Needs Assessment for Antimicrobial Stewardship in an Acute and Complex Care Hospital Specializing in Orthopedic Surgery: A Retrospective Descriptive Study

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ABSTRACT

Background:
Most antimicrobial stewardship (AS) literature has focused on acute care hospitals, with little known about AS needs in specialized facilities, including complex care.
Objective:
To benchmark antibiotic use and identify potential targets for future AS interventions at an acute and complex care orthopedic surgery hospital (ACCOSH).
Methods:
A retrospective study was conducted in patients admitted to the ACCOSH between 1January2015 and 31December2015. The metrics were days of antibiotic therapy (DOT)/1000 patient days, frequency of prolonged therapy, identification of most common antibiotics, and number of microbiology cultures processed.
Results:
Of 2946 patient admissions, 239 (8%; 95%CI:7-9%) patients were prescribed non-perioperative antibiotics (NPAs) and 2343 (80%; 95%CI:79-81%) were prescribed perioperative antibiotics (PAs). A total of 478/3026 NPA courses were prescribed (16%; 95%CI:14-17%). Cephalosporins (29%, 137/478), fluoroquinolones (18%, 88/478), penicillins (17%, 82/478), and intravenous vancomycin (6%, 31/478) were the most common NPAs prescribed. Thirty percent of intravenous NPA courses were stepped down to oral therapy (52/171). The mean DOT/1000 patient days of NPAs was 241 (SD ±65), with a median duration of 7 days (IQR 5-9). Although few NPA courses were >90 days (0.4%, 2/478), 39% were >7 days (188/478). A total of 2548/3026 (84%, 95%CI: 83-85%) antibiotic courses were for PAs, where 2240 courses were for cefazolin (88%, 95%CI:87-89%). While urine was the most common culture source received by microbiology (66%, 961/1454), 24% (235/961) had no growth. The most common urinary isolate was *E. coli* (40%, 57/142). Ciprofloxacin was the most common empiric antibiotic prescribed within 72 hours of an ordered urine culture that grew *E. coli* (18/45, 40%).
Conclusions:
AS initiatives targeting use of cephalosporins, fluoroquinolones, penicillins and intravenous vancomycin, duration of therapy, parenteral to oral step down therapy, perioperative antibiotic choice, assessment of urine samples ordered, drawn and processed, and improved empiric prescribing based on a site-specific antibiogram may be beneficial in an ACCOSH.

BACKGROUND

Antibiotic Stewardship in Acute Care
- Antibiotic resistance is a global threat to public health.
- Overuse of antibiotics is the major driver of antibiotic resistance.
- Up to 50% of antibiotic use in acute care settings is inappropriate.

Antibiotic Stewardship in Acute and Complex Care Orthopaedic Centres – Rationale and Gaps
- The 2017 Accreditation Canada required organizational practice (ROP) for antimicrobial stewardship (AS) has been expanded to include complex continuing care and inpatient rehabilitation.
- Antimicrobial stewardship may be important in acute and complex care hospitals specializing in orthopaedic surgeries because patients may be at risk for both infection and inappropriate antibiotic therapy as a consequence of surgery, prolonged hospitalization with rehabilitation, and patient factors such as age and renal function.
- To date, no data exists to identify the potential AS needs of an acute and complex care hospital specializing in orthopedic surgery.

OBJECTIVE

- The objective of this study was to assess antibiotic use at an acute and complex care hospital specializing in orthopaedic surgery to benchmark antibiotic use and identify potential targets for future AS interventions.

METHODS

Study Design and Setting
- Retrospective descriptive study of antibiotic use among inpatients at a 62 inpatient bed acute and complex care facility in Toronto, Ontario specializing in orthopedic surgery.
- The study period was January 1, 2015-December 31, 2015.
- Institutional Ethics Board approval for ongoing review of antimicrobial stewardship data for quality improvement initiative was obtained originally in February 2010 and undergoes annual review.

Patient Eligibility
- All inpatients admitted to the facility between January 1, 2015 and December 31, 2015 who were prescribed antibiotics and / or had microbiology results were included.

Data Collection
- Data relevant to antibiotic use was obtained from the Pharmacy database of the facility.
- Data relevant to microbiology workload were obtained from the Microbiology database of the facility.
- The number of patient days per month and the number of hospital admissions during the study period were obtained from Decision Support at the facility.
- Patient days per month were used to standardize antibiotic use and microbiology workload to 1000 patient days, to allow benchmarking within and between institutions.

