USE OF PROPHYLACTIC ANTIBIOTICS IN SURGERY AT A MEDICAL CENTER IN SOUTHERN TAIWAN

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Background and Purpose: Use of prophylactic antibiotics to prevent postoperative infection (POI) is a common practice in surgery. This study investigated the amount and cost of surgical prophylaxis in a representative general hospital in Taiwan in order to determine an appropriate course of action to control antibiotic use and decrease the burden of resistance.
Methods: The use of antibiotic prophylaxis for a wide variety of surgical procedures over a 6-month period was retrospectively evaluated in 3,104 patients at a medical center in southern Taiwan.
Results: Timing of perioperative parenteral antibiotics was inappropriate in 738 (23.8%) patients. The average duration of antibiotic use was 6.4 days (2.4 days intravenous + 4.0 days oral). Only 4.9% of patients did not receive prophylactic antibiotics and only 9.2% received a single dose. Prophylaxis exceeded 1 day in 80% of patients and 3 days in 68.2%. The most common regimen was cefazolin plus gentamicin, used in 2,338 (75.3%) procedures. There were 146 POIs in 119 (3.8%) patients. The most common POI was at the surgical site. Aerobic Gram-negative bacilli were most common among the 81 pathogens isolated (54.3%), followed by Gram-positive cocci (34.6%), anaerobes (8.6%) and yeasts (2.4%). The total cost for prophylactic antibiotics was New Taiwan (NT)$ 5,860,242 (~ US$ 169,862). Had a single dose of cefazolin been used for all patients, the cost would have been reduced by 92.1%. Had four doses of cefazolin been used, the cost would have been reduced by 68.5%.
Conclusions: This study documented the excessive use and often inappropriate timing of administration of antibiotics for surgical prophylaxis in a representative medical center in Taiwan. Strategies are needed to improve the appropriate use of surgical antibiotic prophylaxis in Taiwan, not only to reduce costs but, more importantly, to delay the emergence of resistant microorganisms.

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Two converging factors emphasize the need to optimize the use of prophylactic antibiotics in surgery. First, there is increasing global emergence of antimicrobial resistance [1–3]. The problem is complex and multifaceted, but the selective force of antibiotic overuse plays an important role. The second factor is the transition to the era of managed care requiring both cost containment and quality assurance. Antimicrobials account for 13 to 37% of expenditure for drugs in hospitals [4], and 30% of in-hospital antibiotic use is for surgical prophylaxis [5].

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Nosocomial infection is a major problem worldwide. Postoperative wound infection remains the major source of infectious morbidity and mortality in surgical patients. Antimicrobial prophylaxis has been shown to reduce the incidence of postoperative infection (POI) for a variety of surgical procedures; more than 80% of prospective controlled studies demonstrated a significant benefit of antimicrobial prophylaxis in preventing surgical infections [6]. Despite its advantages, surgical prophylaxis is often overused. Fortunately, inappropriate surgical prophylaxis can be readily identified and corrected [7–9].

This investigation was conducted as part of a program sponsored by the Taiwan National Health Research Institutes to define "methods to optimize the use of antibiotics for surgical prophylaxis in Taiwan" [10]. It provided an opportunity to systematically determine how well surgical prophylaxis is used in Taiwan. The current report describes the amount and cost of surgical prophylaxis in a representative general hospital and its findings may suggest a strategy for programs to improve antibiotic use and decrease the burden of resistance.

Materials and Methods

The operating theater records of Kaohsiung Veterans General Hospital were reviewed to identify patients who had undergone operative procedures between January 1 and June 30, 1999. Patients were included in the study if they had undergone an elective procedure involving clean or clean-contaminated surgery as defined by standard criteria [11]. Ten surgical categories were distinguished: colorectal, cardiovascular, chest, general, genitourinary, obstetric and gynecologic, neurosurgical, orthopedic, pediatric and plastic. Patients who underwent otolaryngology, dentistry, ophthalmology, dermatology or ambulatory surgical procedures were excluded. Patients were excluded if they had received an antibiotic for any reason within 1 week prior to surgery.

Data were collected by chart review and recorded on formatted data collection forms. Information was obtained on patient demographic characteristics, surgical department, surgical procedure, surgeons, and dates of admission, operation and discharge. Each course of prophylactic antibiotic was defined by choice of drug, route, timing (first parenteral injection or initiation of oral bowel preparation), dose, duration and cost. POIs were defined according to US Centers for Disease Control (CDC) guidelines [12–14]. They were recorded according to site, time of occurrence and pathogen(s) isolated.

