infants <30 days of age; namely, medical prophylaxis (29.2% [181 of 619]), prophylaxis for neonatal risk factors (27.9% [173 of 619]), prophylaxis for maternal risk factors (16.2% [100 of 619]), and surgical prophylaxis (11.0% [68 of 619]).

Antimicrobials Used for Medical Prophylaxis in Children ≥30 Days of Age

The 3 most common classes of antimicrobials for medical prophylaxis in children ≥30 days of age were trimethoprim/sulfonamides, antifungals, and antivirals (Figure 1). Together, these accounted for two thirds (1233 of 1854 [66.5%]) of all prescriptions for medical prophylaxis. In children ≥30 days of age, 1130 antibiotic prescriptions were written for medical prophylaxis. The 3 most common antibiotic classes for systemic use were trimethoprim/sulfonamides (532 of 1130 [47.1%]), narrow-spectrum penicillins (148 of 1130 [13.1%]), and macrolides/lincosamides (99 of 1130 [8.8%]). Fewer trimethoprim/sulfonamides were prescribed in Asia (RR, 0.725; 95% CI, 0.530–0.992) and Latin America (RR, 0.599; 95% CI, 0.370–0.969). Prescriptions of narrow-spectrum penicillins had an equal distribution globally. Within Northern Europe, the rate was higher than the rest of Europe (RR, 2.221; 95% CI, 1.507–3.272). Macrolides and lincosamides were administered considerably more often to patients in North America (RR, 3.873; 95% CI, 2.516–5.963). Notably, in Northern Europe, this antibacterial class was more commonly used (RR, 5.744; 95% CI, 3.144–10.49). In Asia, significantly more third- or fourth-generation cephalosporins were prescribed (RR, 5.478; 95% CI, 3.078–9.747), as well as carbapenems (RR, 10.55; 95% CI, 2.383–46.69) and glycopeptides/linezolid (RR, 5.539; 95% CI, 2.140–14.33).

Prescription of broad-spectrum and reserve antibiotics for medical prophylaxis varied according to region (Table 2). In Southern Europe and Asia, broad-spectrum antibiotics were prescribed significantly more often (as were reserve antibiotics in Asia), whereas in Australia, their use was more restricted (as were reserve antibiotics in Western Europe; Table 2).

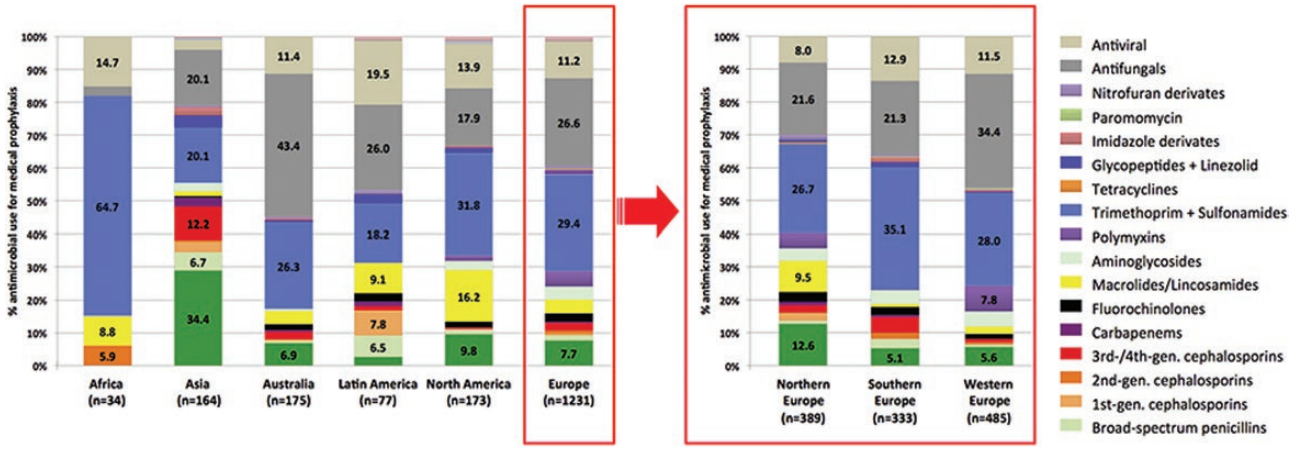

Figure 1. Proportion (%) of children ≥30 days of age with antimicrobial agents for medical prophylactic use (ATC4 level) by United Nations region (numbers of proportions >5% are shown in the graphs).

