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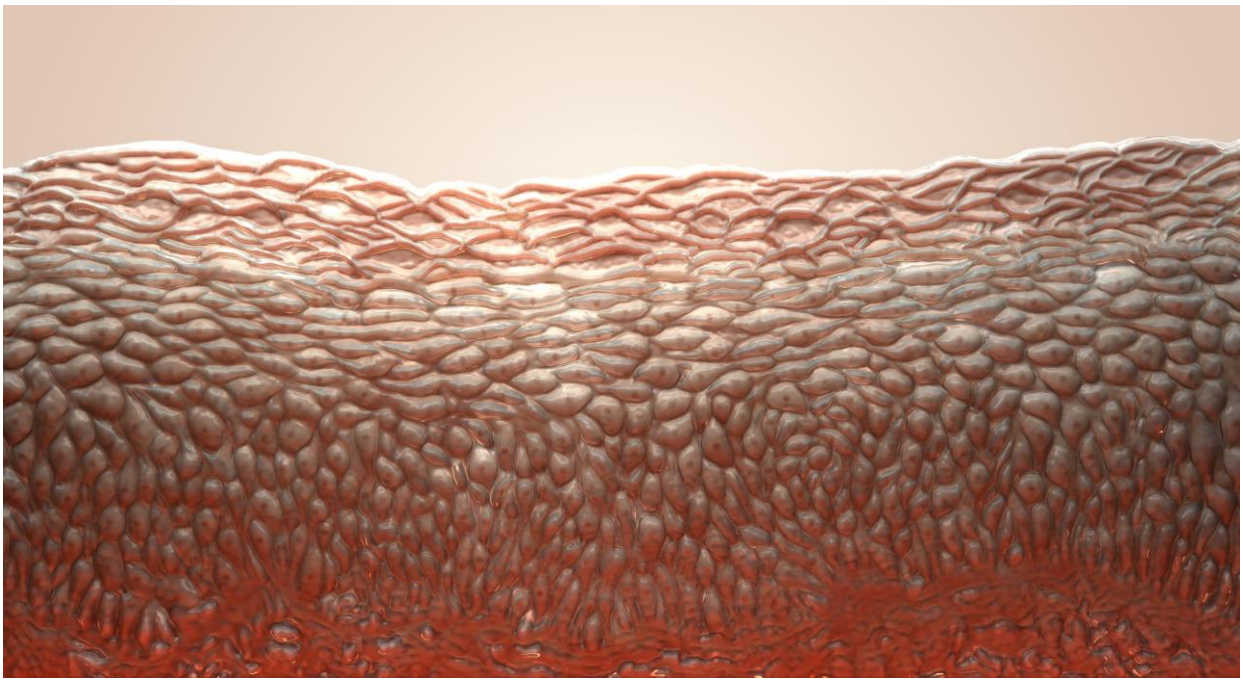
EVIDENCE BRIEF

Duration of Antibiotic Treatment for Uncomplicated Cellulitis in Long-Term Care Residents



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Key Messages

- Recent evidence suggests that short courses of antibiotics (5-7 days) are appropriate for residents with cellulitis that are responding to therapy by day five with no deep-seated infection.
- There are several advantages to short course antibiotic therapy when compared to longer durations, including less side effects,[1,2] less risk of antibiotic-resistant organisms[3,4] and less risk of *C. difficile* infection.[5]

Issue and Research Question

Overuse of antimicrobial therapy in the long-term care (LTC) setting is common and leads to patient harm.[6] Seventy eight (78) % of Ontario LTC residents will receive at least one course of antimicrobial therapy over the course of a year. Skin infections are one of the most common indications for antibiotic therapy in the LTC setting. Approximately 13% of antibiotic courses are prescribed for skin and soft tissue infections, the most common of which is cellulitis.[7]

Sixty three (63) % of prescribed courses of antibiotic treatment in LTC are longer than 10 days. Duration of therapy varies drastically based on prescriber, but not patient characteristics.[8] This data suggests that habit and experience play a large role in antibiotic prescribing patterns in long-term care. Prolonged treatment specifically for skin infections is common. A study in hospitalized patients found that the average length of therapy was 13 days (IQR 10-14 days).[9] Excessive durations of antibiotics are often prescribed for cellulitis because the clinical signs of inflammation (such as redness, swelling and discomfort) persist long after the causative bacteria have been eradicated.

