Constitutional Symptoms Trigger Diagnostic Testing Before Antibiotic Prescribing in High-Risk Nursing Home Residents

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OBJECTIVES: To evaluate the use of diagnostic testing before treating an infection in nursing home (NH) residents suspected of having a urinary tract infection (UTI) or pneumonia.

DESIGN: Prospective longitudinal study nested within a randomized trial, using data from control sites.

SETTING: Six NHs in southeast Michigan.

PARTICIPANTS: NH residents with an indwelling urinary catheter, enteral feeding tube, or both (N = 162) with 695 follow-up visits (189 (28%) visits with an infection).

MEASUREMENTS: Clinical and demographic data—including information on incident infections, antibiotic use, and results of diagnostic tests—were obtained at study enrollment, after 14 days, and monthly thereafter for up to 1 year.

RESULTS: One hundred (62%) NH residents had an incident infection requiring antibiotics, with substantial variations between NHs. In addition to presence of infection-specific symptoms, change in function was a significant predictor of ordering a chest X-ray to detect pneumonia (odds ratio (OR) = 1.7, $P = .01$). Similarly, change in mentation was a significant predictor of ordering a urinalysis (OR = 1.9, $P = .02$), chest X-ray (OR = 3.3, $P < .001$), and blood culture (OR = 2.3, $P = .02$). Antibiotics were used empirically, before laboratory results were available, in 50 of 233 suspected cases of UTI (21.5%) and 16 of 53 (30.2%) suspected cases of pneumonia. Antibiotics were used in 17% of visits without documented clinical or laboratory evidence of infection.

CONCLUSION: Constitutional symptoms such as change in function and mentation commonly lead to diagnostic testing and subsequent antibiotic prescribing. Antibiotic use often continues despite negative test results and should be a target for future interventions. **J Am Geriatr Soc 64:1975–1980, 2016.**

Key words: antibiotic stewardship; nursing homes; functional decline

In the United States, approximately 1.4 million people live in more than 15,000 nursing homes (NHs).[1] These facilities are crucial to meet the postacute and long-term care needs of older adults. Multiple comorbidities are common in this population, which contributes to polypharmacy, often with the eventual development of antimicrobial resistance and inadvertent side effects.[2–5] NHs are increasingly recognized as reservoirs of multidrug-resistant organisms (MDROs).[5,6]

Antibiotics are one of the most frequently prescribed medications in NHs, with 6% to 10% of residents receiving these medications at any given time[2,7] and 50% to 80% receiving at least one prescription over the course of a year.[8–10] An estimated 25% to 75% of antibiotic prescriptions for NH residents do not meet clinical guidelines for appropriate prescribing.[11–16] Empirical antibiotic treatment (preemptive administration of antibiotics before a definitive diagnosis is made) is particularly troubling because it contributes to overuse and can be reduced through thoughtful practical interventions.[2–6]

Diagnosis of infections in older NH residents is particularly challenging because they are often frail, have multiple comorbidities, and commonly have atypical clinical presentations.[17,18] For instance, fever may be low or absent in older persons with infections. Moreover, physician visits tend to be infrequent, with many antibiotics prescribed through telephone orders, often by on-call physicians, and initiated without a preceding physical

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examination or confirmatory diagnostic test.[3,14] Ideally, in the absence of an advanced directive from the resident or primary caregiver limiting medical interventions, NH residents with a suspected infection should have appropriate diagnostic laboratory tests performed and the results reviewed by their primary care provider.[19] Although early administration of antibiotics may be prudent in severe cases, most situations can be managed conservatively while awaiting diagnostic test results.

The aim of this study was to evaluate the use and timing of diagnostic testing before initiating an antibiotic regimen in high-risk NH residents with indwelling devices suspected of having a urinary tract infection (UTI), pneumonia, or both. Presenting symptoms that lead to diagnostic testing and subsequent antibiotic prescribing were of particular interest. Understanding these triggers is crucial to design interventions that change the behavior of physicians, physician extenders, nurses, and care providers and improve patient outcomes.

