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EVIDENCE BRIEF

Duration of Antibiotic Treatment for Pneumonia in Long-Term Care Residents

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Key Messages

- Recent evidence suggests that short courses of antibiotics (5-7 five to seven days) are appropriate for residents with pneumonia that show signs of respiratory stability and clinical improvement.
- 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. Pneumonia is one of the most common indications for antibiotic therapy in the LTC setting. Approximately 36% of antibiotic courses are prescribed for respiratory tract infections (including pneumonia).[7]

Sixty three (63) % of all 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 pneumonia is common. A study in hospitalized patients found that approximately 40% of patients received a duration longer than seven days.[9]

Uncertainty exists regarding the appropriate management of pneumonia 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 pneumonia with a focus on its implications to residents of LTC homes.

Methods

An initial literature search was performed to identify relevant systematic reviews or guidelines pertaining to duration of therapy for pneumonia, particularly in elderly individuals. Following this, a full primary literature search was performed. On December 4, 2017 Public Health Ontario (PHO) Library Services performed a literature search of articles published since 2011 using three databases (MEDLINE, Embase, CINAHL). The search included the concepts “pneumonia,” “antibiotic” and “duration.” English-language articles retrieved by the searches were assessed for eligibility by PHO staff. Articles were included if they were English-language interventional studies comparing short course (<7 days) to longer courses (≥ 7 days) for treatment of pneumonia in adults. Studies were included if different agents were used in each treatment arm. There were no exclusions to setting of pneumonia acquisition.

Main Findings

The initial literature search for systematic review articles resulted in retrieval of a review of antibiotic treatment duration for bacteremia in the critically ill published in 2011.[10] Given the lack of bacteremia trials, this article presented all RCTs evaluating short vs. long course antibiotic therapy for pneumonia. A total of seven English-language RCTs focusing on treatment duration in adults with pneumonia were retrieved.

> **Short course antibiotic therapy (5-7 days) results in similar outcomes compared to long durations (10-14 days) for pneumonia.**

The full primary literature search for articles published since 2011 produced 436 results. After title and abstract screening, four RCTs were included. Including the pre-2011 articles, the total number of relevant studies was 11.[14-24]

The majority of studies (n=9) evaluated duration in patients with community-acquired pneumonia, while the remainder (n=2) included patients with ventilator-associated pneumonia. In terms of setting of treatment, most studies included hospitalized patients (n=8), followed by outpatient and inpatient (n=2) and only outpatients (n=1). There were no studies focusing on LTC as the setting of acquisition or treatment for pneumonia. Short course treatment ranged from 3 to 8 days of therapy, whereas long course treatment ranged from 7-14 days in duration.

Most common outcome measures related to resolution of symptoms at completion of treatment. All studies found no differences in clinical outcomes between short and long course therapy. Appendix A provides detail for each study reviewed.

Discussion and Conclusions

Data from adult patients with pneumonia indicate that short courses of antibiotics (5-7 days) have similar efficacy to longer courses (10-14 days) in terms of clinical cure of infection. These studies include both outpatient and institutionalized patients with infection.

Limitations of this data include a lack of data specifically evaluating older adults, as well as a lack of studies in LTC setting.

Despite this lack of data in the LTC population, this is an important group to evaluate. Residents of LTC homes are more likely to have risk factors for aspiration and subsequent pneumonia (antipsychotic use, dysphagia, neurological conditions).[11] Additionally, cognitive factors may result in delayed reporting and recognition of pneumonia.

Although the risk of pneumonia in LTC residents is elevated, no data exists to support prolonged duration of treatment for those who have a respiratory infection. Additionally, given the lack of benefit of prolonged duration for pneumonia in other patient settings (including patients admitted to acute care wards and intensive care units), short course treatment is desirable for all patients including older residents of LTC homes. A 5-day course is reasonable in patients who have initially responded (respiratory stability and afebrile) and have no evidence of deep-seated infection (e.g., empyema, lung abscess).

Further, 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.[12] 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.[13]

Given the lack of proven efficacy with longer courses, in combination with the risks associated with prolonged antibiotic therapy, short course treatment (5-7 days) should be used whenever possible for management of pneumonia in LTC home residents.

Appendix A: Studies Comparing Duration of Antibiotic Therapy for Pneumonia

Study	Design	Patients	Intervention	Comparator	Outcomes
Tellier et al., 2004[14]	Randomized Double blind Multi-center Modified ITT, Non-inferiority analysis (margin 15%)	Community-Acquired Pneumonia Outpatient and Hospitalized N=581 Mean age = 42 (17% over age 65)	Telithromycin 800 mg PO daily for 5 days	Telithromycin 800 mg PO daily for 7 days Clarithromycin 500 mg PO twice daily for 10 days	Clinical cure at end of therapy: Telithromycin 5 days: 89.3% Telithromycin 7 days: 88.8% Clarithromycin: 10 days: 91.8% Telithromycin 5d – Clarithromycin treatment difference: -2.5% [95% CI -9.7 to 4.7] No statistically significant difference between groups
File et al., 2007[15]	Randomized Double blind Multi-center ITT, non-inferiority analysis (margin 10%)	Community-Acquired Pneumonia Outpatient N=510 Mean age =45 (16 % over age 65)	Gemifloxacin 320 mg PO daily for 5 days	Gemifloxacin 320 mg PO daily for 7 days	Clinical resolution at follow up: 5 days: 95% 7 days: 92% Treatment difference: -3.0 [95% CI: -1.48 to 7.42] No statistically significant difference
Dunbar et al., 2003[16]	Randomized Double blind Multi-center ITT, non-inferiority analysis (margin 15%)	Community-Acquired Pneumonia Outpatient and Hospitalized N=530 Mean age=54	Levofloxacin 750 mg PO daily for 5 days	Levofloxacin 500 mg PO daily for 10 days	Clinical resolution at end of treatment: 5 days: 92.4% 10 days: 91.1% Treatment difference: -1.3 (95% CI: -7.0 to 4.4) No statistically significant difference

