Intensive Care Med (2000) 26: 959–966

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Use of antibiotics in pediatric intensive care and potential savings

Received: 20 October 1999
Final revision received: 5 March 2000
Accepted: 17 March 2000

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Abstract *Objective:* Minimizing unwarranted prescription of antibiotics remains an important objective. Because of the heterogeneity between units regarding patient mix and other characteristics, site-specific targets for reduction must be identified. Here we present a model to address the issue by means of an observational cohort study.
Setting: A tertiary, multidisciplinary, neonatal, and pediatric intensive care unit of a university teaching hospital.
Patients: All newborns and children present in the unit (n = 456) between September 1998 and March 1999. Reasons for admission included postoperative care after cardiac surgery, major neonatal or pediatric surgery, severe trauma, and medical conditions requiring critical care.
Methods: Daily recording of antibiotics given and of indications for initiation. After discontinuation, each treatment episode was assessed as to the presence or absence of infection.
Results: Of the 456 patients 258 (56.6 %) received systemic antibiotics, amounting to 1815 exposure days (54.6 %) during 3322 hospitalization days. Of these, 512 (28 %) were prescribed as prophylaxis and 1303 for suspected infection. Treatment for suspected ventilator-associated pneumonia accounted for 616 (47 %) of 1303 treatment days and suspected sepsis for 255 days (20 %). Patients were classified as having no infection or viral infection during 552 (40 %) treatment days. The average weekly exposure rate in the unit varied considerably during the 29-week study period (range: 40–77/100 hospitalization days). Patient characteristics did not explain this variation.
Conclusion: In this unit the largest reduction in antibiotic treatment would result from measures assisting suspected ventilator-associated pneumonia to be ruled out and from curtailing extended prophylaxis.

Key words Antibiotics Utilisation · Pediatric intensive care · Ventilator-associated pneumonia

Introduction

Infections caused by multiresistant strains are a threat to critically ill patients worldwide [1, 2]. Prolonged antibiotic therapy is believed to contribute to the problem by exerting selective pressure on micro-organisms [3, 4]. Other sources for the occurrence of resistant strains are patients who already harbor such organisms when admitted to the pediatric intensive care unit [5]. Long-term patients are at increased risk of acquiring, harboring, and spreading resistant strains. This long-term selection process has probably facilitated the recent emergence of vancomycin-resistant staphylococci [6]. Resistance patterns appear not to be affected by simple substitution of one antibiotic by another as long as the overall exposure remains unaffected [7]. Thus the reduction in unnecessary antibiotic exposure within intensive care units remains an important objective [8]. Because

Table 1 Criteria for classification of episodes of suspected infection (references are given in parethesis)

Category	Definition	Outcome Classification				
		Proven systemic bacterial infection	Proven localized bacterial infection	Probable infection	Viral infection	Infection unlikely or absent
Microbiological evidence	Positive blood culture for known pathogen except S. epidermidis	positive	negative	negative	negative	negative
	Positive blood culture growing S. epidermidis	positive from two sites	negative	pos from one site	negative	pos from catheter
	Cultures from local site[1]	neg. or pos.	positive [9]	negative	negative	negative
	Viral culture or viral antigen test	–	–	–	positive	–
Clinical suspicion	Physicians explicit statement in the patient's charts	yes	yes	yes	yes	yes
	Diagnostic workup performed[2]	yes	yes	yes	yes	yes
	Prescription[3]	yes	yes	yes	–	–
Objective clinical evidence [10–11]	Thermal instability or fever Tachypnea/Dyspnea or increased ventilator settings Increased rate of apnea or desaturation Recurrent bradycardia (neonates) Pallor, cold limbs or delayed capillary refill time Arterial hypotension Enteral feeding intolerance Seizures or alteration of mental state Acidosis (pH < 7.25, BE < – 10 mmol/l)	Two or more symptoms or signs and absence of any reasonable alternative explanation	At least one of the symptoms or signs, additional signs of localized process and absence of any reasonable alternative explanation	Two or more symptoms or signs and absence of any reasonable alternative explanation	Clinical signs compatible with infection from isolated virus or antigen	Reasonable alternative explanation for symptoms or signs
Laboratory evidence [12]	WBS[4] outside age appropriate reference range [12], older infants: WBC < 5×10^9/L or > 15×10^9/L or increased immature to total neutrophil ratio (> 0.3) or otherwise unexplained thrombocytopenia < 100×10^9/L or plasma level of CRP[5] > 20 mg/l [13]	Two or more signs and absence of any reasonable alternative explanation	Two or more signs and absence of any reasonable alternative explanation	Two or more signs and absence of any reasonable alternative explanation	Less than two signs	Less than two signs
Radiological evidence	Chest X-ray: new consolidation persisting for more than 48 hours [9] CT-scan for identification of focus of infection	–	positive in pneumonia positive if performed	–	–	–

