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Antimicrobial Stewardship

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Long-Term Care Certification in Infection Prevention (LTC-CIP) Preparation Series

Sources

- Content of this module was informed and used with permission from the Association for Professionals in Infection Control and Epidemiology resources:
  - APIC LTC-CIP™ Learning System
  - APIC Text Online

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Exam Content

1. Long-Term Care Settings (15 items)
2. Management and Communication of the Infection Prevention Program (16 items)
3. Identification of Infectious Diseases (18 items)
4. Surveillance and Epidemiologic Investigation (24 items)
5. Prevention and Control of Infectious and Communicable Diseases (24 items)
6. Environment of Care (18 items)
7. Cleaning, Disinfection, Sterilization of Medical Devices and Equipment (15 items)
8. **Antimicrobial Stewardship (11 items)**
9. Employee/Occupational Health (9 items)

Learning Objectives

In this review session, the main topics that will be covered are:

1. The key terms and elements of antimicrobial stewardship programs in Long-Term Care Homes (LTCHs)
2. The proper indications and use of antimicrobials including considerations related to antimicrobial resistance

Antimicrobials and their Use

Basic Principles

- Antimicrobial agents are substances that kill or inhibit the growth of microorganisms (e.g., bacteria, viruses, fungi, or parasites).
- Antibiotics are a type of antimicrobial agent that target bacteria (anti-bacterial) and are usually synthesized by another living microorganism (e.g., fungus).
  - Commonly administered through intravenous or oral routes
  - Less commonly administered through intramuscular, topical, or intraperitoneal routes

Contamination, Colonization and Infection

- Contamination
  - Transient presence of microorganisms on hands, surfaces, devices or equipment
  - Treatment not required as microorganisms can be removed by cleaning, hand hygiene or antisepsis
- Colonization
  - The presence and growth of a microorganism in or on the host
  - Multiplication of the microorganism occurs but with no tissue invasion or damage
  - Treatment not required
- Infection
  - The presence and growth of a microorganism in or on the host
  - Tissue invasion and cellular injury occurs with clinical signs and symptoms
  - Sub-clinical infections may not have obvious clinical signs and symptoms
  - Treatment may be required

Mechanism of Action

- Antimicrobials may affect microorganisms by a variety of mechanisms:
  - Inhibition of cell wall synthesis (e.g., β-lactams such as amoxicillin)
  - Disruption of the function and integrity of the cell membrane (e.g. cyclic lipopeptides such as daptomycin)
  - Inhibition of proper ribosomal RNA function thereby inhibiting protein synthesis (e.g. aminoglycosides such as amikacin)
  - Inhibition of DNA synthesis (e.g. fluoroquinolones such as levofloxacin)

Antibacterial Drugs (1/3)

- β-lactams
  - Penicillins (e.g. amoxicillin)
    - Drug of choice for Group A Streptococci
    - Combine with a β-lactamase inhibitor to overcome resistance (e.g., piperacillin-tazobactam)
  - Cephalosporins (e.g. cephalexin)
    - 4th generation drugs have anti-pseudomonal activity
    - Active against methicillin-resistant *Staphylococcus aureus* (MRSA), *Streptococcus pneumonia*
- Fluoroquinolones
  - Levofloxacin, moxifloxacin
    - Associated with increasing resistance, side effects (e.g. neuropathy)
    - Activity against *Psuedomonas aeruginosa*, Gram negative bacilli
    - Prevents DNA replication, cell division

Antibacterial Drugs (2/3)

- Macrolides
  - Azithromycin, clarithromycin
    - Inhibits bacterial cell protein synthesis
    - Used for atypical pneumonia (e.g. *Legionella* sp.) and Gram positive bacteria
- Aminoglycosides
  - Gentamycin, tobramycin
    - Risk of renal toxicity and ototoxicity (use limited to serious or multidrug resistant infections)
- Glycopeptides
  - Vancomycin
    - Inhibits cell wall and membrane biosynthesis
    - Active against *Enterococcus* sp., *Streptococcus* sp.