Results

A total of 11,344 inpatient procedures were performed between January 1 and June 30, 1999. Charts were analyzed for the 3,936 elective procedures that met the study criteria for clean or clean-contaminated surgery (Table 1). Of these, 832 procedures were excluded for

Table 1. Number of patients who underwent selected elective surgical procedures according to surgical division at Kaohsiung Veterans General Hospital from January through June 1999

Division	Included	Excluded*			Total
		1	2	3	
Colorectal surgery	154	71	1	0	226
Chest surgery	131	31	2	0	164
Cardiovascular surgery	135	50	1	1	187
General surgery	508	130	34	12	684
Genitourinary surgery	359	72	44	2	477
Gynecology	376	23	1	0	400
Neurosurgery	196	53	0	0	249
Obstetrics	136	6	0	1	143
Orthopedic surgery	789	73	38	13	913
Pediatric surgery	85	2	0	0	87
Plastic surgery	235	123	42	6	406
Total	3,104	634	163	35	3,936

*Patients who received antibiotics within 1 week prior to surgery: 1 = antibiotics used for a documented infection preoperatively; 2 = antibiotics used for suspected infection preoperatively; 3 = antibiotics used without symptoms or signs of infection preoperatively.

the following reasons: receipt of an antibiotic within 1 week prior to surgery for documented infections (634 patients), suspected infection (163 patients), or for unidentified reasons (35 patients). The use of prophylactic antibiotics in surgery was determined for the remaining 3,104 patients. Of these procedures, 1,784 (57.5%) were classified as clean surgery and 1,320 (42.5%) as clean-contaminated surgery.

Antibiotic use

Prophylactic antibiotics were used in 95.1% of procedures (Table 2). Among the 151 (4.9%) who did not receive prophylactic antibiotics, 85 procedures were in children who underwent hernia repairs. The remaining 66 cases were spread among a variety of procedure types without a specific pattern of distribution.

Timing

Timing of administration of prophylactic antibiotics in relation to surgical divisions is shown in Table 2. Timing was considered appropriate in 2,215 patients (71.4%) who received preoperative prophylaxis within 2 hours prior to the procedure [15]. Timing was considered inappropriate in 738 (23.8%) patients: i.e., prophylactic antibiotics received more than 2 hours before the incision, or during or after surgery.

Duration

The average number of days of use of prophylactic antibiotic in each division is shown in Table 3. The average duration was intravenous (IV) for 2.4 days plus 4.0 days orally, a total of 6.4 days. Patients who underwent neurosurgery had the longest prophylactic antibiotic use (10.9 days), followed by cardiovascular surgery (9.0 days). All neurosurgery and cardiovascular surgical procedures were classified as clean surgery. Only 286 (9.2%) cases received a single dose of preoperative prophylaxis. Most (238, 82.3%) were general surgery patients who underwent breast, laparoscopic cholecystectomy, hernia and thyroid operations. Prophylaxis exceeded 1 day in 2,509 (80%) patients and exceeded 3 days in 2,116 (68.2%).

Choice of antimicrobial agent

Most prophylactic antibiotics were IV initially, and later switched to oral administration. Both IV and oral antibiotics were used in 1,947 (62.7%) procedures (data not shown). IV antibiotics only were used in 638 (20.6%), and oral antibiotics only were used in 368 (11.9%). The most common IV regimen used in both clean and clean-contaminated surgery was cefazolin plus gentamicin (2,338, 75.3%), followed by cefazolin plus gentamicin and metronidazole (149, 4.8%), cefazolin alone (134, 4.3%), and oxacillin plus gentamicin (108, 3.5%). In 91 procedures in which patients received preoperative oral antibiotic for bowel preparation (most in colorectal surgery), they all also received IV prophylactic antibiotics. Cefoxitin was used during a short period in only 35 of 347 (10.1%) hysterectomies. No other cephalosporins, quinolones or glycopeptides were used during the study period.

Postoperative wound infections

There were 146 POIs in 119 (3.8%) patients (Table 4).