[1] Tracheal aspirate (predominantly one pathogen) (9) or positive urine culture > 106 pathogens/ml or positive culture from normally sterile compartment or positive wound swab in the presence of purulent discharge (10)

[2] A diagnostic sepsis workup comprises blood-cultures, differential WBC, C-reactive protein and physical examination

[3] Prescription of antibiotics other than guideline-directed prophylaxis or increase or change in current medication not indicated by cultures

[4] WBC = white blood cell count [5] CRP = C-reactive protein

of the substantial heterogeneity in resistance patterns, indications for treatment, and reasons for admissions between pediatric intensive care units site-specific targets for potential reduction need to be identified.

To identify targets for potential reduction, it is necessary to monitor antibiotic utilization and relate prescription patterns to indications for treatment, to the outcome of treatment episodes, and to relevant site specific issues such as patient characteristics. We undertook the present observational study as a model to survey the use of antibiotics in neonatal or pediatric intensive care units with the aim of providing an empirical database for future policy changes.

Methods

Patient population

All patients were eligible for inclusion who were admitted to or were present in the level III multidisciplinary neonatal and pediatric intensive care unit between 1 September 1998 and 30 March

1999. During this period 456 patients were admitted (204 girls, 252 boys; median age 0.78 years, mean 3.2 ± 4.6), most of whom (75.9%) were discharged within 1 week. The 45 newborns and children (10% of admissions) who remained in the unit longer than 2 weeks accounted for 1653 of all hospitalization days (49.8%). Further characteristics of the study population are presented in Table 2.

The 19-bed pediatric intensive care unit is the tertiary referral center for eastern and southern Switzerland. The unit provides postoperative care after cardiac surgery or any major pediatric or neonatal surgery, and treatment for children with severe trauma or medical conditions and for outborn neonates with critical illness. Six senior attending specialist pediatric intensive care physicians attend the unit. Each physician is scheduled for up to 2 weeks to resume responsibility for one-half of the unit; the on-call physician changes every 24 h.

Table 2 Patient population

Category	Number (percent)
Total patients	456
Females	204 (44.7)
Median age (mean ± standard deviation) in years	0.76 (3.2 ± 4.6)
Duration of hospitalization	
Less than one week	346 (75.9)
One to three weeks	88 (19.3)
More than three weeks	22 (4.8)
Main reasons for admission	
Newborns	119 (26.1)
– Neonatal respiratory distress	48 (10.6)
– Congenital malformation	43 (9.5)
– Suspected neonatal infection	14 (3.1)
– Other neonatal conditions	14 (3.1)
Infants and children	337 (73.9)
– Post cardiac surgery	74 (16.4)
– Major surgery	41 (9.1)
– Trauma	15 (3.2)
– Suspected systemic infection	37 (8.2)
– Respiratory failure	29 (6.4)
– Loss of consciousness	35 (7.8)
– Circulatory failure (percent)	26 (5.9)
– Observation & triage (percent)	48 (10.6)
– RSV bronchiolitis (percent)	14 (3.1)
– Others (percent)	18 (3.9)

Study design and data collection

We performed an observational cohort study. On working days a trained research fellow (M.R.) checked the patients' records for documentation of antibiotics administered. Further data collection included the physician's record of indication for treatment, basal demographic data, reasons for admission, pediatric risk of mortality score, microbiological data, and results from routine markers of infection. After discontinuation of antibiotic therapy, two investigators (M.R. and J.F.), who were not involved in the care of the patients classified each treatment course prescribed for suspected infection. The four possible categories comprised (a) confirmed systemic or localized infection, (b) uncertain episodes, (c) viral infection, and (d) no infection.