Antibacterial Drugs (3/3)

- Nitroimidazole
  - Metronidazole
    - Use to treat anaerobic infections and parasites
- Sulfonamide
  - Trimethoprim-sulfamethoxazole
    - Inhibits folate synthesis
    - Use for *Nocardia* spp., *Stenotrophomonas maltophila* infections

Antivirals (1/2)

- **Acyclovir** - first widely used antiviral
  - Derivatives valacyclovir and famciclovir are better absorbed and are preferred oral agents for most indications
  - Strong activity against herpes simplex virus (type I and II)
  - Some activity for varicella-zoster virus, Epstein-Barr virus
- **Ganciclovir**
  - First-line for cytomegalovirus (CMV), life-threatening pneumonitis
- Oseltamavir, zanamivir for treatment of influenza A and B infection

Antivirals (2/2)

- Ribavarin is used for RNA and DNA viruses such as Hepatitis C and Respiratory Syncytial Virus
- **Anti-retrovirals (ARVs)**
  - Treatment of Human Immunodeficiency virus (HIV) uses a combination of various drugs to suppress viral replications
  - ARVs may also be used for post-exposure prophylaxis

Mechanisms of Anti-Retrovirals

- Anti-retrovirals have a variety of mechanisms of action involving the inhibition of:
  - Viral entry (e.g. Maraviroc)
  - Fusion of virus with host cell (e.g., Enfuvirtude)
  - Nucleoside/nucleotide reverse transcriptase (e.g., Lamivudine, zidovudine)
  - Non-nucleoside reverse transcriptase (e.g., Efavirenz)
  - Proteases (e.g., Atazanavir)
  - Integrases (e.g., Raltegravir)

Antifungals and Antiparasitics

- Treatment for invasive aspergillosis and disseminated candidiasis
  - Newer agents include triazoles, voriconazole, posaconazole
- Malaria treatment and prophylaxis
  - Chloroquine, primaquine, quinine, mefloquine, doxycycline
- Treatment of Schistosomiasis
  - Praziquantel
- Treatment for nematodes (round worms)
  - Ivermectin, albendazole

Indications for Use

- Indications for antimicrobial use are the reasons why an antimicrobial might be prescribed.
- There are multiple indications for antimicrobial use based on
  - The need to prevent an infection (prophylaxis)
  - The need to treat an infection with a confirmed cause (therapeutic/pathogen-directed)
  - The need to treat an infection with an unconfirmed cause (empiric)

Prophylactic Antimicrobial Therapy

- Prophylactic therapy is intended to prevent an infection before it occurs
  - Example: The administration of antibiotics prior to a surgical procedure or antivirals after a sharps injury
- Antibiotic selection is based on the most likely cause of possible infection
- Additional considerations:
  - Duration of treatment is ideally as short as possible (e.g. surgical prophylactic antibiotics are typically single dose and discontinued within 24 hours after surgery)
  - Colonization with an antimicrobial-resistant organism
    - Colonization with MRSA may warrant use of vancomycin for surgical prophylaxis but generally antimicrobial therapy for colonization is less effective and not routinely indicated.

Empiric Antimicrobial Therapy

- Empiric treatment occurs when an infection is present but the causative agent is not yet identified.
- Antibiotic selection can be made based on:
  - Site of infection
  - Signs and symptoms
  - Common causes of that type of infection
  - Local epidemiology and resistance (e.g., antibiograms)
  - Antimicrobial Stewardship Program (ASP) principles
  - Antibiotic availability and cost
- Follow established, standardized guidelines if available

Therapeutic (Pathogen-Directed) Antimicrobial Therapy

- Therapeutic treatment occurs when the infectious agent has been identified by typical laboratory methods.
- If culture was used, antimicrobial susceptibility can be determined and used to identify the most appropriate antimicrobial choice.
  - Use narrowest spectrum antimicrobial to reduce the risk of antimicrobial resistance emerging.
- If culture is unavailable, antibiograms can be used to assist in selection.

Narrow Versus Broad Spectrum

- Antimicrobial spectrum refers to the range of microorganisms the antimicrobial agent can kill/inhibit.
  - Narrow spectrum antimicrobials are effective against a limited range of microorganisms
    - E.g. fidaxomicin, amoxicillin
  - Broad spectrum antimicrobials are effective against many types of microorganisms
    - E.g. vancomycin, meropenem
    - More readily selects for antimicrobial-resistant organisms (AROs) than narrow spectrum
    - When used for empiric therapy, can be switched to narrow spectrum infectious agent is identified

Antibiotic-Associated Harms

- Overuse or inappropriate use of antibiotics in long-term care settings have been associated with the following harms:
  - Adverse drug events
  - *Clostridioides difficile* infections
  - Contributing to antimicrobial resistance development
  - Increase risk of infections from AROs

Development of Antimicrobial Resistance

- All use of antimicrobials contributes to the development of resistance by exerting selective pressure.
  - Overuse and improper use of antimicrobials exacerbates the problem
  - Microorganisms adapt to survive
- Mechanisms of antimicrobial resistance include:
  - Altering the site the antimicrobial targets
  - Preventing the antimicrobial from entering and/or accumulating
    - Decreased cell wall permeability, efflux pumps (pump out antimicrobials as they enter)
  - Inactivating the drug
- Resistance can arise from genetic mutations or acquiring plasmids carrying resistance genes.