Antimicrobials Used for Surgical Prophylaxis

One quarter of all antimicrobial prophylactic prescriptions were for surgical prophylaxis (905 of 2495 [26.6%]; Table 1). The 4 most common classes of antimicrobials for surgical prophylaxis in children ≥30 days of age were first-generation cephalosporins, narrow-spectrum penicillins, second-generation cephalosporins, and third- or fourth-generation cephalosporins (Figure 2A). Together, these accounted for two thirds (509 of 778 [65.4%]) of all prescriptions for surgical prophylaxis. Overall, the most frequently prescribed class of antibiotics for surgical prophylaxis was first-generation cephalosporins (140 of 761 [18.4%]). This was particularly true for hospitals in North America (RR, 5.929; 95% CI, 4.154–8.463) and Australia (RR, 5.536; 95% CI, 3.839–7.982). Narrow-spectrum penicillins were more commonly prescribed in Northern Europe (RR, 2.721; 95% CI, 1.933–3.830). Second-generation cephalosporins were more frequently used in Western Europe (RR, 1.681; 95% CI, 1.123–2.514). In Asia, more children received third- or fourth-generation cephalosporins (RR, 1.881; 95% CI, 1.348–2.626) and fluoroquinolons (RR, 17.19; 95% CI, 2.085–141.7).

Prescription of broad-spectrum and reserve antibiotics for surgical prophylaxis was high (55.0%; Table 2) and varied according to region (Table 2). Broad-spectrum antibiotics were less frequently used in Northern Europe, Australia, and North America, whereas they were more commonly prescribed in Asia and Western Europe (Table 2). The only region with an increased use of reserve antibiotics for surgical prophylaxis was Southern Europe. Meanwhile, its use in Northern Europe was limited (Table 2).

Table 2. Prophylactic Broad-Spectrum and Reserve Antibiotic Use by Indication and UN Region

	Medical Prophylactic Use						Surgical Prophylactic Use					
	Broad-Spectrum Antibiotics		RR (χ^2 Test) and	Reserve Antibiotics		RR (χ^2 Test) and	Broad-Spectrum Antibiotics		RR (χ^2) and	Reserve Antibiotics		RR (χ^2 Test) and
Region	No.	%	95% CI	No.	%	95% CI	No.	%	95% CI	No.	%	95% CI
Europe	785	50.3	**1.000**	58	3.7	**1.000**	299	56.5	**1.000**	83	15.7	**1.000**
Eastern Europe	9	37.5	n.d.	4	16.7	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Northern Europe	263	49.0	n.s.	19	3.5	n.s.	62	41.3	0.659 (0.537–0.810)	9	6.0	0.307 (0158-0594)
Southern Europe	244	55.7	1.157 (1.044–1.287)	22	5.0	n.s.	155	59.2	n.s.	55	21.0	2.009 (1.318–3.064)
Western Europe	269	47.8	n.s.	13	2.3	0.513 (0.279–0.942)	82	70.1	1.327 (1.143–1.542)	19	16.2	n.s.
Africa	28	50.9	n.d.	0	0	n.d.	5	55.6	n.d.	0	0	n.d.
Asia	192	64.4	1.282 (1.163–1.414)	21	7.0	1.898 (1.170–3.078)	137	69.9	1.234 (1.096–1.389)	23	11.7	n.s.
Australia	91	32.7	0.651 (0.546–0.776)	5	1.8	n.s.	21	31.8	0.562 (0.392–0.806)	5	7.6	n.s.
Latin America	60	52.2	n.s.	6	5.2	n.s.	21	41.2	n.s.	3	5.9	n.s.
North America	107	57.2	n.s.	6	3.2	n.s.	15	27.8	0.491 (0.317–0.759)	4	7.4	n.s.
Grand Total	**1263**	**50.6**		**96**	**3.8**		**498**	**55.0**		**118**	**13.0**	

Abbreviations: CI, confidence interval; n.d., not done; n.s., nonsignificant; RR, risk ratio ([in bold] in comparison to Europe); UN, United Nations.