METHODS

Study Population and Design

The parent study from which data for this longitudinal cohort were taken was a cluster-randomized intervention trial conducted in 12 community-based NHs located in southeast Michigan from May 2010 to May 2013.[20] The goal of the parent study was to design, implement, and evaluate the efficacy of a multicomponent Targeted Infection Prevention (TIP) Program in reducing MDRO prevalence and infections in high-risk NH residents. The institutional review board of the University of Michigan approved the project. Trained research staff employed by the Division of Geriatric and Palliative Care Medicine at the University of Michigan who had clinical experience in NHs collected data. Residents with an indwelling device, including feeding tubes, Foley urinary catheters, or suprapubic urinary catheters, were eligible for this study. Four hundred eighteen residents (six control sites, n = 215; six intervention sites, n = 203) were enrolled in the TIP study over the course of 3 years. For the current study, information was used from the six control sites in the TIP study. Because prospective data were necessary to track incident infections, residents needed two or more visits to be included in the analysis. Fifty-three residents enrolled at the six NHs had a baseline visit only and were excluded, yielding 162 eligible residents with an indwelling device of the 215 persons enrolled.

Participants had a study visit at baseline, after 14 days, and monthly thereafter for a maximum of 1 year (or until death, discharge, or device discontinuation). Follow-up time for each participant was the time from initial enrollment (Day 0) until the last follow-up visit was completed. Clinical and demographic information was obtained at each visit from the source documents at the participating facility including clinical chart review conducted by trained research staff. Descriptive data were recorded at the time of admission, and diagnostic tests and incident infections were prospectively tracked from the first follow-up visit (Day 14) to capture predictors of incident events within the NH.

Diagnostic Tests and Infection Criteria

The diagnostic tests of interest were urinalysis, urinary culture, blood culture, sputum culture, and chest X-ray. Whether any of the diagnostic tests were ordered or completed (yes/no) within 7 days of antibiotic prescribing was assessed by reviewing clinical documentation. For participants to be considered infected, a clinical note was required in their medical records documenting the type of infection and a corresponding prescription of a systemic antibiotic for 3 or more days to treat that infection. Data were also collected from residents who were given systemic antibiotics and had a diagnostic test performed but did not have an infection documented.

Clinical symptoms including acute dysuria; fever (>37.9°C or 1.5°C above baseline temperature); new or worsening urgency, frequency, or incontinence; suprapubic pain; gross hematuria; costovertebral angle (flank) tenderness; rigors; change in mental status; or change in functional status were documented for participants with a diagnosis of a UTI.[21] Change in mental status was defined as a clinician note documenting a new onset of delirium or confusion. Change in function was defined as a clinician note documenting acute functional decline or a change in functional status score using the Lawton and Brody Physician Self-Maintenance Scale, with change in score being a dichotomous variable (change present or absent).[22,23] Symptoms including pleuritic chest pain, fever, cough, new or increased sputum production, change in mental status, and change in functional status were recorded for participants with a diagnosis of pneumonia.[21]

Statistical Analyses

Data were analyzed using a longitudinal panel design. Preliminary analyses began with the characterization of study residents (n = 162), with stratification according to antibiotic use (ever (n = 100) vs never (n = 62)). Differences in means were assessed using two-sample *t*-tests, and differences in proportions were assessed using the Pearson chi-square test. This was followed by an assessment of the variation in infection rates and antibiotic usage across the six NH sites. A random-effects Poisson model for panel data was used and offset by the natural log of person-days under observation to assess differences in infection rates across sites. A similar model was used to assess differences in rates of antibiotic use.

Diagnostic testing within 7 days before (including day of) administration of antibiotics was investigated in residents with UTI or pneumonia who had detailed information regarding timing of tests and dates of antibiotic use (n = 92 residents). Eight residents had missing or incomplete information regarding antibiotic start or stop dates and were excluded. These analyses were stratified according to whether the diagnostic test yielded a positive or negative result, to assess whether types of diagnostic tests and test results influenced antibiotic use. A diagnostic test was considered confirmatory if it was ordered and completed on the same day as the antibiotic order or within the 7 days preceding the antibiotic order.