Discussion/Knowledge Check

Antimicrobial Susceptibility

Antibiograms

- Antibiograms are a profile of the antimicrobial susceptibility of bacterial isolates within a given region or health care setting (e.g., individual long-term care home).
  - Can be used to guide selection of antibiotics
  - Can use to monitor antimicrobial resistance trends and identify targets for stewardship interventions
- Presented as aggregate and cumulative data
  - Percentage of isolates exhibiting susceptibility to a particular antimicrobial

Antibiogram Example

	amikacin		Amoxicillin-Clavulanic acid		Ampicillin / Amoxicillin		Cefazolin		Ceftazidime		Ceftriaxone		Ciprofloxacin		Cloxacillin		Doxycycline	
	#	% S	#	% S	#	% S	#	% S	#	% S	#	% S	#	% S	#	% S	#	% S
Acinetobacter sp.	115	95	3	0	3	0	3	0	122	90	3	0	124	86				
Citrobacter sp.	539	100	288	1	493	0	500	0	374	29	468	19	1421	90			15	87
Enterobacter sp.	1661	100	842	0	1492	0	1583	0	952	42	1534	40	4148	92	25	0	41	34
Escherichia coli - ALL	23299	100	35967	79	59083	55	51558	82	30018	86	53179	87	59570	75			643	32
Haemophilus influenzae			14	100	228	69			14	100	14	100						
Klebsiella sp.	5880	100	8393	92	8581	0	12230	79	7930	91	13387	91	14443	90			47	96
Morganella morganii	239	100	62	0	273	0	265	0	92	25	270	10	398	77				
Pseudomonas aeruginosa	5481	97	240	0	240	0	645	4	11170	90	376	3	11068	85				
Serratia sp.	630	100	132	0	521	0	546	0	109	15	389	26	956	94				

Antimicrobial Stewardship Programs

Antimicrobial Stewardship

- Antimicrobial stewardship promotes the optimal selection of type, duration, route of administration and dosage of antimicrobials to limit unintended consequences of antimicrobial use.
- Stewardship is needed to reduce antibiotic-associated harms.
- The goals of antimicrobial stewardship are to:
  - Optimize clinical outcomes
  - Reduce unnecessary treatment
  - Preserve efficacy of antimicrobials

Antimicrobial Stewardship Program Elements

- Leadership
- Interventions
- Monitoring
- Evaluation
- Future research

Leadership

- A key component of the ASP program is the formation of an ASP team.
- The team requires leadership support to ensure there will be accountability, advocacy and adequate resources (both human and financial).
  - Senior management lead
    - Advocate for resources including expertise and designating the ASP as a priority
    - Provide support for training in ASP initiatives
    - Monitoring ASP performance
  - Program lead
    - Monitor program development and coordinate program measures
    - Could be a quality improvement specialist, project coordinator or clinical lead

ASP Team Members (1/2)

- In addition to formal leadership for the ASP team, other members include:
  - Medical lead
    - Involved in reviewing data, championing initiatives and reinforcing the standardization of prescribing
    - Could be a medical director or nurse practitioner
  - Nursing lead
    - Reinforce best practices to prevent infections (e.g., prevention of pressure ulcers, advocating for prompt removal of indwelling urinary catheters when no longer necessary)
    - Reinforce assessment and documentation standardization
  - Pharmacy expertise
    - Provide expertise on optimizing the selection, dosage and duration of antimicrobials
    - Perform medication reviews and assess appropriateness of antimicrobial use
    - Promote awareness and the importance of the ASP

ASP Team Members (2/2)

- In addition to formal leadership for the ASP team, other members include:
  - IPAC expertise
    - Support the ASP by contributing surveillance data on health care-associated ARO and C. difficile infections
    - Promoting IPAC best practices to reduce the risk of infections
  - Laboratory expertise
    - Provide antibiograms to support the optimal selection of antimicrobials
  - Additional local resources
    - Partnering or engaging with public health units or other health care organizations (e.g. a local hospital) to solicit additional support or resources

Interventions

- It is important to understand what is and what is not appropriate antimicrobial use.
- Set minimum criteria for initiation of antimicrobial treatment
  - Identify the signs and symptoms for common infections that need to be present to prompt initiation of antimicrobial therapy
  - Communicate need to reassess choice of antimicrobial agent once laboratory results are available
- Use standardized treatment guidelines
  - Guide the selection, dose, route of administration and duration of antimicrobial treatment

Identifying Priorities

- Focus on the highest risk infection types (i.e., those most commonly associated with inappropriate antibiotic treatment in LTCHs).
  - Asymptomatic bacteriuria
  - Upper respiratory/viral infections
  - Wound infections
- Prolonged antibiotic use
  - E.g., review treatment for complicated cases such as chronic diabetic foot infections
- Practices where there is no timely review of antibiotic therapy