Outcome classification

Each treatment course was classified based on microbiological evidence, clinical suspicion of infection, objective clinical evidence, and laboratory evidence. Possible outcomes were confirmed systemic bacterial infection, confirmed localized infection, probable infection, viral infection, and infection unlikely or absent. Criteria are outlined in Table 1 [9, 10, 11, 12, 13]. Ventilator-associated pneumonia was diagnosed when the four criteria were met, and chest radiography revealed an otherwise unexplained new infiltrate persisting for more than 48 h [9]. Differences in classification were resolved by consensus.

Definitions, classification, and existing guidelines for antibiotic treatment

Antibiotics, which were given enterally, were regarded as systemic treatment based on pharmacokinetics and the intention to treat. Blood levels of drugs were not monitored except for those of vancomycin and gentamicin. Any prophylactic treatment that was continued longer than defined by guidelines constituted a change to therapy for suspected infection. Antibiotic treatment was regarded as appropriate when prescribed for episodes classified as confirmed or probable infection. Antibiotics were considered probably inappropriate when prescribed for viral infection, for episodes classified as infection absent or unlikely, and when physicians failed to discontinue antibiotics beyond the intended duration of prescription.

During the study period we did not change the guidelines as to antibiotic prescriptions. These guidelines stated that therapy for suspected infection should be discontinued after 48 h provided blood cultures remain negative, and the patient showed no other signs suggestive of infection. Therapy for confirmed or probable infection was continued for 7, 10, 14, or 21 days depending on the isolated or suspected pathogen and the site of infection. Perioperative prophylaxis was prescribed, for example, for cardiac surgery (48 h), for abdominal surgery with opening of the bowel (5 days), and for facial surgery (7 days). Patients with open fractures of the skull or open basal skull fracture receive 6 weeks of trimpethoprim/sulfomethoxazole. Patients with congenital or acquired immunodeficiency were treated to achieve appropriate prophylaxis covering *Pneumocystis carinii*. All cases of resistance were discussed with the infectious disease specialists of the hospital.

Statistical analysis

The basis of measurement was the calendar day. A patient who received antibiotics, or who was present in the unit on any calendar day during the study period contributed one exposure day or one hospitalization day. Exposure rates were calculated as the proportion of days on antibiotics per 100 hospitalization days. To account for the fact that patients were hospitalized, discharged, started on, or taken off antibiotics throughout the day we omitted the discharge or discontinuation day from all analyses referring to the length of stay or to the duration of treatment. The Kaplan-Meier method (log-rank test) with half-cycle correction was employed to compare the duration of antibiotic treatment between subgroups. In this context, we regarded patients who were discharged on antibiotics as censored.

To test whether the observed variation in antibiotic exposure rates followed showed cyclic variation we performed the Wallis-Moore test [14]. Nonlinear (harmonic) regressions were fit employ-

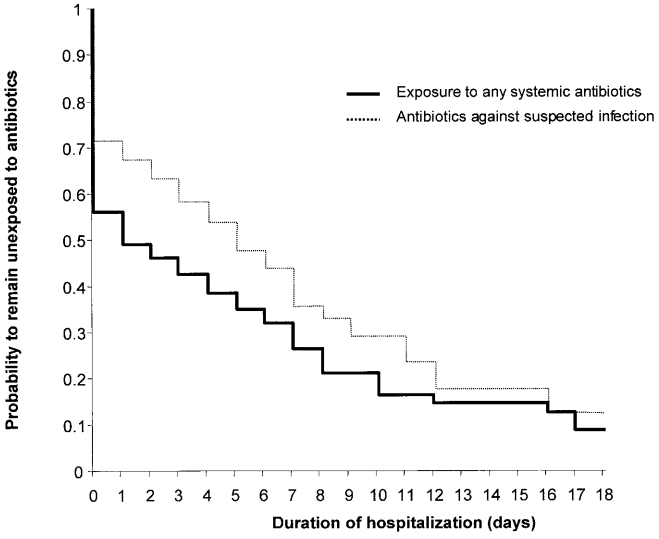

Fig. 1 Probability of remaining unexposed to antibiotic therapy in relation to length of stay. *Bold line* time until first systemic antibiotic treatment; *dotted line* time until first treatment for suspected infection

