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Letters to the Editor

Evaluation of surgical site infection antibiotic prophylaxis among patients receiving antibiotics for active infection

Sir,

Standard practice for the prevention of surgical site infection (SSI) includes administration of prophylactic antibiotics within 1 h prior to incision [1]. Often, hospitalized surgical patients receive antibiotics to treat a suspected or confirmed infection, which may or may not be related to the surgical procedure. Among these patients, it is unclear if additional doses of antibiotics closer to the time of incision are necessary to prevent SSIs. Notably, patients with evidence of infection prior to surgery are excluded from many quality measures evaluating pre-operative antibiotic prophylaxis [2]. Consequently, the administration of duplicative prophylactic antibiotics may be unnecessary and potentially harmful due to concentration-dependent antibiotic toxicities.

We sought to determine the frequency and associated risks of inappropriate antibiotic surgical prophylaxis. This single-centre, retrospective cohort study evaluated adult inpatients that were receiving antibiotics for a suspected or confirmed infection and underwent a surgical procedure between 1st January 2015 and 31st March 2015. The primary outcome was the percentage of patients who received appropriate antibiotic prophylaxis. Appropriate antibiotic prophylaxis was defined as adequate microbiological spectrum of activity based on the site of surgery [3], without duplication of microbiological coverage if additional prophylactic antibiotics were given prior to incision. Inappropriate antibiotic prophylaxis included patients who received inadequate microbiological spectrum of activity based on the site of surgery, or those who received additional antibiotics despite already receiving adequate coverage from treatment antibiotics. Microbiological history was evaluated up to 90 days before surgery to determine if any additional coverage may have been necessary (e.g. vancomycin for a recent meticillin-resistant *Staphylococcus aureus* infection).

Secondary outcomes included antibiotic-related adverse events, SSI rates, 14-day all-cause mortality and 30-day re-admission. Antibiotic-related adverse events were evaluated up to 24 h after the completion of antibiotics for surgical prophylaxis. Reactions evaluated included: documented hypersensitivity requiring the administration of diphenhydramine, epinephrine, corticosteroid or bronchodilator; infusion-related reaction associated with antibiotic administration, requiring early discontinuation and/or diphenhydramine administration; and nephrotoxicity defined as an increase in serum creatinine >50% above baseline.

This evaluation included 499 patients, 326 (65%) of whom received appropriate antibiotic prophylaxis. Among the 173 (35%) patients who received inappropriate antibiotic prophylaxis, 151 (87%) received additional antibiotics at the time of surgery that were duplicative and unnecessary. The remaining 22 (13%) patients did not receive additional antibiotic prophylaxis, despite requiring an expanded spectrum of activity therapy for the surgical procedure. Among the 326 patients who received appropriate antibiotic prophylaxis, 271 (83%) patients received treatment antibiotics with an adequate spectrum of activity and did not receive any additional antibiotics for prophylaxis. The remaining 55 (17%) patients appropriately received additional antibiotic(s) prior to incision in order to achieve an adequate spectrum of activity for prophylaxis.

Baseline characteristics between the inappropriate and appropriate groups were generally similar (Table I). The inappropriate group had more clean surgeries than the appropriate group (46% vs 28%, $P<0.01$). Overall, seven patients experienced an antibiotic-related adverse event. More patients who received inappropriate antibiotic prophylaxis experienced an adverse event (3% vs 0.6%, $P=0.05$). Five patients experienced an infusion-related reaction, including two patients with Red Man syndrome with vancomycin. The remaining two patients experienced nephrotoxicity. There were no differences in SSIs, mortality and re-admission (Table I). Among patients who received additional antibiotics for prophylaxis, 69% of antibiotics were ordered through an electronic order set. The rate of appropriate antibiotic prophylaxis was lower when providers ordered prophylactic antibiotics through an order set than when an order set was not used (27% vs 64%, $P<0.001$).

This evaluation among surgical patients who received antibiotics for the treatment of infection reveals an area of opportunity for antimicrobial stewardship. Although the majority of patients received appropriate antibiotic prophylaxis, 35% of patients received inappropriate prophylaxis, which was associated with a higher rate of adverse events. Importantly, no difference in SSIs was observed, which suggests that antibiotics do not need to be redosed immediately prior to incision when patients are already receiving treatment dosing of antibiotics. Although order sets are often employed to improve pre-operative management and ensure appropriate use of antibiotic prophylaxis, we observed an inverse effect in this scenario. This is likely due to the lack of patient-specific assessment, which is required to compare the patient's treatment antibiotics with those required for surgical prophylaxis.

Table I
Baseline characteristics and outcomes

	All patients N=499	Appropriate N=326	Inappropriate N=173	P-value
Age, years, mean ± SD	56.8 ± 15.6	55.3 ± 16.2	57.6 ± 15.3	0.11
BMI, kg/m^2, mean ± SD	29.2 ± 9.1	28.3 ± 8.7	29.6 ± 9.3	0.11
Male	293 (59)	196 (60)	97 (56)	0.38
Any antibiotic allergy	38 (24)	24 (23)	14 (26)	0.74
Serum creatinine, mg/dL, mean ± SD	1.6 ± 1.9	1.5 ± 1.5	1.6 ± 2.1	0.30
Comorbidities				
Cardiovascular disease	286 (57)	187 (57)	99 (57)	0.99
Diabetes	164 (33)	110 (34)	54 (31)	0.57
Immunocompromised[a]	120 (24)	77 (15)	43 (9)	0.75
ESRD	106 (21)	74 (15)	32 (6)	0.27
Positive microbiological culture in the last 90 days	163 (33)	101 (40)	62 (36)	0.27
Surgery type				0.54
Emergent	426 (85)	276 (85)	150 (87)	
Elective	73 (15)	50 (15)	23 (13)	
Wound classification				<0.01
Clean	169 (34)	90 (28)	79 (46)	
Clean-contaminated	242 (49)	173 (53)	69 (40)	
Contaminated	88 (18)	63 (19)	25 (15)	
Antibiotic-related adverse events	7 (1.4)	2 (0.6)	5 (3)	0.05
Surgical site infection	1 (0.2)	1 (0.3)	0 (0)	0.99
14-day all-cause mortality	43 (9)	33 (10)	10 (6)	0.10
30-day re-admission	151 (30)	97 (30)	54 (31)	0.75

SD, standard deviation; BMI, body mass index; ESRD, end-stage renal disease.
Data are *N* (%) unless otherwise specified.
[a] Defined as haematological malignancy, human immunodeficiency virus or solid organ transplantation.

Limitations of this evaluation include the relatively small sample, which may have resulted in a lack of power to detect a difference in SSI rate and other outcomes. Additionally, the evaluation did not include a comprehensive review of confounders that may have contributed to outcome differences. To our knowledge, this is the first study to evaluate this specific clinical scenario. Future antimicrobial stewardship efforts should focus on determining methods to improve appropriate prescribing of antibiotics for surgical prophylaxis in the setting of active infection.

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