Predictors of diagnostic testing were evaluated using multilevel random-effects logit models, with the likelihood

function approximated using the adaptive Gauss-Hermite quadrature method. Use of individual diagnostic tests was modeled separately using the independent variables demographic data on admission (age, sex, weight, number of comorbidities from Charlson Comorbidity Index), symptoms (fever, chills, dysuria or hematuria, urgency, frequency, suprapubic pain, incontinence for UTI; fever, cough, sputum, mental status change, chest pain for pneumonia); change in Physical Self-Maintenance Scale score (change present or absent).[22] Two-tailed alpha was set at .05. Data were analyzed using Stata/MP version 13.1 (StataCorp LP, College Station, TX).

RESULTS

Demographic Characteristics

The 162 eligible NH residents with indwelling devices from six NH facilities were observed for an average follow-up of 104 ± 122 days, with 857 visits overall (including 695 follow-up visits). Seventy-nine (48.8%) residents had an indwelling urinary catheter, 54 (33.3%) had a feeding tube, and 29 (17.9%) had both. Of the 162 residents, 100 (61.7%) received one or more courses of antibiotics at some time during follow-up (344 prescriptions). Resident characteristics are shown in Table 1. The mean age of residents was 72.2 ± 13.5, 57% were male (n = 93), and 86% were non-Hispanic white (n = 118). Mean Charlson Comorbidity Index score was 2.9 ± 2.1 at baseline. Mean age, sex, race, admission weight, number of comorbidities, and physical functioning of residents who were prescribed antibiotics were similar to those of residents who were not. Antibiotic use was more common in residents with a urinary catheter ($P < .001$) than in those who had a feeding tube only and in those who ever had a pressure ulcer ($P < .001$).

Table 2 describes the variation in antibiotic use between the six NH facilities. The results are given according to visits, with each resident having had multiple visits and the mean number of visits being 5 ± 4 per person. For 27.7% (189/683) of the follow-up visits, a new infection had occurred within the past 30 days, with significant variation in the proportion infected across the six NHs (range 13.5–40.6%, $P = .008$). The rate of new infection per 1,000 device-days was 11.7 (Table 2). Antibiotics were prescribed in 17% of 494 visits without any documentation of the presence or type of infection.

Predictors of Diagnostic Testing

Residents who had a fever (>37.5 C or 1.5 C above baseline temperature) were more likely to have a chest x-ray, a sputum culture, and blood culture when compared with residents without fever. Furthermore, change in mental status (defined by new-onset delirium or confusion) predicted evaluation of an infection by ordering urinalysis, chest x-ray and blood cultures). Similarly, change in function was predictive of chest x-ray, sputum culture and blood culture ordering.

As expected, having at least one clinical symptom of a UTI was strongly predictive of ordering a urinalysis (adjusted odds ratio (aOR) = 5.3, $P < .001$) and urinary culturing urine culture (aOR = 5.3, $P < .001$). Similarly, having symptoms specific to pneumonia was predictive of ordering a sputum culture (aOR = 17.2, $P < .001$) and a chest X-ray (aOR = 6.5, $P < .001$). Symptoms suggestive of UTI (aOR = 2.5, $P = .01$) also predicted obtaining blood cultures.

Antibiotic Use and Diagnostic Testing for UTI and Pneumonia

Three hundred forty-four prescriptions were written for indications of pneumonia or UTI in 92 residents; 38% (n = 131) of these were written or started before a laboratory test was performed, and 62% (n = 213) were started after a confirmatory diagnostic test consistent with the infection. The average number of antibiotic days was 7 for the treatment of a UTI (range 1–60 days) and 7.5 for pneumonia (range 1–29 days) based on residents who had information regarding diagnostic testing and antibiotic use.