Uncertainty exists regarding the appropriate management of uncomplicated cellulitis in residents of LTC homes, particularly with respect to the appropriate duration of therapy. This document will summarize the literature pertaining to treatment duration for uncomplicated cellulitis, particularly as it relates to residents of LTC homes.

Methods

An initial Cochrane Database search was performed to determine if there were any relevant systematic reviews or guidelines pertaining to duration of therapy for uncomplicated cellulitis, particularly in older individuals. Following this, a full primary literature search was performed. On April 11, 2017, Public Health Ontario (PHO) Library Services performed a literature search of articles published since 2004 using three databases (MEDLINE, Embase, CINAHL). The search included the concepts “cellulitis,” “antibiotic” and “duration.” Both primary literature and review articles were searched to comprehensively capture all relevant literature. English-language articles retrieved by the searches were assessed for eligibility by PHO staff. Articles were included if they were interventional studies comparing short course (<7 days) to longer courses (≥ 7 days) for treatment of cellulitis. Studies were included if different agents were used in each treatment arm; however, single dose treatment studies were excluded.

Main Findings

The initial literature search for articles published since 2004 retrieved 2248 references. After title and abstract screening, three eligible studies were found on this topic.
No systematic reviews were found on this topic.

> **Short course antibiotic therapy (5-7 days) results in similar outcomes compared to long durations (10 days) for uncomplicated cellulitis.**

Of the three studies,[10,11,12] a total of 1,420 patients with acute skin infections were included. Studies were all randomized controlled trials, two of which used non-inferiority designs.[11,12] Short course therapy ranged from 5 to 6 days, whereas longer course therapy was 10 days in each study. One study used the same drug (levofloxacin)[10] in both long and short course groups, whereas the other two used a different medication within the same class (tedizolid in short course, linezolid in long course group).[11,12] No studies focused on long-term care residents specifically; however, a number of cellulitis patients were hospitalized; 13% in Hepburn et al,[10] 42% in Moran et al,[12] not reported in Prokocimer et al.[11] The mean age range was 43 to 52 years of age. One study allowed for short course if patients had at least minimal improvement by day five of therapy, whereas the others were fixed courses of treatment regardless of symptom improvement.

All studies found no difference in clinical outcomes between short and long course therapy. Outcomes included resolution of infection both early in therapy and after completion of the treatment course. No differences in overall rates of adverse events were reported between study groups.

Appendix A is a table summarizing all studies comparing short course (less than 7 days) to long course (7-14 days) of antibiotics for treatment of uncomplicated cellulitis.

Discussion and Conclusions

Data from adult patients with cellulitis indicate that short courses of antibiotics (5-6 days) have similar efficacy to longer courses (10 days) in terms of clinical cure of infection. These studies included both outpatient and inpatients.

Limitations of this data include:

- Lack of data in older adults
- No studies in LTC setting
- Antibiotic agents used are not currently recommended for first line therapy for cellulitis

Older adults are at increased risk of infections, including those involving the skin. This is in part due to reduced immunocompetence, thinning of the skin and reduced blood flow. Additionally, cognitive factors may result in delayed reporting and recognition of skin infections.

On the other hand, given the lack of data to support prolonged duration of therapy for cellulitis, in addition to the paucibacillary nature of these infections, short course treatment is desirable for all patients with uncomplicated infection including older residents of LTC homes. A short course is reasonable in patients who have initially responded to infection by day five, have no un-drained collection or lesion requiring debridement, no deep-seated infection and adequate circulation at the site of infection.

