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Antibiotic Stewardship Related to CDI in Long-Term Care Facilities

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Introduction

Clostridioides difficile (previous name *Clostridium difficile*) is a major burden to the healthcare system with an unaccountable contribution from long-term care facilities (LTCF) [1]. To reduce this burden, every year Joint Commission standards have recognized prevention of *Clostridioides difficile infection* (CDI) as one of the National Patient Safety Goals. Generally, most of the focus remains on prevention measures such as strict isolation, hand hygiene with soap and water, and environmental disinfection to reduce CDI transmission. These measures are restricted in application to a group of patients with suspected or confirmed CDI. The key strategy to prevent *C. difficile* colonization, even prior to the manifestation of infection, is reducing inappropriate antibiotic use.

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Need for Antimicrobial Stewardship in Long-Term Care Facilities

Exposure to antibiotics in previous 3 months, multiple courses of antibiotic therapy, and length of antibiotic treatment alter the gut flora and are associated with high risk for *C. difficile* colonization [2]. Even a single dose of high-risk antimicrobials such as clindamycin, fluoroquinolones, and cephalosporins increases risk for CDI.

Commonly, LTCF residents have complex medical conditions lowering their threshold to antibiotic exposure. Residents receive at least one course of antibiotic every year [3]. Old age and rise in antibiotic utilization have resulted in high *C. difficile* acquisition rates (8–33%) at LTCFs [3]. Current estimated CDI incidence rate in LTCF is 2.3 cases/10,000 resident days [4].

To combat antibiotic-resistant bacteria and infections, the White House released a national action plan to achieve a goal of 50% reduction in incidence of CDI by 2020. Effectively, the Centers for Medicare and Medicaid Services (CMS) proposed regulatory rule to implement antimicrobial stewardship programs in all hospital settings including LTCF [2].

Since the regulatory advent, acute care hospital data is the strongest evidence on the effectiveness of stewardship programs. A multidisciplinary stewardship program in an acute care hospital setting reported a significant decrease in CDI rates ($p = 0.002$) sustained over a 7-year period by limiting utilization of third-generation cephalosporins [5]. A systematic review and meta-analysis of 16 studies restricting cephalosporin and fluoroquinolone use showed protective benefit with a 52% risk reduction in CDI cases [6]. Following a CDI outbreak at a VA facility, Climo et al. performed a prospective cohort study observing the effect of restriction of clindamycin use on CDI rates. The study reported sustained reduction in CDI cases (11.5 cases/month compared with 3.33 cases/month; $p < 0.001$) and cost savings (an estimated $47,782 by preventing 237 CDI cases) over a 3-year time period [7]. Successful reduction in CDI rates post-emergence of robust antibiotic stewardship programs "(ASPs)" in an acute care setting supplements as a strong need for similar action in LTCFs.

ABCs of Antimicrobial Stewardship Program

Antimicrobial or antibiotic stewardship (ASP) entitles efficient antibiotic utilization for an appropriate indication with the right antibiotic, at right dose and route of administration, and for a right duration of time. The primary objective of ASP is to establish a multidisciplinary team to promote education and awareness on increasing antimicrobial resistance, implement policies, and monitor the appropriate use of antibiotics. The scope of ASP is vast, extending beyond prevention of CDI to the reduction in incidence of other multidrug-resistant organisms (MDROs) and antibiotic-associated adverse events, reducing healthcare expenditures through antibiotic cost savings, and overall improving patient care, safety, and quality of life.

As LTCF system differs from acute care hospitals, multidisciplinary expert panels from the Society for Healthcare Epidemiology of America (SHEA), Association for Professionals in Infection Control (APIC), and Infectious Diseases Society of America (IDSA) recommend infection preventionists in LTCFs to step up and incorporate antimicrobial stewardship activities in the infection control programs (Category IB) [2]. The guidance tool published by the Centers for Disease Control and Prevention (CDC) recognized as a standard to establish ASP at any acute care and long-term care facility [8]. Table 7.1 highlights core elements in stewardship with specific recommendations directed to LTCFs on gradual implementation of strategies over time for stability and sustainment of stewardship program.