Figure 1 displays whether a diagnostic test was obtained in the 7 days before the onset of an antibiotic regimen. Physicians did not use the most-recent diagnostic test(s) before prescribing antibiotics in 21.5% of instances in which a UTI was suspected (50/233) and in 30.2% of instances in which pneumonia was suspected (16/53) (Figure 1). In 233 instances of UTI, urinalysis was the most commonly performed diagnostic test before prescribing an antibiotic (n = 161, 69.1%), followed by a urine culture

Table 1. Characteristics of Residents with Indwelling Urinary Catheters and Feeding Tubes from Six Targeted Infection Prevention Study Nursing Homes (N = 162)

Resident Characteristic	Antibiotics Prescribed, n = 100	No Antibiotics Prescribed, n = 62	Total, N = 162	*P*-Value
Age, mean ± SD	72.7 ± 13.2	71.4 ± 14.0	72.2 ± 13.5	.54
Male, n (%)	61 (61)	32 (52)	93 (57)	.24
Non-Hispanic white, n (%)	73 (86)	45 (85)	118 (86)	.87
Weight, pounds, mean ± SD	180.9 ± 64.7	167.0 ± 61.1	175.4 ± 63.5	.19
Charlson Comorbidity Index score, mean ± SD	3.0 ± 2.0	2.8 ± 2.2	2.9 ± 2.1	.50
Ever had pressure sore, n (%)	65 (65)	18 (29)	83 (51)	<.001
Physical Self-Maintenance Scale score, mean ± SD[a]	22.1 ± 3.8	21.9 ± 4.4	22.0 ± 4.0	.81

[a]Range 6–30, higher scores reflecting greater dependence.
SD = standard deviation.

Table 2. Variation in Antibiotic Use Between Nursing Homes (NHs)

Characteristic	NH						
	I	II	III	IV	V	VI	All
Visits, n	96	177	100	93	107	122	695
Visits with ≥1 infections, n (%)[a]	13 (13.5)	57 (32.4)	20 (21.1)	23 (25.6)	43 (40.6)	33 (27.5)	189 (27.7)
Infection rate (per 1,000 device-days)	4.6	16.3	8.9	9.5	16.6	10.5	11.7
Days of antibiotic use with urinary tract infection or pneumonia, mean ± SD	10.5 ± 3.2	10.9 ± 6.6	10.5 ± 4.9	8.5 ± 6.2	13.1 ± 6.5	12.5 ± 6.4	11.3 ± 6.2
Charlson Comorbidity Index score, mean ± SD[b]	3.3 ± 2.6	3.1 ± 2.2	1.9 ± 1.1	3.0 ± 2.8	2.6 ± 1.7	3.4 ± 1.9	2.9 ± 2.1
NH ownership	Nonprofit	Profit	Profit	Profit	Nonprofit	Profit	

[a]New infection within last 30 days. Infection was unknown at 12 visits.
[b]At first visit.

Table 3. Constitutional Symptoms and Diagnostic Tests

Symptom	Diagnostic Test				
	Urinalysis	Urine Culture	Chest X-Ray	Sputum Culture	Blood Culture
	Odds Ratio (95% Confidence Interval) *P*-Value				
Fever	1.2 (0.6–2.2) .67	1.1 (0.6–2.0) .86	4.8 (2.5–9.0) <.001	6.3 (2.0–19.7) .002	26.9 (10.2–70.6) <.001
Change in mentation	1.9 (1.1–3.1) .02	1.3 (0.8–2.2) .32	3.3 (1.9–5.7) <.001	0.2 (0.03–1.8) .17	2.3 (1.2–4.6) .02
Change in function	1.4 (1.0–2.1) .07	1.3 (0.9–1.9) .21	1.7 (1.1–2.5) .01	2.5 (1.4–4.4) .002	2.1 (1.4–3.2) .001