There are several risks to prolonged courses of antimicrobial therapy. Due to physiological changes associated with aging, older adults are more susceptible to the negative consequences of antibiotics, including adverse effects and drug interactions.[13] Prolonged antimicrobial therapy has been shown in many studies to result in a greater risk of acquiring antibiotic resistant organisms.[3,4] Additionally, longer durations of antimicrobial therapy are associated with increased risk of *C. difficile* infection (CDI).[5] Older adults are already more susceptible to CDI and more likely to suffer morbidity and mortality from this infection.[14]

Given the lack of proven efficacy with longer courses, in combination with the risks associated with prolonged antibiotic therapy, short course treatment should be used whenever possible for management of uncomplicated cellulitis in LTC home residents.

Appendix A: Studies Comparing Duration of Antibiotic Therapy for Uncomplicated Cellulitis

Study	Design	Patients	Intervention	Comparator	Outcomes
Hepburn, 2004[10]	Randomized Double blind Single-center ITT, superiority analysis	Uncomplicated cellulitis, presenting to emergency department or a or ambulatory clinic in adults (13% hospitalized) (with at least minimal improvement by 5 days of therapy) n=87 randomized mean age = 52.5 y	5 days treatment: Complete 5 days of antibiotic therapy with levofloxacin 500 mg PO daily Plus placebo for an additional 5 days	10 days treatment: Complete 5 days of antibiotic therapy with levofloxacin 500 mg PO daily Plus levofloxacin for an additional 5 days	Resolution of infection (at day 14) with no symptom recurrence (at day 28): 5 days: 98% 10 days: 98% P>0.05 No serious adverse events reported
Prokocimer, 2013 ESTABLISH-1[11]	Randomized Double blind Multi-center ITT, Non-inferiority (margin=10%) analysis	Acute bacterial skin and skin structure infections in adults (complicated: at least 1 local and 1 regional or systemic manifestation). Gram positive infection suspected or documented.	Tedizolid 200 mg PO once daily x 6 days	Linezolid 600 mg PO bid x 10 days	Early clinical response (48-72h): Tedizolid: 79.5% Linezolid: 79.4% Treatment difference 0.1% [95% CI, −6.1% to 6.2%]) Sustained clinical response (day 11): Tedizolid: 69.3% Linezolid: 71.9% Treatment difference -2.6% [95% CI, −9.6% to 4.2%])

Study	Design	Patients	Intervention	Comparator	Outcomes
		n=667 randomized mean age = 43.3 y			Adverse events: Tedizolid: 40.8% Linezolid: 43.3% No statistically significant difference
Moran G, 2014 ESTABLISH-2[12]	Randomized Double blind Multi-center ITT, Non-inferiority (margin=10%) analysis	Patients ≥ 12 years with acute bacterial skin and skin structure infections Minimum lesion area 75 cm^2 and suspected or documented gram positive pathogen (42.5% hospitalized) n=666 randomized mean age = 46 y	Tedizolid 200 mg daily x 6 days IV → PO Switch if clinical improvement and afebrile	Linezolid 600 mg BID x 10 days IV → PO Switch if clinical improvement and afebrile	Early clinical response (48-72h): Tedizolid: 85% Linezolid: 83% Treatment difference 2.6% [95% CI, −3.0% to 8.2%]) End of treatment response: Tedizolid: 87% Linezolid: 88% Treatment difference -1.0% [95% CI, −6.1% to 4.1%]) Adverse events: Tedizolid: 45% Linezolid: 43% No statistically significant difference

Specifications and Limitations of Evidence Brief

The purpose of this Evidence Brief is to investigate a research question in a timely manner to help inform decision making. The Evidence Brief presents key findings, based on a systematic search of the best available evidence near the time of publication, as well as systematic screening and extraction of the data from that evidence. It does not report the same level of detail as a full systematic review. Every attempt has been made to incorporate the highest level of evidence on the topic. There may be relevant individual studies that are not included; however, it is important to consider at the time of use of this brief whether individual studies would alter the conclusions drawn from the document.

Additional Resources

- Duration of Antibiotic Treatment for Pneumonia in Long-Term Care Residents (Evidence Brief)
- Shorter is Smarter: Reducing Duration of Antibiotic Treatment for Common Infections in Long-Term Care (Fact Sheet)
- Shorter is Smarter: Reduce Duration of Antibiotic Therapy in Long-Term Care (Infographic)
- Duration of Antibiotic Treatment for Uncomplicated Urinary Tract Infection in Long-Term Care Residents (Evidence Brief)

References

1. Milo G, Katchman EA, Paul M, Christiaens T, Baerheim A, Leibovici L. Duration of antibacterial treatment for uncomplicated urinary tract infection in women. Cochrane Database Syst Rev. 2005;(2):CD004682.