ing the principles outlined elsewhere [15]. To search for factors potentially explaining the variation in weekly exposure rates, multivariable regression analysis was calculated, entering weekly exposure rates as dependent variable and patient characteristics/physician assignment as independent variables. Differences in proportions were tested by the χ^2 statistic or by the Mantel-Haenzel-adjusted χ^2 test. All statistical tests were two-tailed with a type I error of less than 5% indicating statistical significance. All analyses were performed using SAS software (version 6.12, SAS, Cary, N.C., USA), or Prism Software (version 3, GraphPad, San Diego, Calif., USA).

Results

Antibiotic exposure and treatment episodes

A total of 258 patients (56.6% of admissions) were exposed to systemic antibiotic therapy. Of these, 187 (40.1%) received one or more courses of treatment for suspected infection. The remaining 71 patients (15.6%) were given guideline-directed antibiotic prophylaxis. Figure 1 displays the probability of remaining unexposed to antibiotics in relation to duration of hospitalization. Table 3 presents the outcome adjudication of the treatment episodes. Independent classification by the two investigators showed a good agreement (Cohen's $\varkappa = 0.76$).

Exposure days and indication for therapy

Patients received systemic antibiotic therapy on 1815 hospitalization days (54.6%). The relative proportion of hospitalization days under systemic therapy increased as patients remained in the unit. The rate amounted to 44.4% per 100 days in patients hospitalized for up to 3 days, compared with 60.2% in patients after the second week of hospitalization ($p < 0.001$). Of the 1815 exposure days to systemic antibiotic treatment, 512 (28%) were given as guideline-directed prophylaxis and 1303 were prescribed for suspected infection (Table 4). Treatment for suspected ventilator-associated pneumonia accounted for 612 (47%) of 1303 treatment days and suspected sepsis for 251 days (20%). The proportion of patients treated for suspected pneumonia increased with duration of hospitalization ($p < 0.01$). Patients were classified as having no infection or viral infection during 552 (40%) of the 1303 treatment days. The rate of probably unwarranted antibiotic therapy in suspected ventilator-associated pneumonia was 33%, corresponding to 15% of all treatment days for suspected infection. Table 4 shows the distribution of treatment days for other indications in relation to the duration of hospitalization. On several occasions, physicians failed to discontinue antibiotics after the intended length of treatment (48 h, 7 days, 10 days, and 14 days). Failure to discontinue accounted for 77 excess exposure days (4.3% of all treatment days).

Table 3 Treatment episodes and outcomes

	No. of patients (percent)	No. of courses
Any systemic antibiotics	258 (56.6)	
Prophylaxis only	71 (15.6)	
Treated for suspected infection	187 (41.0)	217
1 course	172 (92.0)	172
2 courses	10 (5.3)	20
3 or more courses	5 (2.7)	25
Independent outcome assessment	**No. of courses**	**Treatment days (mean/median)**
Total	217	1815
Proven infection	89	1049 (11.7/6)
Uncertain episodes	56	391 (7.0/5)
No infection	55	301 (5.4/3)
Viral infection	17	74 (4.4/3)

Identified pathogens and resistance patterns

Of the 288 blood cultures collected during the study from 192 patients, 31 cultures were positive (10.8%, 27 patients). The isolates comprised: *Staphylococcus epidermidis* (6), *S. aureus* (3), other staphylococci (1), *Streptococcus pneumoniae* (2), group B streptococci (1), other streptococci (2), *Stomatococcus mucilaginosus* (1), enterococci (1), *Citrobacter coseri* (1), *Pseudomonas*