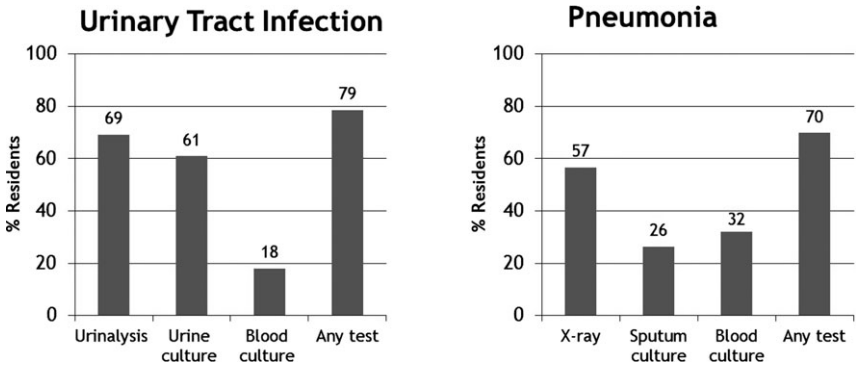

Figure 1. Percentage of residents who received antimicrobials and had the diagnostic test performed within 7 days of antibiotic prescription for urinary tract infection (UTI) or pneumonia. Physicians did not order any test before prescribing antibiotics in 21% of UTIs and 30% of cases of pneumonia. Column labels represent the percentage. Any test = any of the three tests listed; X-ray = chest X-ray.

(n = 142, 60.9%). In approximately one-third of instances, there was no request for a urinalysis, or the results were not available before initiation of treatment for a suspected UTI. Blood cultures were conducted in 18% of instances (n = 42) before antibiotic prescribing in residents with a suspected UTI. In 53 instances of treatment for pneumonia, a chest X-ray was the most commonly performed diagnostic test (n = 30, 56.4%) before prescribing an antibiotic, followed by a sputum culture (n = 14, 25.4%).

Figure 2 is a representation of antibiotic use after the review of diagnostic test results. In those observations in which a UTI was identified, a positive urinalysis or urine culture led to antibiotic administration in 89.7% of instances (209/233). The vast majority of antibiotics were discontinued if results of a urinalysis or chest X-ray were negative, although in 25 (17.6%) cases, antibiotics for a UTI were continued despite negative results. Blood culture results were often negative when residents received antibiotics for UTI (81.0%) or pneumonia (88.2%).

DISCUSSION

Empirical antibiotic use in older NH residents is troubling, prompting national calls to redesign infection control and prevention programs in NHs.[3] The current study explored predictors of diagnostic testing, variations in antibiotic

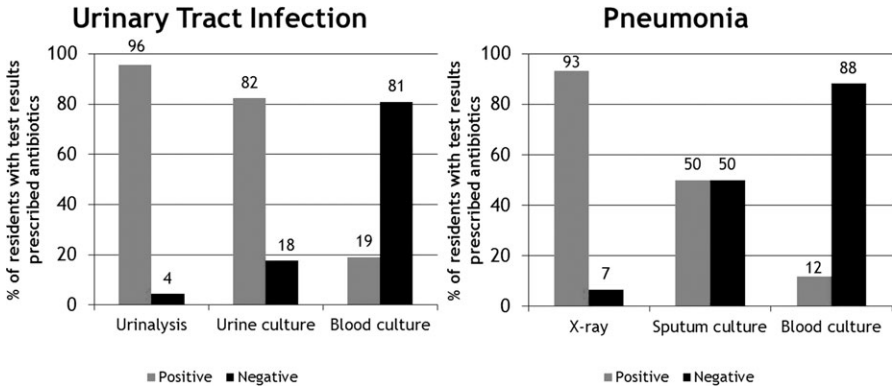

Figure 2. Percentage of antibiotic use in residents after review of laboratory test results. The majority of antibiotics were discontinued if results of a urinalysis or chest X-ray were negative, but in 25 (18%) urine cultures, antibiotics for a urinary tract infection (UTI) were continued despite negative results. X-ray = chest X-ray.

usage, and the extent to which different diagnostic tests influence decisions regarding antibiotic prescriptions. Along with infection-specific symptoms, a change in function and mentation often trigger diagnostic testing. Test-guided antibiotic use exceeds empiric prescribing, although antibiotics were initiated without diagnostic testing in one-fifth of suspected UTIs and one-third of suspected pneumonia infections. The use of antibiotics in NH residents often continues despite negative laboratory tests for suspected infection. These results suggest that diagnostic testing should be used more promptly and effectively to reduce inappropriate antibiotic use.