Statistical Analysis
- Descriptive analyses were completed using Microsoft Excel 2010 software (Microsoft Corporation, Redmond, Washington) and GraphPad Instat (version 3.05, 32 bit for WIN 95/NT, created September 27, 2000).
- Interval data are reported as means with standard deviation or median with interquartile range (IQR), based on whether or not data passed the test for normality (GraphPad Instat).
- Nominal data are reported as a percentage with a 95% confidence interval (CI).

Disclosures: Authors of this poster have the following to disclose concerning possible personal or financial relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:
- Claudiu Serbanescu – Nothing to disclose
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METHODS

Outcome Measures

Antibiotics:
- The primary benchmark metrics for non-perioperative antibiotics were days of antibiotic therapy (DOT) per 1000 patient days (PDs), frequency of prolonged antibiotic therapy > 7 days and > 90 days, and identification of most common antibiotics prescribed during the study period.
- The secondary antibiotic outcomes for non-perioperative antibiotics were DOT/1000 PDs categorized by antibiotic class, specific antibiotic, intravenous antibiotics, oral antibiotics, antibiotics with activity against methicillin resistant *Staphylococcus aureus* (MRSA) [vancomycin IV, trimethoprim-sulfamethoxazole IV/PO, levofloxacin IV/PO, moxifloxacin IV/PO, clindamycin IV/PO] and *Pseudomonas aeruginosa* [ciprofloxacin IV/PO, meropenem, ceftazidime, piperacillin-tazobactam 4.5g], days of IV antibiotic therapy saved by parenteral to oral step down, and empiric therapy for presumed urinary tract infection (UTI).
- The benchmark metric for perioperative antibiotics was DOT/1000 PDs for each specific antibiotic and duration of therapy.

Microbiology:
- The primary benchmark metric for microbiology was an assessment of workload for processing cultures drawn for inpatients expressed as the number for each source sent to microbiology/1000 PDs.
- Secondary microbiology outcomes were the number of cultures for inpatients which were received and processed by microbiology that revealed no growth and the number of preoperative urine cultures with a designation in the microbiology profile of "not indicated".
- An institution specific antibiogram was developed for the most frequent bacteria isolated during the study period.

RESULTS

Demographic Characteristics:
- 2,946 patients were admitted to the hospital
- 239 (8%; 95% CI: 7-9%) patients were prescribed non-perioperative antibiotics
- 2,343 (80%; 95% CI: 79-81%) patients were prescribed perioperative antibiotics
- Mean age of patients on non-perioperative antibiotics was 72 ± 15 years (range 18 – 101)
- 145 (61%) were female
- Total number of patient days at the site during study period was 18,700 days

Antibiotic Use:
- Most antibiotic courses were for perioperative antibiotics (2548/3026, 84%; 95% CI: 83-86%)
- Of 478 antibiotic courses prescribed for presumed infection (16%; 95% CI: 14-17%), 39% of courses were for > 7 days (188/478) and only 0.4% were continued for > 90 days (2/478)
- Median duration of non-perioperative antibiotic use was 7 days (IQR 5-9)
- Cefazolin was the most commonly used antibiotic for surgical prophylaxis (88%, 2240/2548; 95% CI: 87-89%)
- Most perioperative antibiotic courses had a duration of ≤ 24 hours (2323/2548, 91% of total perioperative antibiotics)