Table 4 Indication for antibiotic therapy

	Hospitalization days (percent of hospitalization days) Duration of hospitalization			
	All	< 1 week	1 to 3 weeks	> 3 weeks
Total hospitalization days	3322	1118	1024	1180
Without antibiotics	1507 (45.4)	656 (58.7)	422 (41.2)	427 (36.2)
Systemic antibiotics given	1815 (54.6)	462 (41.3)	602 (58.8)	753 (63.8)
Indications	Number of treatment days (percent of column including prophylaxis)			
Suspected sepsis no focus	251 (13.8)	83 (18.0)	87 (14.5)	81 (10.8)
Suspected pneumonia	612 (33.7)	100 (21.7)	210 (34.9)	302 (40.1)
Suspected catheter infection	56 (3.1)	5 (1.1)	13 (2.2)	38 (5)
Suspected peritonitis or necrotizing enterocolitis	84 (4.6)	21 (4.6)	25 (4.2)	38 (5)
Suspected meningitis	96 (5.3)	48 (10.4)	48 (8)	–
Suspected urinary tract infection	126 (6.9)	32 (7)	50 (8.3)	44 (5.8)
Suspected wound infection	51 (2.8)	–	41 (6.8)	10 (1.3)
Other suspected infections	24 (1.3)	17 (3.7)	7 (1.2)	–
Prophylaxis because of congenital or acquired immunodeficiency	120 (6.6)	10 (2.2)	11 (1.8)	99 (13.1)
Prophylaxis against urinary tract infection	126 (6.9)	8 (1.7)	20 (3.3)	98 (13)
Prophylaxis post surgery	262 (14.4)	132 (28.7)	87 (14.5)	43 (5.7)
Prophylaxis other indications	7 (0.4)	4 (0.9)	3 (0.5)	–

aeroginosa (3), *Neisseria meningitidis* (3), *Klebsiellae* (3), *Haemophilus influencae* (1), *Serratia marcenses* (2), and *Candida albicans* (1). Twenty-one micro-organisms (68 %) showed in vitro resistance to one or more antibiotics to which they would naturally be susceptible. Multiresistance to all first-line antibiotics (ampicillin, gentamicin, third-generation cephalosporines) was observed in six isolates (19 %). Seven of ten staphylococci were resistant to aminopenicillins and three were multiresistant.

Prescribed drugs

On average, patients received 1.57 drugs per exposure day. Drug preferences varied considerably with dura-

Table 5 Risk of exposure to different antibiotics in relation to patients length of stay

Antimicrobial agent	No. of exposure days (percent)	LOS[a] < 1 wk	LOS 1 to 3 wk OR[b] (95 % Cl)	LOS > 3 wk OR (95 % Cl)
Penicillin	23 (0.7)	1.0	1.7 (0.74–3.9)	–[c]
Aminopenicillin	379 (11.4)	1.0	1.1 (0.9–1.4)	0.2 (0.16–0.3)
Aminopenicillin & Clav. acid	530 (16)	1.0	1.9 (1.5–2.5)	2.3 (1.8–2.9)
Cephalosporine 1st gen.	54 (1.6)	1.0	0.02 (0.01–0.08)	0.16 (0.08–0.3)
Cephalosporine 3rd gen.	244 (7.3)	1.0	1.5 (1.1–2.1)	1.6 (1.1–2.2)
Aminoglycosides	494 (14.9)	1.0	1.4 (1.1–1.7)	0.6 (0.5–0.8)
Sulfonamides	305 (9.2)	1.0	2.1 (1.4–3.1)	5.4 (3.9–7.5)
Quinolones	96 (2.9)	–	1.0[d]	10.2 (4.9–21.2)[d]
Clindamycin	73 (2.2)	1.0	2.9 (1.4–5.8)	3.6 (1.9–6.9)
Metronidazole	199 (6)	1.0	2.3 (1.6–3.5)	2.5 (1.7–3.6)
Macrolide	33 (1)	1.0	0.2 (0.1–0.7)	1.1 (0.5–2.2)
Meropeneme	162 (4.9)	1.0	15.5 (6.4–37.5)	41.3 (20.5–83.1)
Glycopeptides (Teicop. Vanc.)	280 (8.4)	1.0	5.2 (3.4–8.0)	7.9 (5.3–11.6)
Others	14 (0.4)	1.0	4.4 (0.6–32.6)	8.6 (1.5–47.9)
Tubercolostatics	17 (0.5)	1.0	0.6 (0.2–1.6)	–[c]
Systemic antimycotics	38 (1.1)	1.0	3.5 (1.5–8.3)	2.1 (0.8–5.3)
Enteral antimycotics	154 (4.6)	1.0	5.9 (3.3–10.6)	7.9 (4.6–13.6)

Numbers add up to more than 1815 exposure days because patients usually received more than one drug simultaneously.