Table 2. Timing of administration of prophylactic antibiotic in patients who underwent selected elective surgical procedures, according to surgical division, at the Kaohsiung Veterans General Hospital from January through June 1999

Division (*n*)	Nil*	Preoperative			After incision, but during surgery	After surgery
		≤ 1 hr	> 1 hr to ≤ 2 hr	> 2 hr†		
Colorectal surgery (154)	1	9	67	1	1	75
Chest surgery (131)	1	73	28	12	6	11
Cardiovascular surgery (135)	12	38	9	1	–	75
General surgery (508)	4	331	97	32	9	35
Genitourinary surgery (359)	20	98	146	49	2	44
Gynecology (376)	1	302	50	9	7	7
Neurosurgery (196)	0	125	29	9	13	20
Obstetrics (136)	4	103	–	2	4	23
Orthopedic surgery (789)	13	330	326	44	20	56
Pediatric surgery (85)	85	–	–	–	–	–
Plastic surgery (235)	10	35	19	7	–	164
Total (3,104)	151 (4.9%)	1,444 (46.5%)	771 (24.8%)	166 (5.3%)	62 (2%)	510 (16.4%)

*No prophylactic antibiotic used perioperatively; †preoperative intravenous antibiotics only, excluding oral antibiotics for bowel mechanical preparation.

Table 3. Average number of days of antibiotics following surgery among patients who underwent selected elective surgical procedures, according to surgical division, at Kaohsiung Veterans General Hospital from January through June 1999

Division (*n*)	Average no. of days of antibiotics*		
	Intravenous	Oral†	Total
Colorectal surgery (154)	2.9	1.6	4.4
Chest surgery (131)	3.6	4.8	8.4
Cardiovascular surgery (135)	2.0	7.1	9.0
General surgery (508)	1.3	1.6	2.9
Genitourinary surgery (359)	2.5	4.8	7.2
Gynecology (376)	2.3	3.5	5.8
Neurosurgery (196)	5.9	5.1	10.9
Obstetrics (136)	1.6	4.2	5.8
Orthopedic surgery (789)	2.9	4.8	7.6
Pediatric surgery (85)	0	0	0
Plastic surgery (235)	1.4	4.2	5.5
Total (3,104)	2.4	4.0	6.4

*Defined as 0 if a single dose of prophylactic antibiotic was given preoperatively; †including number of days antibiotics were prescribed after discharge.

Table 4. Occurrence of postoperative infections by specific site for patients who underwent selected surgical procedures, according to surgical division, at Kaohsiung Veterans General Hospital from January through June 1999

Division (*n*)	Infections, *n* (%)	Site of infection					
		UTI	SSI	PBSI	LRTI	SBSI	Other*
Colorectal surgery (154)	9 (5.8)	3	2	4	1	–	1
Chest surgery (131)	8 (6.1)	1	5	–	1	–	1
Cardiovascular surgery (135)	2 (1.5)	–	1	–	–	–	1
General surgery (508)	33 (6.5)	6	25	3	2	–	4
Genitourinary surgery (359)	14 (3.9)	9	4	–	–	2	1
Gynecology (376)	4 (1.1)	1	3	–	–	–	–
Neurosurgery (196)	27 (13.8)	17	5	1	13	2	3
Obstetrics (136)	1 (0.7)	1	–	–	–	–	–
Orthopedic surgery (789)	19 (2.4)	2	17	1	–	–	1
Pediatric surgery (85)	2 (2.4)	–	–	–	–	–	2
Plastic surgery (235)	0 (0.0)	–	–	–	–	–	–
Total (3,104)	119 (3.8)	40	62	9	17	4	14

UTI = urinary tract infection; SSI = surgical site infection; PBSI = primary bloodstream infection; LRTI = lower respiratory tract infection; SBSI = secondary bloodstream infection. *Others: 5 central venous pressure-line infections, 3 acute tonsillitis, 3 upper RTIs, 1 osteomyelitis, 1 bed sore, and 1 bronchiolitis.

The most common were surgical site infections (SSIs; 62, 52.1%). The rate of SSI was 1.2% (21/1,784) after clean surgery and 3.1% (41/1,320) after clean-contaminated surgery. Most SSIs occurred in general surgery and orthopedics. Most SSIs in general surgery (18/25) were complications after clean-contaminated surgery. All SSIs in orthopedics occurred after clean surgery. Neurosurgery had the highest rate of POI (13.8%), most of which were urinary tract and lower respiratory infections; only five (2.6%) were SSIs. Only two of the 286 patients who had received a single dose of preoperative antibiotic (mostly in general surgery) developed a POI.