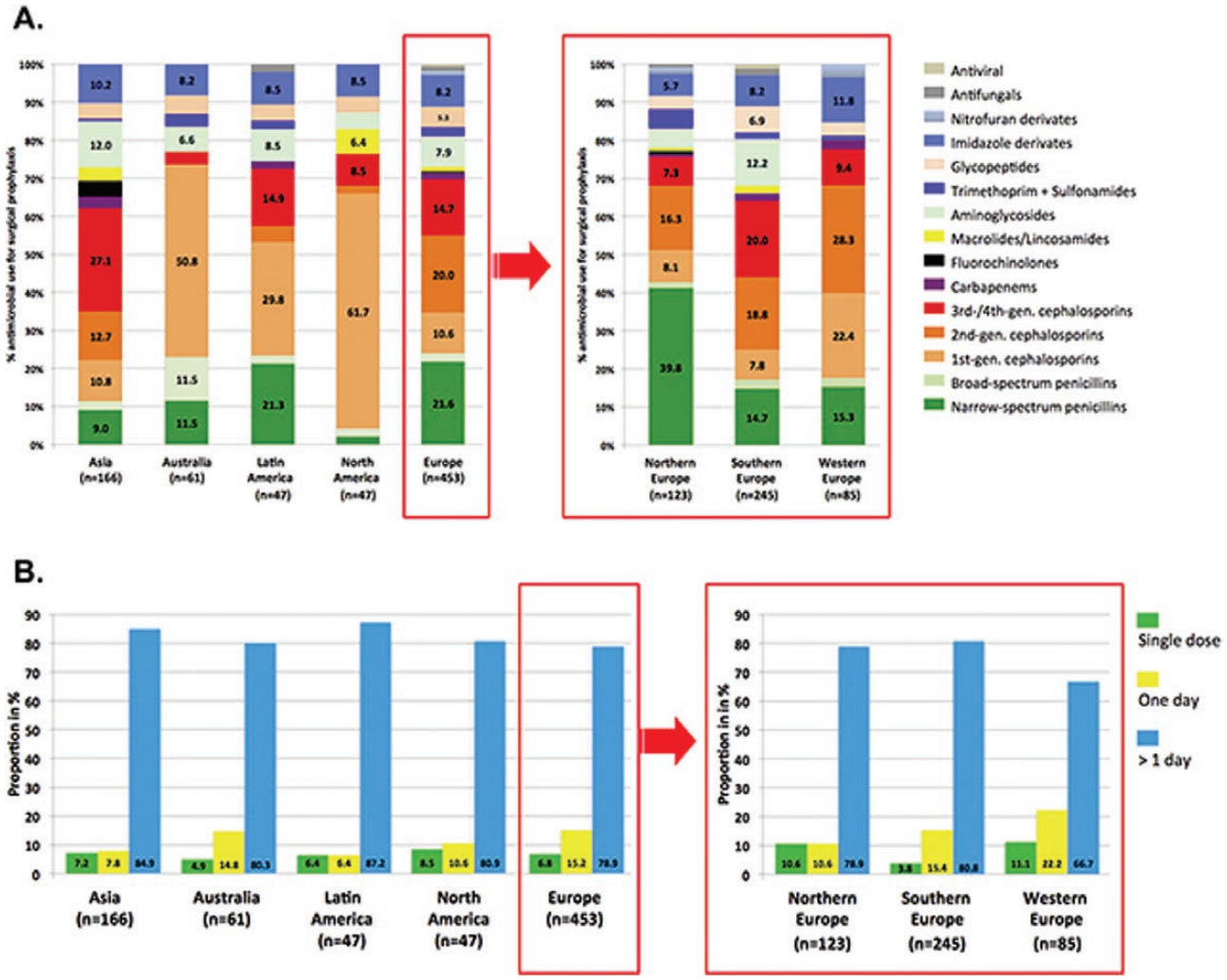

Figure 2. (A) Proportion (%) of children ≥30 days of age with antimicrobial agents for surgical prophylactic use (ATC4 level) by United Nations (UN) region (numbers of proportions >5% are shown in the graph). (B) Proportion (%) of children ≥30 days of age with surgical prophylactic use by duration and UN region.