[a] LOS = length of hospitalization in the ICU.

[b] OR = odds ratio. Patients hospitalized for less than one week are regarded as reference group. An odds ratio higher than 1 corresponds to a greater risk of exposure for patients in this group.

[c] Not prescribed for patients hospitalized for longer than three weeks.

[d] Not prescribed for patients hospitalized for less than one week

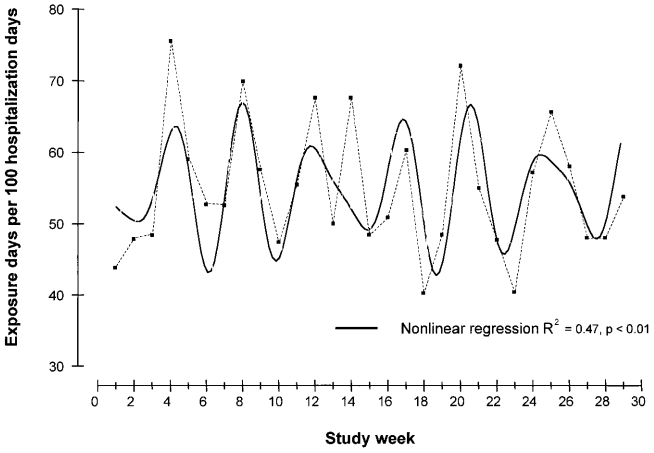

Fig. 2 Exposure rate to any systemic antibiotic treatment during the 29-week study period. Each point on the curve corresponds to the aggregated days of exposure divided by the total of hospitalization days for consecutive 7-day periods. The noninterrupted line denotes the nonlinear regression line simulating seasonality by overlaying two sine-wave functions with a period duration of 4.2 and 3.1 weeks, respectively

tion of hospitalization. Aminopenicillins and aminoglycosides accounted for nearly one-half of all drugs prescribed during the first 3 days of hospitalization. As patients continued to remain in the unit, physicians more frequently prescribed glycopeptides, meropeneme, and amoxicillin plus clavulanic acid as drugs of first choice. Table 5 displays the odds of being exposed to specific antibiotics, comparing patients hospitalized for less than 7 days to patients hospitalized for longer periods.

Variation in prescription rate

We observed a considerable variation in weekly prescription rates (range: 40.1–77 per 100 hospitalization days). Figure 2 displays the variation during the 29-week study period. A nonlinear regression model simulating seasonality by overlaying two sine-wave functions explained 47 % of the variance ($p < 0.001$). The sine-wave functions had a period duration of 4.2 weeks (95 % confidence interval 4.0–4.4 weeks) with an amplitude of 8 per 100 hospitalization days and a period duration of 3.1 (2.9–3.3) weeks with an amplitude of 4.4 per 100 hospitalization days. This observation prompted us to generate post-hoc hypotheses attempting to explain the variation by patient characteristics. We performed several regression analyses with exposure rate per week as dependent variable and variables arising from patient data (e. g., admission categories, caseload of surgical patients) and physicians' rosters as the independent variables. None of the investigated models revealed a statistically significant association.

Discussion

In this study we related the use of antibiotic treatment to indication, presence of infection, and length of stay. The overall exposure rate to antibiotics and the distribution of indications for treatment were similar to those reported from other pediatric and adult units [16, 17, 18]. A striking finding was the high rate of antibiotics prescribed for suspected pneumonia. The rate of suspected ventilator-associated pneumonia by far exceeded the rate of confirmed infections, which occurred at similar rates as reported [9, 19]. After the third day of hospitalization, exposure for suspected ventilator-associated infection accounted for nearly 40 % of all treatment days, corresponding to one-fourth of all hospitalization days. The prescription rate for suspected bloodstream infection was 2.4 times lower, underscoring the need to improve diagnostic measures for ruling out pneumonia [20].

