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Major articles

Evaluating the impact of an antimicrobial stewardship program on the length of stay of immune-competent adult patients admitted to a hospital ward with a diagnosis of community-acquired pneumonia: A quasi-experimental study

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stepped-wedge design
time-variant survival analysis
length of stay

Background: The purpose of this study was to demonstrate an antimicrobial stewardship intervention can reduce length of stay for patients admitted to hospital with community-acquired pneumonia (CAP).
Methods: Starting April 1, 2013, consecutive adult patients with CAP admitted to an acute care community hospital in Barrie, Ontario, Canada, were eligible for enrollment until March 31, 2015. The antimicrobial stewardship intervention was a prospective audit and feedback recommendation implemented in a stepped-wedge design across 4 wards. The primary outcome was time to hospital discharge, and secondary outcomes included time to antibiotic discontinuation and a composite outcome of 30-day readmission or all-cause mortality. The intervention effect was estimated by survival (time to discharge and antibiotic discontinuation) and logistic (30-day readmission or all-cause mortality) regression analyses.
Results: Complete data were available for 763 patients. The primary outcome was observed in 196 (82%) control patients and 402 (77%) intervention patients. Length of stay was reduced by 11% (95% confidence interval [CI], −9% to 35%). Time to antibiotic discontinuation was shortened by 29% (95% CI, 10%-52%). Odds ratio for 30-day readmission or all-cause mortality was 0.79 (95% CI, 0.49-1.29).
Conclusions: A prospective audit and feedback intervention did not significantly reduce length of hospital stay in CAP patients despite reducing overall antibiotic utilization.

In the province of Ontario, Canada, pneumonia is the leading cause of death from bacterial infections and accounts for >18,000 years of life lost per annum.[1] Pneumonia accounts for most antibiotic utilization in both hospital and outpatient settings.[2,3] Evidence-based guidelines for the diagnosis and management of pneumonia are available to physicians.[4,5] There exists significant unwarranted variation from these guidelines that is associated with both increased mortality and antibiotic utilization.[6-10] Unwarranted variation refers to the absence of patient- or disease-specific reasons to justify practice variation from evidence-based guidelines. Antimicrobial stewardship interventions (ASis) are defined as any intervention that minimizes unwarranted variation in antibiotic utilization from evidence-based practice, with the intent of improving patient safety and quality of care.[11] ASis can be operationalized in different ways, but prospective audit and feedback (persuasive approach) and restricted antimicrobial prescribing policies (restrictive approach) appear to be the most effective interventions to achieve the goals of antimicrobial stewardship.[11-13]

ASis directed to community-acquired pneumonia (CAP) patients have failed to demonstrate reductions in length of hospital stay (LOS).[12,13] LOS accounts for the most costs for CAP compared with any reductions in antibiotic utilization attributable to ASis.[14] Given the high operational costs of antimicrobial stewardship programs that use prospective audit and feedback interventions, it is important to demonstrate that these programs can minimize the costs of caring for CAP patients. Of the 3 randomized controlled trials

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in CAP patients, only the study by Fine et al modeled length of stay as a time-to-event occurrence.[15-17] In this study, the ASi consisted of a prospective chart audit starting on day 3 of hospitalization and physician feedback in the form of a recommendation, suggesting optimal timing of conversion from intravenous to oral antibiotics. The intervention was modeled as a time-invariant exposure in the final model despite the timing of the recommendation varied by up to 7 days from the time of enrollment. The hazard ratio (HR) for discharge was 1.16 (95% confidence interval [CI], 0.97-1.38) for the intervention group, suggesting a nonsignificant reduction in length of stay of 16%. Not accounting for time-variant bias may have diluted the ASis effect toward an HR value of 1.[18] In addition, Fine et al did not use a competing risks model, potentially leading to a biased ASi effect estimate.[19]