Study	Design	Patients	Intervention	Comparator	Outcomes
Leophonte et al., 2002[17]	Randomized Double blind Multi-center Non-inferiority analysis (margin 10%)	Community-Acquired Pneumonia Hospitalized N=204 Mean age = 64	Ceftriaxone 1 g IV daily for 5 days	Ceftriaxone 1 g IV daily for 10 days	Clinical resolution at 10 days: 5 days: 81.9% 10 days: 82.6% No significant difference between groups. 5 days non-inferior to 10 days.
Siegel et al., 1999[18]	Randomized Double blind Single Center ITT analysis	Community-Acquired Pneumonia Hospitalized N=46 Mean age = 61	Cefuroxime 7 days Cefuroxime 750 mg IV q8h x 2 days then Cefuroxime axetil 500 mg PO q12h x 5 days	Cefuroxime 10 days Cefuroxime 750 mg q8h x 2 days then Cefuroxime axetil 500 mg PO q12h x 5 days	Clinical resolution: 7 days: 87.5% 10 days: 90.9% Treatment difference: 3.4% {95% CI: -14.5 to 21.3%] No statistically significant difference between groups.
El Moussaoui et al., 2006[19]	Randomized Double blind Multi-center non-inferiority analysis (margin 10%)	Community-Acquired Pneumonia (with substantial improvement at 72h) Hospitalized N=121 Median age = 54-60	3 days Amoxicillin IV x 3 days	8 days Amoxicillin IV x 3 days then Amoxicillin PO x 5 days	Clinical success rate 3 days: 93% 8 days: 93% Treatment difference: 0.1% [95% CI: -9% to 10%] 3 days non-inferior to 8 days.

Study	Design	Patients	Intervention	Comparator	Outcomes
Chastre et al., 2003[20]	Randomized Double blind Multi-center ITT, non-inferiority analysis (margin 10%)	Ventilator-Associated Pneumonia Hospitalized in ICU N=402 Mean age = 61	8 days (antibiotic selection at discretion of physician)	15 days (antibiotic selection at discretion of physician)	Mortality 8 days: 18.8% 15 days: 17.2% Treatment difference: 1.6% [90% CI: -3.7% to 6.9%] Recurrence 8 days: 28.9% 15 days: 26% Treatment difference: 2.9% [90% CI: -3.2% to 9.1%] 8 days non-inferior to 15 days with less antibiotic use and less emergence of resistance. Non-fermenting gram negative (e.g., *Pseudomonas aeruginosa*) organisms may require longer treatment.
Zhao, 2016[21]	Randomized Open label Multi-center ITT analysis Non-inferiority trial (margin 10%)	Community-Acquired Pneumonia Hospitalized N=457 Mean age = 41	Levofloxacin 750 mg IV x 5 days	Levofloxacin 500 mg IV/PO*x 7-14 days *IV/PO switch when fever decrease, WBC normal, and able to take oral drugs	Clinical efficacy at end of treatment: 5 days: 91.40% 7-14 days (mean 10.4 d): 94.27% Treatment difference: -2.87 [95% CI -7.64 to 1.90] 5 days non-inferior to 7-14 days.
Uranga, 2016[22]	Randomized Multicenter	Community-Acquired Pneumonia	Antibiotic duration minimum x 5 days	Antibiotic duration per physician	Clinical success at day 10: Intervention (median 5 days): 56.3% Control (median 10 days): 48.6%

Study	Design	Patients	Intervention	Comparator	Outcomes
	ITT analysis Non-inferiority trial	Hospitalized N=312 Mean age = 65	stopped if: - temp≤37.8°C x 48hr - AND ≤ 1 CAP associated sign of clinical instability		P=0.18 5 days based on clinical stability non-inferior to longer course.
Zhao, 2014[23]	Randomized Open label Multi-center Non-inferiority trial (margin 10%)	Community-Acquired Pneumonia Hospitalized N=241 Mean age = 41	Levofloxacin 750mg IV x 5 days	Levofloxacin 500mg IV x 7-14 days	Overall efficacy at 7-14 days after last dose: 5 days: 86.2% 7-14 days: 84.7% Treatment difference: 1.6 (95% CI [-7.8, 10.9]) Short course non-inferior to longer course.
Capellier 2012[24]	Randomized Open-label Multicenter Equivalence analysis (margin=10%)	Ventilator-associated pneumonia Hospitalized in ICU N=225 Mean age = 49	Beta-lactams x 8 days (combined with aminoglycoside x 5 days)	Beta-lactams x 15 days (combined with aminoglycoside x 5 days)	Clinical cure rate at day 21: 8 days: 85.3% 15 days: 84.5% Treatment difference: 0.9% [95% CI -8.4 to 10.3] 8 days non-inferior to 15 days.

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 Uncomplicated Cellulitis 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)

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