The 4 most common classes of antimicrobials for surgical prophylaxis in infants <30 days were aminoglycosides, narrow-spectrum penicillins, imidazole derivates, and glycopeptides (Figure 3A). Together, these accounted for 69.3% (88 of 127) of all surgical prophylaxis prescriptions. Overall, the most frequently prescribed class of antibiotics for surgical prophylaxis was aminoglycosides and narrow-spectrum penicillins (28 of 127 [22.0%] each). For glycopeptides, prescription was the highest in European hospitals (RR, 2.474; 95% CI, 1.020–5.999). Within Europe, narrow-spectrum penicillins were used only in Northern Europe ($P < .0001$ [no RR or CI]). In North America, more children received first-generation cephalosporins (RR, 6.324; 95% CI, 2.696–14.83).

Duration of Surgical Antibiotic Prophylaxis

In the vast majority of cases, surgical prophylaxis was given for longer than 1 day. In children ≥30 days of age, 80.1% of cases (623 of 778; range, 68.2%–87.2%) received prophylaxis for over 24 hours (Figure 2B). A single dose was administered only in a small minority of cases (6.8% [range, 3.7%–10.6%]). A similar prescription pattern was observed among infants <30 days of age (Figure 3B). In 80.0% of these cases (99 of 127), surgical prophylaxis was given for more than 1 day.

DISCUSSION

This cross-sectional survey represents the first assessment of antimicrobial prescription practices for prophylaxis in pediatric patients hospitalized worldwide. The majority of prescriptions was for medical prophylaxis (73.4%), with only one quarter for surgical prophylaxis. This rate was even higher in infants <30 days of age (ie, 83.5%). Among those, the 3 main indications—medical prophylaxis, prophylaxis for neonatal risk factors, and prophylaxis for maternal risk factors—accounted for 73.3% of all prescriptions (data not shown). For half of the medical prophylaxis prescriptions in neonates (ie, 50.4%),