Wound cultures

Clinical specimens were sent for culture in 91 of 119 (76.5%) infected patients. Twenty-eight (23.5%) POIs were diagnosed clinically without culture and 17 of 62 (27.4%) SSI specimens were not cultured. A total of 81 isolates were cultured from 45 patients with SSIs (Table 5). Aerobic Gram-negative bacilli were the most common cultured pathogens (54.3%) isolated. The three

Table 5. Number of pathogens involved in postoperative surgical site infections among patients who underwent selected elective surgical procedures at Kaohsiung Veterans General Hospital from January through June 1999

Gram-positive cocci	28	Gram-negative bacilli	44
Enterococcus spp.	11	*Escherichia coli*	12
Methicillin-resistant *Staphylococcus aureus*	6	*Pseudomonas aeruginosa*	6
Methicillin-susceptible *S. aureus*	5	*Klebsiella pneumoniae*	6
Coagulase-negative staphylococci	2	*Serratia marcescens*	2
viridans-Gr. streptococci	2	*Morganella morganii*	5
Other streptococci	2	*Citrobacter* spp	2
Anaerobes	7	*Enterobacter cloacae*	3
Prevotella spp	2	*Proteus* spp	2
Peptostreptococcus	2	*Pseudomonas* sp	1
Bacteroides	2	*Aeromonas* spp	2
Veillonella	1	*Burkholderia cepacia*	1
Gram-positive bacilli	1	*Klebsiella oxytoca*	1
Yeast	2	*Providencia rettgeri*	1
		Comamonas acidovorans	1

most common pathogens, *Escherichia coli*, *Staphylococcus aureus* and *Enterococcus* spp, accounted for 42.0% of the isolates. In general surgery, 25 SSIs had pathogen(s) cultured. Gram-negative bacilli were involved in three of seven clean surgery wounds and 12 of 18 clean-contaminated wounds. In orthopedics, 14 SSIs had pathogen(s) cultured, of which eight were Gram-negative bacilli.

Costs

The total cost of prophylactic antibiotic use during the study period was New Taiwan (NT)$ 5,860,242 (~ US$ 169,862). This does not include the costs of pharmacy and administration. The average cost per procedure was NT$ 1,897 (US$ 55). Had a single dose of cefazolin been used for all patients, the total cost would have been NT$ 461,254, a reduction of 92.1%. Had four doses of cefazolin been used, the total cost would have been NT$ 1,845,018, a reduction of 68.5%.

Discussion

There is considerable evidence that appropriate use of antimicrobial agents for surgical prophylaxis can reduce the incidence of POI [7, 16]. Several guidelines for prophylactic use of antimicrobial agents are available to help with indications, choice of drug, and duration of prophylaxis [17–22]. Unfortunately, poor compliance with standard guidelines has been reported [23–28].

We found that antibiotic prophylaxis in surgery was virtually universal regardless of indication or surgical division. Only 4.9% of all patients undergoing surgical procedures did not receive a prophylactic perioperative antibiotic. Clean procedures constituted 57.5% of all surgical procedures and accounted for 33.9% of all SSIs, which is consistent with the findings of a previous study [29]. Although antibiotic prophylaxis has been clearly shown to reduce the incidence of POI in clean-contaminated and contaminated procedures, there is still no clear consensus regarding its use in clean surgery other than for high-risk procedures. Prophylaxis is indicated only for specific clean surgical procedures where the benefits of preventing a rare infection exceed the risks and costs of prophylaxis. These include procedures with foreign material, grafts or prosthetic devices. There are now data to support the use of prophylaxis in some low-risk procedures. A study by Platt et al showed a significant reduction in the overall incidence of wound infection by 17% in hernia repair and breast surgery [30]. Lewis et al also reported a 75% reduction in SSI in low-risk patients who underwent elective clean surgery [31]. Despite these reports, the low risk of infection after many clean procedures precludes further conclusive tests of the efficacy of prophylactic antibiotics [32].

Burke established the timing of administration of antibiotics in the early 1960s [33]. It is essential that antibiotic prophylaxis be initiated in close proximity to the time of the surgical procedure in order to achieve effective tissue concentrations at the time of incision and throughout the operation [15, 21, 22, 34]. The major exception is cesarean section, for which the first dose of prophylaxis should be delayed until the umbilical cord is clamped to avoid placental transfer of the antibiotic to the fetus [16, 35–38]. For longer procedures, readministration of the drug is indicated at intervals of one or two times the half-life of the drug [35, 39]. If a systemic antibiotic is used, IV administration of an appropriate dose in the operating theater just before the induction of anesthesia is practical [24, 34]. "On call" dosing is no longer acceptable because it may result in premature administration of the antibiotic and insufficient tissue concentration of drug during the operative procedure [7]. However, in this study we found that, when preoperative antibiotics were used, they were constantly prescribed as an on call order and were administered before sending patients to the theater. This resulted in administration of prophylactic antibiotic(s) 2 hours earlier than incision in 5.3% of procedures. Inappropriate timing of administration of prophylactic antibiotics occurred in nearly 24% of all surgical procedures. The timely preoperative administration of prophylactic antibiotics is considered an important issue in quality assurance in surgical care [40].