Table 1: Non-perioperative Antibiotic Use During Study Period*

Antibiotic Use	Number of Antibiotic Orders	% of Total Antibiotic Orders	95% Confidence Interval Antibiotic Orders	DOT/1000 patient days[b]	Interquartile Range for DOT/1000 patient days
By route[c]:					
Total antibiotics, any route	478	100		241±65	(174-277)
IV	171	36	31% - 40%	120±49	(88-177)
PO	304	64	59% - 68%	121±30	(95-146)
Other	3	1	0% - 1%	NA	NA
By indication:					
IV to PO Step Down	52	30[d]	26% - 35%	21±13[d]	(17-28)[d]
MRSA activity	80	17	13% - 20%	36±15	(25-40)
Pseudomonas activity	85	18	14% - 21%	35±25	(19-43)
By class, specific drug:					
Penicillins	82	17	14% - 21%	53±25	(31-66)
Ampicillin	11	2	1% - 4%	9±10	(1-17)
Amoxicillin	31	6	4% - 9%	13±7	(10-13)
Amoxicillin/Clavulanate	11	2	1% - 4%	5±8	(0-6)
Penicillin G IV	6	1	0% - 2%	10±11	(0-12)
Penicillin V PO	1	0	0% - 1%	0	(0-0)
Cloxacillin IV	7	1	0% - 3%	6±8	(0-8)
Cloxacillin PO	2	0	0% - 1%	0	(0-0)
Piperacillin/Tazobactam 3.375G	4	1	0% - 2%	3±6	(0-4)
Piperacillin/Tazobactam 4.5G	9	2	1% - 3%	7±11	(0-5)
Cephalosporins	137	29	25% - 33%	71±34	(46-89)
Cefazolin	27	6	4% - 8%	23±24	(5-33)
Cephalexin	64	13	10% - 16%	27±12	(18-35)
Cefprozil	1	0	0% - 1%	0	(0-0)
Cefuroxime axetil	4	1	0% - 2%	0	(0-0)
Ceftazidime	4	1	0% - 2%	0	(0-0)
Ceftriaxone	37	8	5% - 10%	18±9	(15-22)
Carbapenems	11	2	1% - 4%	6±9	(0-7)
Ertapenem	6	1	0% - 2%	3±7	(0-4)
Meropenem	5	1	0% - 2%	0	(0-2)
Total Beta Lactams	230	48	44% - 53%	131±45	(101-163)
Fluroquinolones	88	18	15% - 22%	30±13	(24-35)
Ciprofloxacin PO	62	13	10% - 16%	23±13	(14-24)
Ciprofloxacin IV	5	1	0% - 2%	2±3	(0-2)
Levofloxacin PO	19	4	2% - 6%	5±6	(0-7)
Levofloxacin IV	1	0	0% - 1%	0	(0-0)
Moxifloxacin PO	1	0	0% - 1%	0	(0-0)
Macrolides	12	3	1% - 4%	4±4	(0-5)
Azithromycin PO	7	1	0% - 3%	2±4	(0-3)
Azithromycin IV	4	1	0% - 2%	2±3	(0-1)
Clarithromycin PO	1	0	0% - 1%	0	(0-0)
Lincosamides	9	2	1% - 3%	10±12	(0-17)
Clindamycin PO	5	1	0% - 2%	5±10	(0-4)
Clindamycin IV	4	1	0% - 2%	5±7	(0-7)
Glycopeptide	37	8	5% - 10%	27±14	(20-37)
Vancomycin IV	31	6	4% - 9%	23±14	(16-34)
Vancomycin PO	6	1	0% - 2%	3±4	(0-7)
Sulfonamides	28	6	4% - 8%	7±7	(2-9)
Trimethoprim-Sulfamethoxazole PO	28	6	4% - 8%	7±7	(2-9)
Tetracyclines	11	2	1% - 4%	4±4	(0-6)
Doxycycline PO	7	1	0% - 3%	2±2	(0-4)
Minocycline	1	1	0% - 1%	0	(0-0)
Tetracycline	1	0	0% - 1%	0	(0-0)
Urinary Antiseptics	36	8	5% - 10%	12±8	(7-14)
Nitrofurantoin	34	7	5% - 9%	12±7	(7-14)
Trimethoprim PO	2	0	0% - 1%	0	(0-0)
Other	27	6	4% - 8%	17±15	(5-20)
Metronidazole PO	11	2	1% - 4%	5±6	(0-7)
Metronidazole IV	9	2	1% - 3%	5±7	(0-6)
Rifampin PO	7	1	0% - 3%	7±9	(0-9)

DOT = days of therapy, IQR = interquartile range, IV = intravenous, PO = by mouth, MRSA = methicillin resistant *Staphylococcus aureus*, NA = not applicable.
*Study period was January 1, 2015 to December 31, 2015 (12 months), and the total number of patient days was 18 700.
[a] Data provided as mean ± SD for data that passed the test for normality and median for data that failed the test for normality.
[b] Adds to more than 100% due to rounding rules.
[c] % of Total IV orders
[d] Represents the number of days of IV therapy saved per 1000 patient days with IV to PO stepdown therapy