Antibiotic exposure rates increased with length of stay. The difference in antibiotic utilization between short-term and long-term patients was attributable to the higher incidence of treatment for suspected pneumonia in the latter, and to the increased use of prophylaxis in long-term patients. The few long-term patients, who account for a large proportion of hospitalization days, are particularly at risk of becoming living reservoirs for the selection and harboring of multiresistant strains.

Physicians showed a remarkable cyclic variation in prescription rates. We found no association between utilization rates and patient characteristics or physician rosters. Since physicians were aware of the aims of the ongoing study, a Hawthorne effect from recurrent attempts to lower prescription rates is possible. As yet, however, the observed cyclic variation remains elusive.

We recorded a wide heterogeneity in the choice of drugs. The prescription rate of drugs reserved for the treatment of resistant strains was high. Patients who had been hospitalized for more than 14 days received glycopeptides on every 4th exposure day or every 6th hospitalization day. A recent study showed that alternative treatment strategies which reduce the utilization rates of vancomycin or teicoplanin can be implemented without impairing patient outcomes [21]. The diversity of drugs is testimony to the range of prescribing physicians involved. In our unit each specialist – neurosurgeons, cardiothoracic surgeons, pediatric surgeons, infectious disease specialists, immunologists, intensive care physicians, and nephrologists – share the right to order treatment. Our data illustrate that the bottom line to such cacophony is an increased utilization rate of drugs reserved for treating resistant strains.

Guideline-directed prophylaxis accounted for 28 % of treatment days, and almost one-half of these exposure days were accounted for by postoperative prophy-

laxis. As a consequence of this study, we reviewed the existing evidence from the literature. The benefit of extended prophylaxis for the individual patient is at least controversial [22, 23] and is probably confined to certain procedures [24]. As a first consequence we reevaluated our guidelines and restricted surgical prophylaxis to one preoperative dose, except for indications supported by evidence (see e. g., [24]). Moreover, adhering to existing guidelines alone (e. g., discontinuation of antibiotics after 48 h when infection is unlikely) would have curtailed exposure by 4 % of all treatment days. In summary, our data demonstrate that scrutinizing the rationale for each individual course of treatment may easily reduce the overall rate of antibiotic exposure by a considerable margin. Such quality improvement can be achieved at virtually no cost.

Several limitations of our study must be acknowledged. First, other units may care for entirely different patient populations. Thus, other targets for potential savings may be identified. However, while our findings may be site specific, we believe that the general principle of determining actual antibiotic prescription patterns and relating these to patient outcomes is a generalizable approach. Second, due to the lack of a true gold standard as to the diagnosis of infection, the outcome adjudication by two independent investigators did not protect against misclassification. We do not claim to have ascertained the true absence or presence of infection, except for patients with positive blood cultures and clinical signs of infection. However, the similarity between the incidence rate of infections observed in our study and reports from other units caring for similar populations [11, 25] supports the appropriateness of the outcome assessment.

Our primary aim was to identify targets for potential reduction in the administration of antibiotics. Assuming that improved diagnostic strategies and revised guidelines achieve the limiting of postoperative prophylaxis to few indications, and to save 50 % of all exposure days in patients who are not infected, the exposure rate of antibiotics would have dropped from 55 to 35 or 40 per 100 hospitalization days. These savings would have leveled the differing rates between short-term and long-term patients. It is beyond the scope of this observational study to quantify the potential cost savings of such reduction, partly because we are unable to assess the cost of additional testing, which might be triggered by more stringent utilization of antimicrobial drugs. The impact on costs, occurrence of resistant strains, and patient outcomes remains to be elucidated.

Conclusion

We employed a straightforward but laborious approach to determine antibiotic prescription patterns and targets for potential reduction in unnecessary exposure. In this multidisciplinary pediatric intensive care unit we demonstrated a great variability of exposure rates. Relevant reduction could result by cutting the treatment for suspected ventilator-associated respiratory tract infection and from shortening prophylactic strategies which are not supported by evidence.

Acknowledgements The study was supported by grants from the Stanley Thomas Johnson Foundation, Berne, Switzerland, and from the Alice Bucher Foundation, Lucerne, Switzerland.

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