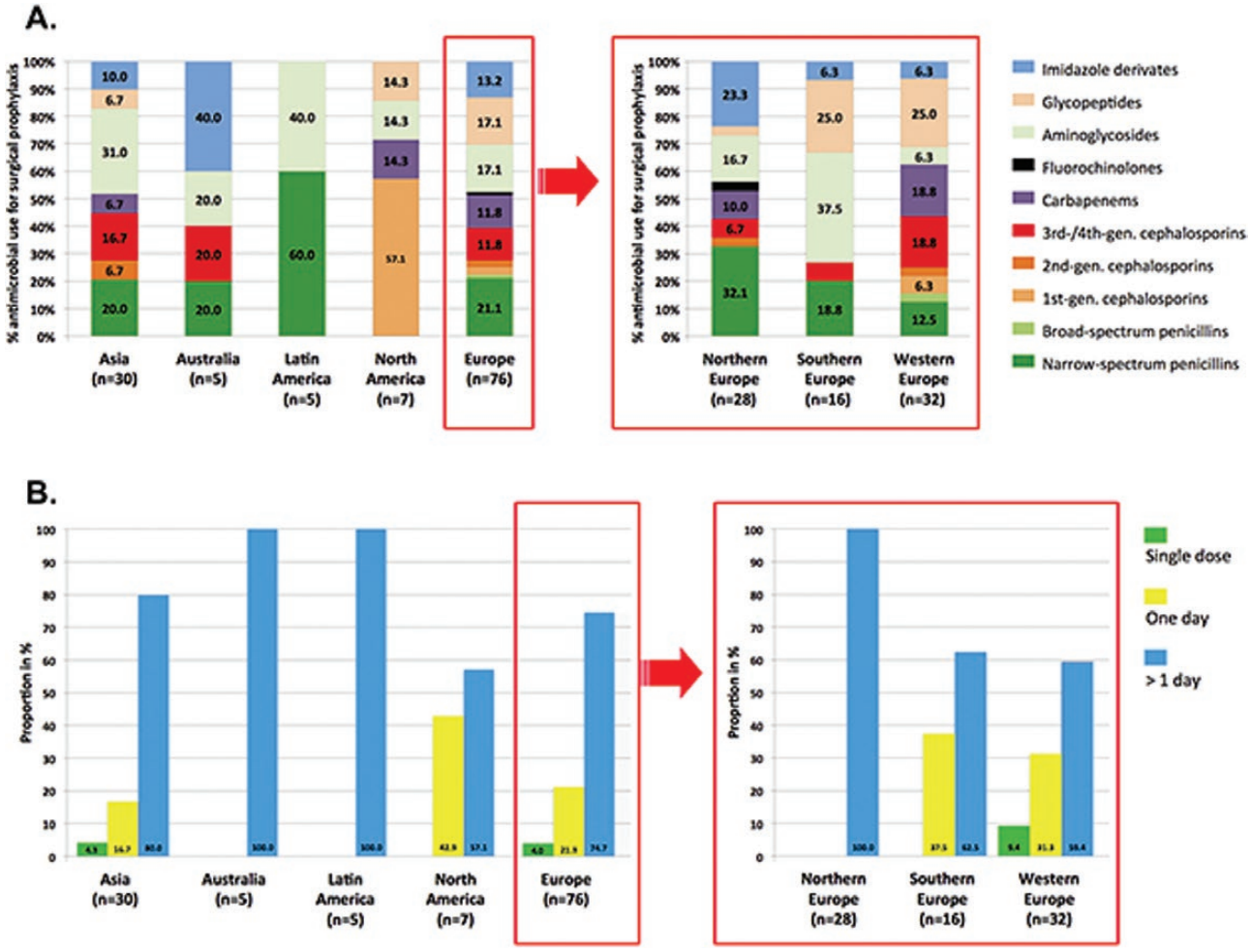

Figure 3. (A) Proportion (%) of infants <30 days of age with antimicrobial agents for surgical prophylactic use (ATC4 level) by United Nations (UN) region (numbers in proportions >5% are shown in the graph). (B) Proportion (%) of infants <30 days of age with surgical prophylactic use by duration and UN region.

broad-spectrum antibiotics were used (data not shown). Despite our study's lack of data regarding the specific indications for medical prophylaxis, this high rate cannot be considered evidence-based [13]. The high rate of prophylactic prescribing is similar to data shown by the 2008 European Surveillance of Antibiotic Consumption (ESAC) PPS study, which included 32 pediatric departments in 21 European countries and analyzed systemic antimicrobial prescriptions from 1799 children [14]. The ESAC study showed that in 171 cases, antimicrobials were given for prophylaxis [14], and in 66% of cases, a medical prophylaxis was the indication [14]. In our study, there was a higher prevalence of medical prophylaxis in Western Europe, Australia, and North America. This overrepresentation is likely due to the greater number of patients admitted to highly specialized tertiary-care pediatric hospitals that provide care to those with oncological or other complex underlying diseases [10]. Regarding medical prophylaxis, oncological diseases were the most common underlying conditions in children ≥30 days of age. These and other variations in practice among the regions may be explained by disparities among hospital care systems as well as by the patient case-mix in the different parts of the world [15]. In comparison to the ESAC PPS 2008 study, our study showed a lower rate of parenteral administration (46.6% vs 62.5% in 2008) [14]. More importantly, however, the ESAC PPS study reported route of administration at a patient level, whereas our data were based on a prescription level. For this reason, meaningful trends cannot be deduced from comparing the two. GARPEC (Global Antimicrobial Resistance, Prescribing, and Efficacy Among Neonates and Children) [16], the global follow-up study of ARPEC, will use the same PPS method. In the future, this will allow us to draw comparisons over time.

We have identified several key strategies for improving prophylactic prescription practices. The first performance indicator is the high rate of antimicrobial combination prescriptions. In 36.7% of cases, 2 or more systemic antimicrobials were administered. This result is in line with the 37.4% shown by the ESAC PPS 2008 study conducted among European hospitals only [14]. The high rate of combination therapy in our study

was observed for both medical (38.9%) and surgical prophylaxis (28.8%), with the latter percentage clearly indicating inappropriate usage. Multiple studies in adults have shown that antibiotic combinations do not provide additional coverage and do no result in lower rates of postoperative surgical site infections (SSIs) [5, 6]. According to a study by Tamma et al [17], even in pediatric patients with Gram-negative sepsis—a high-mortality disease—combination antibiotic therapy did not translate into a survival benefit. Both the ASHP report and World Health Organization (WHO)'s global guidelines state that for most surgical procedures, a single-agent regimen (eg, a first-generation cephalosporin) is the preferred option [5, 18]. In addition to the lack of clinical benefits offered by combination therapies, these therapies have numerous potential negative ramifications, including drug interactions, the need for drug monitoring, increased costs, and additional side effects.