Barriers in Long-Term Care Facilities

Despite comprehensive guidance, hardly 25–60% of LTCFs have formal ASPs [9]. Majority of these programs lack written policies, financial and leadership support, as well as dedicated staffing. Infection prevention personnel commonly leads stewardship efforts without adequate support. The facility-based ASPs perform limited basic activities such as monitoring antibiotic use,

Table 7.1 Core elements of antimicrobial stewardship program

Core elements	Stakeholders	Goals and objectives
Commitment Key element for success of program	Administrative leadership Clinical leadership: medical director, director of nursing services, director of staff development Infectious disease specialist Infection prevention and healthcare epidemiology staff Pharmacist Microbiology Information technology	Goal: To establish and sustain ASP Objectives: –Provide formal written statement of support to improve and monitor antibiotic use –Provide financial support for stewardship activities –Include stewardship duties as part of work requirement and annual performance review –Support for staff training and education –Support for stewardship activities with engagement of multidisciplinary group

Accountability	Physician leader, preferably infectious diseases trained	Goal: To lead and monitor stewardship program Objectives: –Establish stewardship committee/workgroup composing infection preventionist (must), nursing director, medical director, consulting pharmacist, administrator, physician champion, nurse champion, nurse aide champion, and resident and family council representative –Plan, develop, and implement stewardship policies, procedures, and protocol –Direct communication and feedback to providers and staff on adherence to antimicrobial prescribing per policy –Review and monitor outcomes of stewardship activities
Drug expertise	Pharmacy leader as co-champion	Goal: To co-lead, promote, monitor, and support stewardship activities Objectives: –Develop facility-specific antibiogram based on local susceptibility pattern –Participate in development of stewardship policies, procedures, and protocol –Review adherence to antibiotic prescribing policy –Provide recommendations to stewardship committee/workgroup based on outcomes and resistance data

(continued)

Table 7.1 (continued)

Core elements	Stakeholders	Goals and objectives
Action	Antimicrobial stewardship committee	Goal: To implement strategies to improve antibiotic use Objectives: –Perform baseline assessment on antibiotic prescribing practices for common infections, average duration of antibiotic treatment, and CDI rate. –Identify simple, measurable, and modifiable targets to review and monitor change in antibiotic use before and after ASP intervention. –Routine communication of implemented policies, procedures, and protocols with all providers and staff –Recommend LTCFs to implement at least one of the below measurable strategies during start of ASP: *Publish antibiotic prescription policy advising providers to include dose, duration, and indication for each recommended antibiotic *Publish facility specific guidelines on treatment of CDI based on severity. Include treatment of other common infections (urinary tract infection, pneumonia, skin and soft tissue infection, invasive infections) in guidelines *Provide guidance on ordering appropriate diagnostic studies based on clinical assessment (e.g., *C. difficile* PCR, toxin assay) *Provide access to standard published guidelines on recommended duration of antibiotic treatment *Implement antibiotic time-out/stop protocol to promote 48–72 hours reassessment of appropriate antibiotic use based on clinical and diagnostic evaluation *Implement prior authorization to reduce inappropriate antibiotic use *Optimize antibiotic use by providing prospective audit and feedback to providers *Empower pharmacy-led initiatives to automate optimal antibiotic dosing, route of administration, and evaluation of drug-drug interactions

Tracking and reporting	Antimicrobial stewardship committee	Goal: To periodically monitor, track, and report outcome measures within the committee and annual review with staff and providers Objectives: Track and monitor at least one of the below outcome measures, corresponding to implemented strategy, to analyze success of the ASP: –Antibiotic use: measure days of therapy/1000 resident days of care –Change in CDI rate: based on restriction of high risk antibiotics –Cost savings: antibiotic costs, healthcare costs –Adherence to facility specific treatment guidelines –Prevalence of antibiotic resistance
Education	Physician providers, prescribers, clinical staff Nursing staff Residents and family	Goal: To educate, raise awareness, and obtain support to improve antibiotic use and reduce CDI Objectives: –Educate physicians and nursing staff on cause-effect relationship of improper use of antibiotics, development of antibiotic resistance, and rise in CDI rates –Review published facility-specific guidelines and protocols with staff (in the form of didactic presentations, posters, flyers, reminders) on appropriate antibiotic use –Provide feedback on facility-wide antibiotic use and to individual providers on antibiotic utilization per policy –Provide education to residents and families during admission to facility (in the form of posters, flyers, and direct communication) on ASP in an effort to improve antibiotic use and reduce facility-onset infections particularly CDI

appropriateness, providing antibiogram, and tracking CDI rates. Thus, partial implementation of core elements has resulted in unstable and poorly sustained ASP in LTCFs. The major barriers for stewardship deficiencies in LTCFs include remote facilities with lack of on-site infectious diseases trained physician, lack of specialized pharmacist, and lack of diagnostic resources such as on-site microbiology lab [9]. Poor staff knowledge on stewardship, poor response by providers to inappropriate prescribing practices, less engaged physician and staff in stewardship initiatives, and antibiotic pressure by patient/family have attributed to failure of stewardship initiatives [10, 11]. Overall, limited resources, complex patient population, and different culture of practice in LTCFs prohibit successful implementation and sustainment of ASP.