This study found that only 9.2% of all patients undergoing surgical procedures received a single dose of prophylactic antibiotic. Prophylaxis exceeded 1 day in 80% of patients and exceeded 3 days in 68.2%. However, a single dose of antibiotic before surgery is sufficient prophylaxis for most surgical procedures [41]. The duration of administration needs to be extended only in special circumstances, such as gross contamination secondary to a ruptured viscus or severe trauma. No further benefit is conferred by the administration of additional doses after the patient has left the theater [35, 42]. Continued use predisposes to superinfection by antimicrobial-resistant bacteria in the hospital environment [28] and development of *Clostridium difficile*-related diarrhea [23, 43]. Prolonged use may originate from the mistaken belief that extending the duration of prophylaxis beyond the immediate perioperative period will decrease the incidence of postoperative infection [44].

Results from this study showed that 74.6% of patients undergoing surgical procedures received either combined IV and oral antibiotics, or oral antibiotics alone as prophylaxis. Oral antibiotics, except those for patients undergoing surgical procedures involving the bowel, were consistently used either after surgery or after IV administration. International guidelines for surgical prophylaxis recommend that IV administration of antibiotics is optimal to ensure adequate levels in tissues during most operative procedures [17–22]. The exception to this principle is colorectal operations: preoperative oral administration of antibiotics appears to be an effective alternative to IV administration in preventing SSIs in such procedures. However, in this study, dual-route administration of antibiotics was found in all such procedures.

Gentamicin was used in more than 80% of procedures, despite the fact that it has not been demonstrated to be effective as a prophylactic agent in a prospective clinical trial in clean surgery [16]. Excess use of gentamicin is associated with a marked increase in gentamicin resistance within the hospital environment [45]. Gentamicin is not recommended for prophylaxis in surgery because of nephrotoxicity and ototoxicity.

Postoperative wound infection is the most common nosocomial infection in patients undergoing surgery [46]. In this study, the rate of POI for selected clean and clean-contaminated procedures was 3.8%. SSIs accounted for half of all POIs. The rates of SSI in clean and clean-contaminated surgical wounds were 1.2% and 3.1%, respectively. This figure is similar to results from a 10-year prospective study in almost 63,000 wounds [47]. However, because information on POIs was retrospectively collected from chart records and microbiologic results, the attack rate found in this study constitutes an underestimation of the true rate of POIs, including SSI. It has been estimated that 12 to 84% of SSIs are detected after patients are discharged from the hospital [14]. We also noted that culture was not performed in almost one-quarter of patients with POI, which may also have led to an underestimation of the true rate of SSI if the local treatment of SSIs by surgeons was not recorded.

For most SSIs, pathogens originate from the endogenous flora of the patient's skin, mucous membranes or hollow viscera. These organisms are usually aerobic Gram-positive cocci (e.g., staphylococci), but may include fecal flora (e.g., anaerobic bacteria and Gram-negative bacilli). In our study, Gram-negative bacilli were the most commonly cultured pathogens from SSIs. Their occurrence in two-thirds of 18 SSIs after clean-contaminated general surgery is a reasonable expectation. However, the reason for the high prevalence of pathogenic Gram-negative bacilli in cultured SSIs in orthopedic procedures — all clean surgery — remains unclear. It may be partly explained by excessive use of antibiotics that increase the risk of colonization with hospital-acquired pathogens and later lead to superinfection by antimicrobial-resistant bacteria in the hospital environment [28].

The findings that neurosurgery had the highest rate of POI, despite the fact that most surgical procedures were clean and that a long duration of prophylaxis was used, may be explained by prolonged use of ventilator support and indwelling urinary catheters. Prolonged use of antibiotics in neurosurgery may be counterproductive, allowing the emergence of resistant microorganisms in intubated and catheterized patients. The excessive cost of prolonged use of prophylactic antibiotics cannot be justified based on international guidelines [23, 26, 48].

The current findings of problems with selection of proper antibiotics for prophylaxis, inappropriate timing of administration, and prolonged use reflects similar problems in other hospitals in Taiwan [49]. Strategies to improve the appropriate use of prophylactic antibiotics in surgery should be undertaken nationwide to reduce costs of antibiotics and emergence of resistant microorganisms. Fortunately, there is a vast body of evidence on how to best apply cost-effective methods to antimicrobial prophylaxis in surgery.

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