Before Prescription Interventions (1/2)

- Standardization of resident assessment
  - Situation-Background-Assessment-Recommendation (SBAR) tools provide a standardized framework for communication between health care workers (e.g., nurses to physicians).
- Diagnostic testing stewardship
  - Established guidelines for diagnostic testing can reduce treatment decisions based on incidental findings or positive lab results in the absence of clinical signs/symptoms of infections.
    - E.g., a positive urine culture from a resident with no signs/symptoms of a urinary tract infection may indicate asymptomatic bacteriuria which does not need treatment

Before Prescription Interventions (2/2)

- Audit and Feedback to the Prescriber
  - Compare prescribing practices between peers
  - Compare to accepted guidelines
  - Prescribers should regularly review their own prescribing reports
- Education
  - Consistent message on the importance of antimicrobial stewardship to all stakeholders (i.e. prescribers, clinical staff, residents, families)
    - Education strategies need to be mindful of barriers to behavior change
  - Required ASP practices in LTCHs

At Prescription Interventions (1/2)

- Indication
  - Treatment indication should be documented for review later
- Optimize Selection
  - Use antibiograms to inform empiric treatment
- Optimize administration route
  - Oral therapy is preferred, timely transitions from intravenous to oral therapy should be promoted
- Allergy verification
  - Allergy assessments and penicillin skin testing if indicated to prevent inappropriate avoidance of lower risk treatments

At Prescription Interventions (2/2)

- Preauthorization
  - Prescribers must obtain approval for use of certain antibiotics from a designated position of expertise (e.g., pharmacist)
  - Labour intensive and LTCHs may not have access to available expertise

After the Prescription

- Antibiotic “time-outs”
  - Regular prompts to review the status of the resident to ensure treatment is still warranted
  - Consult with any relevant laboratory or diagnostic imaging results
  - Assess treatment: should it be stopped, switched or continued?
- Pharmacy medication reviews (prospective audit and feedback)
  - Antibiotic orders are reviewed and feedback is provided to the prescriber
  - Prescribers can stop or change treatment based on the feedback
  - Labour intensive and LTCHs may not have access to available expertise

Strategies for Implementing ASP Interventions

- Use multiple strategies to address behavior change.
  - Education sessions, infographics, algorithms, pocket guides
- Algorithms can be used to simplify and standardize decision-making.
- Start small with one or two practice changes at a time.
  - Focus on areas that can be improved such as diagnostic stewardship to support appropriate urine testing or *C. difficile* testing.

Monitoring (1/2)

- Collecting data for the ASP is important to ensure the program is effective
  - Sources of data include laboratory reports, chart reviews, sentinel reporting systems, rounds
- Monitoring of process measures
  - Assessing compliance with ASP initiatives
    - Compliance with adherence to start criteria
    - Compliance with new ASP practices (e.g. were reassessments performed if time-outs were implemented)
  - Low adherence rates should be investigated to identify and address barriers

Monitoring (2/2)

- Monitoring of outcome measures
  - Antibiotic starts
    - Determine the rate of new antibiotic starts overall or for specific types of infections
  - Days of Therapy (DOT)
    - Number of a days that a resident is on a unique antibiotic (i.e., if a resident is on two antibiotics simultaneously for five days, the DOT is ten)
    - A reduction in DOT may indicate that the ASP is effective in reducing unnecessary antimicrobial use
  - Costs
    - ASPs have been associated with reduced costs therefore monitoring costs associated with antibiotic prescribing (e.g., focusing on high-cost antibiotics)
  - Healthcare-associated *C. difficile* infection (CDI) rates

Evaluation (1/2)

- Ongoing quality improvement and feedback is needed to ensure the ASP is effective and sustainable
- Need to consider strategies to maintain momentum in the event of staff turnover, loss of organizational support or staff reverting to previous processes
- Consider if additional education is needed for ASP team members

Evaluation (2/2)

- Feedback
  - Data from process and outcome measures should be routinely shared with ASP team members
  - Can use data to reflect on current practices, identify new strategies to address existing barriers
- Integrate changes
  - ASP practices should be integrated in the work culture of the LTCH
    - Strategies should be incorporated into policies and procedures, orientation packages and employee resources
    - Can also be included in resident and family resources

ASP Challenges in Long-term Care

- Atypical presentation of symptoms may delay diagnosis
- Cognitive impairment may affect communication of symptoms
- Age-related risk of infections due to impaired immune response
- Frequent hospitalizations

Discussion/Knowledge Check

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