Table 2: Microbiology

Number (%)	Total	Urine	Blood	Biopsy	Hardware	Sputum	Swab
Total cultures received by lab for INPATIENTS*	1454 (100)	961 (66)	92 (6)	198 (14)	21 (1)	4 (0.3)	178 (12)
Total cultures received by lab for INPATIENTS per 1000 Patient Days	78	51	5	11	1	0.2	10
Total microbial load by source**	245 (17)	142 (15)	2 (2)	46 (23)	5 (24)	3 (75)	47 (26)
Gram negative***	122 (50)	109 (77)	0 (0)	8 (17)	0 (0)	0 (0)	5 (11)
Escherichia coli	61 (25)	56 (39)	0 (0)	5 (11)	0 (0)	0 (0)	0 (0)
Escherichia coli (ESBL producer)	1 (0.4)	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Klebsiella pneumoniae	6 (2)	6 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Klebsiella oxytoca	1 (0.4)	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Citrobacter species	5 (2)	5 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Morganella morganii	2 0.8	2 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Serratia marcescens	3 (1)	3 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Enterobacter cloacae complex	6 (2)	6 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Proteus mirabilis	11 (4)	7 (5)	0 (0)	1 (2)	0 (0)	0 (0)	3 (6)
Pseudomonas aeruginosa	24 (10)	21 (15)	0 (0)	1 (2)	0 (0)	0 (0)	2 (4)
Other gram negative [^]	2 (0.8)	1 (0.7)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
Gram positive	111 (45)	30 (21)	2 (100)	38 (83)	5 (100)	0 (0)	36 (77)
MRSA	5 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (11)
MSSA	11 (4)	1 (0.7)	1 (50)	2 (4)	1 (20)	0 (0)	6 (13)
Coagulase negative staphylococci	37 (15)	1 (0.7)	0 (0)	16 (35)	3 (60)	0 (0)	16 (34)
Enterococcus faecalis	30 (12)	20 (14)	0 (0)	6 (13)	0 (0)	0 (0)	3 (6)
Enterococcus faecium	5 (2)	4 (3)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
Other gram positive[^^]	24 (10)	4 (3)	1 (50)	13 (28)	0 (0)	0 (0)	6 (13)
Other microbes[^^^]	12 (5)	3 (2)	0 (0)	0 (0)	0 (0)	3 (100)	6 (13)
Total negative**	639 (44)	243 (25)	83 (90)	160 (81)	17 (81)	1 (25)	135 (76)
No growth**	623 (38)	235 (21)	81 (95)	160 (75)	13 (62)	0 (0)	134 (70)
Sent when preoperative urine cultures were not indicated**	2 (0.1)	2 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Not processed**^^	14 0.9	6 0.5	2 (2)	0 (0)	4 (19)	1 (25)	1 (0.5)

*** Percentage out of total cultures received by lab for this row**
**** Percentage out of total cultures received by lab for this source for this row**
***** Percentage out of total microbial load for that source for this section unless otherwise indicated.**
[^] Other gram negative: Pseudomonas stutzeri, Stenotrophomonas maltophilia
[^^] Other gram positive: aerobic spore forming bacilli, *Bacillus* spp., Beta-haemolytic streptococcus group B, *Corynebacterium striatum*, Diphtheroid bacilli, *Finegoldia magna*, *Propionibacterium acnes*, *Streptococcus anginosus*, Viridans group streptococci, *Enterococcus avium*, *Staphylococcus haghamensis*.
[^^^] Other microbes: Yeast, Commensal organisms, Normal flora
^^ Not processed: samples were not processed due to unlabelled specimen, cancelled by nursing, specimen too old, inappropriate specimen for culture, contamination, broken container, specimen received in unsuitable packaging, and delay in transport

Table 3. Empiric Antibiotics Used for Presumed UTI (Where final culture result indicated *E. coli*)

Antibiotic	Number	(%)	95% Confidence Interval
Ampicillin	1	(2)	-2% - 7%
Amoxicillin	8	(18)	7% - 29%
Amoxicillin / Clavulanate	0	(0)	-
Cloxacillin PO	0	(0)	-
Cloxacillin IV	0	(0)	-
Cefazolin	0	(0)	-
Cephalexin	5	(11)	2% - 20%
Cefuroxime axetil	1	(2)	-2% - 7%
Ceftriaxone	2	(4)	-2% - 10%
Ciprofloxacin PO	18	(40)	26% - 54%
Ciprofloxacin IV	0	(0)	-
Levofloxacin PO	0	(0)	-
Levofloxacin IV	0	(0)	-
Azithromycin PO	0	(0)	-
Azithromycin IV	0	(0)	-
TMP/SMX PO	1	(2)	-2% - 7%
TMP/SMX IV	0	(0)	-
Nitrofurantoin	9	(20)	8% - 32%
Metronidazole PO	0	(0)	-
Metronidazole IV	0	(0)	-
Total by counting # step down (column W)	45	(100)	