2. Vogel T, Verreault R, Gourdeau M, Morin M, Grenier-Gosselin L, Rochette L. Optimal duration of antibiotic therapy for uncomplicated urinary tract infection in older women: a double-blind randomized controlled trial. CMAJ. 2004;170(4):469-73. Available from: http://www.cmaj.ca/content/cmaj/170/4/469.full.pdf

3. Chastre J, Wolff M, Fagon JY, Chevret S, Thomas F, Wermert D, et al. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: a randomized trial. JAMA. 2003;290(19):2588-98. Available from: https://jamanetwork.com/journals/jama/fullarticle/197644

4. Goessens WH, Verbrugh HA. [Antibiotic resistance: epidemiological developments and preventive measures]. Ned Tijdschr Geneeskd. 2007;151(13):748-52.

5. Owens RC, Donskey CJ, Gaynes RP, Loo VG, Muto CA. Antimicrobial-associated risk factors for Clostridium difficile infection. Clin Infect Dis. 2008;46 Suppl 1:S19-31. Available from: https://academic.oup.com/cid/article/46/Supplement_1/S19/455084

6. Daneman N, Bronskill SE, Gruneir A, Newman AM, Fischer HD, Rochon PA, et al. Variability in antibiotic use across nursing homes and the risk of antibiotic-related adverse outcomes for individual residents. JAMA Intern Med. 2015;175(8):1331-9. Available from: https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2337257

7. Loeb M, Simor AE, Landry L, Walter S, McArthur M, Duffy J, et al. Antibiotic use in Ontario facilities that provide chronic care. J Gen Int Med. 2001;16(6):376-83. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1495221/

8. Daneman N, Gruneir A, Bronskill SE, Newman A, Fischer HD, Rochon PA, et al. Prolonged antibiotic treatment in long-term care: role of the prescriber. JAMA Intern Med. 2013;173(8):673-82. Available from: https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/1669102

9. Jenkins TC, Sabel AL, Sarcone EE, Price CS, Mehler PS, Burman WJ. Skin and soft-tissue infections requiring hospitalization at an academic medical center: opportunities for antimicrobial stewardship. Clin Infect Dis. 2010;51(8):895-903. Available from: https://academic.oup.com/cid/article/51/8/895/331695

10. Hepburn MJ, Dooley DP, Skidmore PJ, Ellis MW, Starnes WF, Hasewinkle WC. Comparison of short-course (5 days) and standard (10 days) treatment for uncomplicated cellulitis. Arch Intern

Med. 2004;164(15):1669-74. Available from: https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/760487

11. Prokocimer P, De Anda C, Fang E, Mehra P, Das A. Tedizolid phosphate vs linezolid for treatment of acute bacterial skin and skin structure infections: the ESTABLISH-1 randomized trial. JAMA. 2013;309(6):559-69. Available from: https://jamanetwork.com/journals/jama/fullarticle/1570280

12. Moran GJ, Fang E, Corey GR, Das AF, De Anda C, Prokocimer P. Tedizolid for 6 days versus linezolid for 10 days for acute bacterial skin and skin-structure infections (ESTABLISH-2): a randomised, double-blind, phase 3, non-inferiority trial. Lancet Infect Dis. 2014;14(8):696-705.

13. Faulkner CM, Cox HL, Williamson JC. Unique aspects of antimicrobial use in older adults. Clin Infect Dis. 2005;40(7):997-1004. Available from: https://academic.oup.com/cid/article/40/7/997/373878

14. Miller M, Gravel D, Mulvey M, Taylor G, Boyd D, Simor A, et al. Health care-associated Clostridium difficile infection in Canada: patient age and infecting strain type are highly predictive of severe outcome and mortality. Clin Infect Dis. 2010;50(2):194-201. Available from: https://academic.oup.com/cid/article/50/2/194/328758

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