Recommended Solutions and Resources to Overcome Barriers

Few studies have explored barriers in LTCFs to provide guidance on practical solutions and resources to facilitate ASP. The Society for Post-Acute and Long-Term Care Medicine developed an antibiotic stewardship policy template, specific for LTCFs [12]. The policy provides guidance on implementation of ASP to meet CMS requirements. Acknowledging the lack of physician availability, the policy promotes use of provider-friendly algorithms like revised McGeer criteria and Loeb minimum criteria to diagnose common infections per surveillance definitions and to determine need for initiation of antibiotic therapy. Additional simple guidance to promote appropriate antibiotic use in LTCF is provided by Zarowitz et al. using treatment algorithms tailored toward infections commonly encountered in older adults (urinary tract infections, upper respiratory tract infections, pneumonia, skin and soft tissue infections) [13].

Alternative recommended strategy to prevent CDI is gaining consultation from infectious diseases (ID) expert. A 160-bed VA based LTCF showed a 30% reduction in total antimicrobial use and a significant reduction in CDI rate ($p = 0.04$) post-implementation

of ID consultation services [14]. Appointing an ID expert by individual LTCF or group of LTCFs can be an effective way to combat antimicrobial usage in resource-limited setting.

One of the important overlooked cause for continued high burden of CDI in healthcare facilities is the constant transfer of residents from LTCFs to acute care hospitals (ACH) and vice versa. Thus, strong ASPs in LTCFs will make a major impact in reducing overall CDI rates. A 212-bed LTCF in Massachusetts collaborated with local ACH to obtain stewardship support via telemedicine. The local ASP team led by infectious diseases expert conducted daily chart reviews, generated reports on antimicrobial use, and gave feedback to LTCF providers through emails. Three-year post-implementation results demonstrated a reduction in high-risk antimicrobial use and hospital-acquired CDI rates ($p = 0.02$) [15]. Another LTCF collaborated with the local hospital-based ASP to promote education to physicians, staff, pharmacist, and resident family members on appropriate antibiotic use. On a 12-month follow-up, the LTCF reported reduced fluoroquinolone use by 37% but with non-significant reduction in CDI incidence by 19% [16]. There is a strong need for such collaborations to mitigate staffing and financial issues promoting utility of infectious diseases and pharmacy consultations from local ACHs for stewardship activities. Ultimately, these collaborations reduce overall burden of infections and antibiotic resistance in community and thus increase sustainability of ASP in LTCF.

Impact of Stewardship in Long-Term Care Facilities on CDI Rates

Outcome studies published since the implementation of ASP in LTCFs have reported simultaneous reduction in CDI rates and improvement in antimicrobial use [17, 18]. Limited studies have specifically analyzed reduction in the CDI rates. A 50-bed LTCF in the southeast United States reported a 23% reduction in CDI rates sustained over a 1-year period. The facility had successful reduction in CDI by implementing a tiered approach including infection prevention and stewardship measures reducing general

antibiotic use and restricting use of clindamycin and cephalosporins [19]. Bunch et al. reported institution of ASP in addition to ongoing infection prevention measures in a 55-bed LTCF. During the 6-year study period, there was a 33% reduction in antibiotic cost per patient day, and CDI SIR rate reduced from 1.25 to 0.25 (two-tailed p-value = 0.0009) [20]. Valiquette et al. reported significant decline in CDI cases (p = 0.007) with establishment of stewardship program reducing high-risk antimicrobial use (cephalosporins, ciprofloxacin, clindamycin, macrolides), post-failure of impact of infection prevention strategies [21]. Few studies have reported no significant impact of stewardship efforts on CDI outcomes. Two LTCFs reported 21–25% reduction in antimicrobial use secondary to stewardship interventions. However, both studies observed no change in CDI rates [22]. Inapt impact of stewardship on CDI outcomes has been attributed to inadequate infection prevention measures [23].

Summary

Compared to acute care hospital setting, establishing and maintaining ASP in LTCF remains a challenge. Leadership support, staff education, and routine review and feedback by engaged ASP leaders are the essential pillars for the success of stewardship program. Reduction in CDI, particularly, necessitates multidisciplinary, bundled approach and collaboration with infection prevention to produce an impact. There is a need for further research on effective ways to sustain stewardship program and improve outcome measures in the resource-limited LTCFs.

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