The second quality indicator is the high rate of prophylactic broad-spectrum antibiotic prescribing worldwide. In our study, this accounted for half the cases of both medical and surgical prophylaxis. This prescription pattern was particularly notable in Asia (for both indications) and in Western Europe (for surgical prophylaxis). In Asia, colonization and infection rates with multiresistant organisms are the highest in the world—a fact that may explain the higher use of broad-spectrum antibiotics in this region [1]. Use of broad-spectrum antibiotics itself is associated with an increased risk of antimicrobial resistance [1]. This is particularly true for third- and fourth-generation cephalosporins as well as for fluoroquinolones [1].

The third performance indicator is the prolonged (>24 hour) duration of surgical prophylaxis. In our study, 80% of surgical patients—including infants <30 days as well as children ≥30 days of age—received surgical prophylaxis for >1 day. The new WHO guidelines on prevention of SSIs strongly recommend against prolonging surgical antibiotic prophylaxis (SAP) beyond a single dose due to the lack of benefit in reducing SSIs [18]. According to WHO, prolongation should only be considered in cardiac, vascular, and orthognatic surgery for a period of up to 24 hours. However, the quality of evidence demonstrating a beneficial effect is low to very low [18]. Unfortunately, our study protocol did not include questions about the type of surgery associated with SAP. Although extended therapy does not decrease the risk of postsurgical infections, its prolonged use is in fact associated with adverse events and antimicrobial resistance [19].

It is important to recognize limitations of our study. The study design is cross-sectional and provides a snapshot of antimicrobial prescribing practices at the hospital level. Participation was voluntary and the researcher did not receive payment. Both of these factors could lead to a participation bias whereby primarily highly motivated parties participated in the survey. However, how this bias might influence the observed rates is unclear. There are no generally accepted consensus definitions of medical prophylaxis. For this reason, definitions of prophylaxis were not preset in the study protocol. There is a clear overlap between medical prophylaxis for maternal or neonatal risk, early empiric therapy, and then prolonging antibiotic therapy in high-risk babies in settings with a very high prevalence of hospital-acquired infection. However, it is clear that a consensus definition of medical prophylaxis is needed for research purposes. Training of researchers collecting hospital data was not performed in person; rather, it was done by means of an online training tool, a frequently asked questions list, and a helpdesk. Therefore, data accountability cannot be independently validated. Nevertheless, data were subjected to inconsistency checking, with requests for clarification directed towards participating centers when needed. Despite the large number of patients included in the study, it should be noted that tertiary care hospitals were overrepresented. For this reason, the generalizability of the data for other types of pediatric hospitals cannot be guaranteed. Moreover, geographic regions outside Europe were underrepresented. Accordingly, findings are only representative for the hospitals captured. Finally, but crucially, we were hampered in our determination of whether or not antibiotic classes were used appropriately by the fact that indications for prophylaxis were not specifically collected with the survey.

Although acknowledging the above limitations, we nevertheless believe our study contains several unique strengths. The survey was global and hospitals from 41 countries participated. A large number of patients (3400 prescriptions for prophylaxis) were eligible and included in the current analysis. The study used a standardized protocol, which ensured uniformity of data and of conclusions to be drawn from it. Such a standardized method facilitates comparisons among hospitals and countries, while also paving the way for longitudinal analyses when the survey becomes repeated [16]. Therefore, the PPS method easily can be used to test the efficacy of interventions deployed for the purpose of improving prophylactic antimicrobial prescribing practices. Finally, the PPS method may provide a vital tool for initiating and evaluating interventions that are part of an antibiotic stewardship program. The survey method is inexpensive and therefore also feasible in resource-limited countries.

CONCLUSIONS

Our study is the first PPS on prescription practices for systemic antimicrobial agents used for surgical and medical prophylaxis for pediatric patients hospitalized worldwide, and it reveals several potential targets for quality improvements. We conclude that the following interventions are needed: (1) reduce the high rate of antimicrobial combination prescriptions, especially in medical prophylaxis; (2) limit the high rate of broad-spectrum antibiotic usage; and (3) combat the extended duration of surgical prophylaxis.

Notes

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