Site Specific Antibiogram
- The site specific antibiogram revealed similar resistance rates to the hospital wide antibiogram (Results not displayed)

DISCUSSION

- This retrospective descriptive study assessed antibiotic use in an acute and complex care facility specializing in orthopaedic surgery.
- To the best of our knowledge, this is the first study to provide metrics for antibiotic use in an orthopedic patient population, and therefore, this study serves to benchmark antibiotic use in an orthopedic patient population and identify potential targets for future antimicrobial stewardship interventions.
- Eight percent of patients admitted to this orthopedic centre during the study period were treated with non-perioperative antibiotics.
- Perioperative antibiotics constituted the majority of the antibiotic use (84%).
- The most commonly used non-perioperative antibiotics were cephalosporins (29%), fluoroquinolones (18%), penicillins (17%), and IV vancomycin (6%).
- Intravenous to oral step-down antibiotic therapy was implemented in 30% of IV antibiotic courses.
- Of the non-perioperative antibiotic courses, many were continued for more than 7 days (39%).
- The mean days of therapy per 1000 patient days for non-perioperative antibiotics was 241 ± 65, and the median duration of non-perioperative antibiotic use was 7 days (IQR 5-9).
- The metric of DOT/1000 patient days for non-perioperative antibiotics corresponds to about half of the use seen in our acute care facility (Sunnybrook Health Sciences Centre – Bayview Campus), and therefore, may justify a 0.5 full time equivalent position for an antimicrobial stewardship pharmacist.
- A duration of 24 hours maximum was used for the majority of perioperative antibiotic courses (91%), as recommended in the IDSA/SHEA guidelines .
- Urine was the most frequent source received by microbiology for processing (66%), 24% of urine samples had no growth, and *E. coli* (non- ESBL) was the most commonly cultured bacteria (39%) among culture positive urine samples.
- The prevalence of MRSA at the facility was only 0.3%.
- Based on our findings, potential targets of future antimicrobial stewardship interventions identified include implementing a prospective audit and feedback initiative of the most frequently used non-perioperative antibiotic classes (cephalosporins, fluoroquinolones, penicillins and vancomycin IV); assessing duration of therapy to minimize potentially unnecessary prolonged antibiotic use (>7 days); evaluating the potential to improve parenteral to oral step down antibiotic therapy; and the exploration of initiatives to potentially reduce the number of urine samples for culture and susceptibility ordered, drawn and processed by microbiology.
- Initiatives that should be explored related to urine cultures include education of health care professionals about urinary tract infections versus asymptomatic bacteriuria, implementing microbiology policies that reduce upstream laboratory testing of urine sources sent to microbiology, and prospective audit programs to evaluate patients for whom a urine culture has been ordered with utilization of an annually updated site specific antibiogram.

Limitations:
- Retrospective and descriptive study that analyzed data from a single facility
- Limited 1 year study period
- Associated with a teaching hospital
- Uncertainty in linking an antibiotic course with a specific culture, diagnosis (i.e. for UTI), or indication (i.e. perioperative vs. non-perioperative, targeted vs. empiric)
- Despite these limitations, this study provides:
  - Benchmarking data for antibiotic use at an acute and complex care facility specializing in orthopaedic surgery, which has not been done before
  - Identification of potentially problematic issues with antibiotic therapy in an acute and complex care facility which may benefit from antimicrobial stewardship initiatives
- Future studies evaluating the implementation of antimicrobial stewardship interventions proposed to target one or more areas of potential need identified in this study are planned and will be shared in a future publication.

CONCLUSION

Areas of antibiotic use at this acute and complex care facility which may benefit from antimicrobial stewardship include potentially excessive use of cephalosporins, fluoroquinolones, penicillins and IV vancomycin. There are opportunities to reduce duration of therapy, promote parenteral to oral step down therapy, and improve prescribing based on a site- specific antibiogram.

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