Inappropriate antibiotic use leads to poor outcomes, including adverse drug events, higher healthcare costs, and antimicrobial resistance.[3,9] Although many criteria are used to judge the appropriateness of antibiotics prescribed, the majority of longitudinal surveillance studies find at least 50% of antibiotic courses to be inappropriate.[11–16] One study[14] found that information derived from laboratory test results or physical examination figured in the antibiotic prescription process approximately 50% of the time, and a survey of more than 200 NH residents noted the presence of infection-specific signs and symptoms in only 46% of the residents for whom antibiotics were ordered.[16] Also in that study, appropriate cultures were obtained in only 58% of suspected UTIs and sputum cultures in 3% of suspected lower respiratory tract infections.[16] In the current study, antibiotics were used in the previous 30 days for 99% of visits at which a UTI or pneumonia was identified (as defined according to study criteria) and in 17% of visits at which the resident did not have an infection. More than one-third of antibiotic prescriptions for UTI or pneumonia were written or started before a laboratory test was performed.

The current authors also show that changes in function and mentation commonly trigger further diagnostic testing. Professional societies such as the Infectious Disease Society of America emphasize functional assessment as part of the infectious disease evaluation in older adults.[24] Nevertheless, although a progressive infection can present as a change in function or mentation, not all of these changes are due to an infection. Further research on minimum differential diagnostic considerations in individuals with acute functional and mental status changes in hospitals and NHs is urgently needed. In particular, defining the probability of infection when a resident has an isolated functional or mental status change has the potential to substantially change physician prescribing practices.

This study highlights how different diagnostic tests influence decisions concerning antibiotic prescription in NHs. After review of test results, the prescribing physician or physician extender must reach a treatment decision, sometimes with incomplete information. Although failing to treat older adults based on a negative test result reduces inappropriate antibiotic use and thus enhances their safety, frontline providers may have concerns regarding the potential rapid decline if an infection remains untreated. Thus, the benefits of treating people with clinically suspected infections but negative diagnostic tests must be balanced against the contributory development of antibiotic resistance and other adverse events in the larger population as a whole.[25,26] With a growing body of evidence demonstrating the effectiveness of simple educational interventions in recognition of infections and management considerations, a proactive approach can be implemented to curb and eventually eliminate inappropriate antibiotic usage in NHs.[4,20,27–29]

Strengths of this study are its prospective longitudinal design that involved high-risk residents from multiple free-standing NHs. Trained research staff collected data. The authors note several limitations. Information was not collected on the prescribing clinicians' specialty. In addition, the focus of this study was NH residents in southeast Michigan who had an indwelling device and were at higher potential risk of infection than most NHs resident, so the results may not be generalizable to all NH residents. Moreover, the analysis of diagnostic testing focused on individuals who received antibiotics; information was not collected on individuals for whom a test was ordered but no antibiotic was prescribed. This would be an important population to examine in future studies.

In conclusion, a relatively high percentage of empiric antibiotic use was found in NHs in the absence of clinical evidence of infection with substantial variations between NHs. Although the indications for laboratory testing appeared appropriate, the results of laboratory testing did not necessarily inform decision-making regarding antibiotic treatment. Further studies to improve antibiotic stewardship in NHs should address clinical decision-making based

on symptomatology and the interpretation of diagnostic test results. Avenues for rapid, yet accurate, testing may be worth exploring so that antibiotics can be expeditiously targeted to those who would most likely benefit. Such approaches should augment efforts to improve antibiotic stewardship, reduce MDROs, and enhance the quality of life of NH residents.

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