Quasi-experimental, or observational, study designs are commonly used to evaluate real-world programs. This study design is at risk for estimating a biased average treatment effect because of the absence of investigator-controlled treatment assignments and frequent absence of contemporaneous controls. The problem of contemporaneous controls can be minimized by using a stepped-wedge study design.[20] This design provides investigators with the opportunity to implement an intervention in a sequential manner over a number of time periods across all units (clusters). Not only does this provide a contemporaneous control group both within and across units, but all patients will ultimately receive the intervention, which is important for those interventions in which a preponderance of evidence suggests overall patient benefit. The problem of treatment assignment ignorability can be minimized by using a matching strategy, such as a propensity score analysis that attempts to condition the average treatment effect on observable random variables used to minimize selection bias.[21]

In the present study, we estimated the effectiveness of an ASi using a prospective audit and feedback intervention to reduce the length of stay for patients admitted to hospital with CAP. The ASi was implemented on 4 wards in a single hospital using a stepped-wedge design to ensure contemporaneous controls, and the time to hospital discharge was modeled using survival analysis. In addition, the ASi was modeled as a time-variant exposure variable, and outcomes such as death were treated as both censored and competing events.

MATERIALS AND METHODS

The study protocol has been published elsewhere.[22]

Setting

The study took place at a single-site, 339-bed, community-based, university-affiliated hospital located in Barrie, Ontario, Canada. This is the sole hospital, serving 128,000 Barrie residents. Patients admitted to 4 medical wards were enrolled in the study. All study patients were admitted to the hospitalist service.

Participants

Consecutive adult patients (≥18 years old) were enrolled for a 2-year period starting on April 1, 2013. Inclusion criteria for enrollment were diagnosis of pneumonia by the admitting physician, LOS ≥48 hours, and prescription of either an oral second- or third-generation cephalosporin, any oral respiratory fluoroquinolone, or any intravenous antibiotic ≥48 hours. Exclusion criteria included recent hospitalization in the preceding 3 months, receiving immunosuppressants, neutropenia, immunocompromised, admission to an intensive care unit, or life expectancy ≤3 months.

Intervention

The ASi consists of a prospective chart audit and physician feedback persuasive approach.[23] The ASi occurred anytime after 48 hours postadmission. An infectious diseases–trained pharmacist (L.M.) and infectious diseases–trained physician (G.D.) conducted every ASi. The ASi recommendations were consistent with the Infectious Diseases Society of America CAP guidelines[4] and the Canadian Thoracic Society guidelines for the management of chronic obstructive pulmonary disease.[24] All ASi recommendations were documented in the patient's electronic medical record and communicated directly to the attending hospitalist. All patients were contacted by telephone at 30 days postdischarge for follow-up of antibiotic use and to determine 30-day readmission and all-cause mortality events.

Design

This is a quasi-experimental stepped-wedge controlled study intended to measure the effectiveness of a real-world program.[25] The ASi was implemented in a nonrandomized stepped-wedge design across 4 medical wards (Fig 1).[20] The target of the ASi was the hospitalist, whereas the unit of analysis was individual patient outcomes adjusted for potential clustering effects within the hospital wards.

Sample size

Sample size for the study was fixed and had been previously estimated at 400-500 eligible patients per calendar year.[14] This study enrolled 763 patients, and 78.3% experienced the primary outcome (598 events). Setting power at 0.8 and statistical significance (2-sided) α at 0.05, the estimated ASi effect needed for detection was ≥20% reduction in length of stay.[26]

Outcomes

The primary outcome of the study is LOS. Patients are administratively censored at 14 days postadmission. Potential competing outcomes are death, transfer from the ward to an intensive care unit, or transfer from the ward to another hospital. The secondary

Ward	Type	Period																							
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
		2013m4	2013m5	2013m6	2013m7	2013m8	2013m9	2013m10	2013m11	2013m12	2014m1	2014m2	2014m3	2014m4	2014m5	2014m6	2014m7	2014m8	2014m9	2014m10	2014m11	2014m12	2015m1	2015m2	2015m3
3GA	Medicine	c	c	c	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3GC	Medicine	c	c	c	c	c	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
4GC	Medicine	c	c	c	c	c	c	c	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3SA	Medicine	c	c	c	c	c	c	c	c	c	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	c=control period (N=24); x=intervention period (N=96)																								

Fig 1. Sequential implementation of antimicrobial stewardship interventions across 4 medical wards over the 24-month study period.