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Antibiotic treatment of community-acquired pneumonia: a questionnaire survey in Danish general practice

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Abstract

Background

Discrepancies exist in Danish guidelines for the treatment of bacterial community-acquired pneumonia (CAP). This study aimed to investigate how GPs treat adults with CAP and explore associations between GP characteristics and treatment duration.

Methods

In autumn 2020, GPs in the North Denmark Region were asked to complete an electronic questionnaire on antibiotic prescribing for CAP. Information about GP gender, age, experience and type of practice was obtained. Multivariable logistic regression was used to analyse the association between GP characteristics and treatment duration.

Results

A total of 298 GPs were invited to participate of whom 108 completed the survey.

Penicillin V was used as first line treatment for CAP by all participants. Treatment duration varied from five (54.6%) to ten days (8.3%).

A 5-day course of penicillin was less likely to be prescribed by male GPs (odds ratio (OR) 0.35, 95% confidence interval (CI) 0.13 to 0.94) and more likely to be prescribed by GPs with 5-9 years of experience in general practice (OR 5.03, 95%CI 1.09 to 23.21) compared to those with 10-19 years of experience.

Conclusion

Variation in antibiotic treatment of CAP emphasises the importance of generating solid evidence about the optimal duration regarding both effectiveness and safety.

Introduction

In the pursuit of changing the trend of the increasing numbers of resistant bacteria throughout the world, it is of high importance to reduce the consumption of antibiotics [1]. In humans, the majority of antibiotics are prescribed in primary care and mainly in the general practice setting [2,3]. Especially acute respiratory tract- and urinary tract infections are often treated with antibiotics in general practice, with acute lower respiratory tract infections (LRTI) being a common indication [3]. The severity of a LRTI can vary widely – from mild symptoms to a life-threatening condition. According to Statistics Denmark, a total of 47,968 patients were hospitalised (3.6% of all hospitalizations) and 1,911 persons died from pneumonia (3.5% of all deaths) during 2018 [4].

Pneumonia acquired outside the hospital setting is referred to as community-acquired pneumonia (CAP) [5]. In Denmark, *Streptococcus pneumoniae* (*S. pneumoniae*) is the most common bacterial pathogen causing CAP [6]. However, other bacteria such as *Mycoplasma pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Chlamydia pneumoniae*, *Staphylococcus aureus*, and *Legionella pneumophila* are known to cause a bacterial pneumonia [6]. Importantly, not only is *S. pneumoniae* known to be the most common cause of bacterial CAP, but an infection due to this specific pathogen also poses an increased risk of a severe disease course and of being admitted to hospital [6].

Most patients with an acute cough have a viral infection and only few patients have a bacterial pneumonia. However, the diagnosis of CAP can be hard to establish and consequently an overuse of antibiotics for LRTI patients exists [7].

In Denmark, penicillin V is recommended as the drug of choice for antibiotic treatment of bacterial CAP, as about 95% of *S. pneumoniae* are sensitive to this antibiotic [2]. Most *S. pneumoniae* are also sensitive to macrolides [2], however, treatment with penicillin V is

recommended as it is a narrow-spectrum penicillin selecting less for resistant bacteria than more broad-spectrum antibiotics.

In 2016, new recommendations for treatment of LRTIs in general practice were launched by the Danish Medicine Council (RADS) [8]. These recommendations suggest that antibiotic treatment of CAP should be changed from penicillin V 1 MIE (660 mg) x 3 in seven days to penicillin V 1 MIE (660 mg) x 4 in five days. The rationale given for these changes were to minimise the risk of treatment failure and to reduce the selection of resistant bacteria [8].

Importantly, discrepancies exist in Danish guidelines for treatment of bacterial CAP as the guideline from the Danish College of General Practitioners (DSAM) recommends antibiotic treatment three times a day for seven days [9]. Two Danish medical web portals;

Promedicin.dk recommends antibiotic treatment four times a day for five days [10], and

Lægehåndbogen leaves it to the GPs to decide which one of the antibiotic treatment regimens they will provide for their patients [11].

The evidence behind the recommendations of a five-day treatment period is limited [12].

However, the recommendation of seven days of treatment is not based on scientific evidence but has nevertheless gained acceptance over the years. As for now, the Danish GPs are left in a dilemma, and each GP has to decide on which guidelines to follow.

The aim of this study was to investigate how Danish GPs treat adults with CAP. Furthermore, the association between GP characteristics and antibiotic treatment duration was explored.

Methods

Setting

Danish GPs act as primary care providers and gatekeepers to more extended services in the healthcare sector. Almost every citizen is listed with a GP and treatments are free of charge

for the patients. The GPs are paid through a combination of capitation fees and fee-for-services [13].

Design

GPs in the North Denmark Region were asked to complete an electronic questionnaire regarding antibiotic treatment of adults with bacterial CAP. The invitation was sent out by the Danish Organisation of General Practitioners (PLO) to all members in the North Denmark Region. In mid-September 2020, each GP received an email with information about the study and a link for the survey. One reminder was sent out after two weeks for all recipients, and the survey was closed on 5 October 2020. Participation was voluntary, and an economic compensation corresponding to ten minutes (138.36 DKK) was offered each GP [14].

The questionnaire was generated in the web-based tool SurveyXact [15].

Firstly, two members of the research team (LiB, MPH) developed a preliminary questionnaire based on the content of the various guidelines in Denmark [8-11, 16, 17]. Next, all members of the research team, comprising four GPs, one statistician, and two researchers within the field of antibiotic use, commented on this draft. Some questions were revised, some deleted, and new questions were proposed. Once again, the revised list of questions was sent to all members of the research team and they were asked to comment on this new draft. After two “rounds of commenting”, all team members agreed on the content of the questionnaire.

Lastly, four GPs were asked to test the final electronic questionnaire resulting in no further revisions.

Data

Each GP completed a questionnaire regarding antibiotic treatment of adults (≥ 18 years), without any known chronic respiratory disease, diagnosed with bacterial CAP in general practice.

The GPs were asked about 6 items:

- 1) First choice of antibiotic treatment: penicillin V, clarithromycin, roxithromycin, amoxicillin, amoxicillin with clavulanic acid, or other choice of antibiotics.
- 2) Dose: 1 mill IE / 1.2 mill IE three or four times a day, or other choice of dosage (mg) provided orally.

Of note – the GPs were not asked to differentiate between issuing a dose of 1 mill. IE (660mg) or 1.2 mill. IE (800 mg), but only if the dose was provided times three or four.

- 3) Treatment duration (days).
- 4) Whether patients with severe symptoms are treated for a longer period than those with mild/moderate symptoms – and if so, how many days?
- 5) Whether patients are recommended to stop treatment when symptoms resolved.

Of note - no specific time frame for antibiotic treatment prior to discontinuation was stated in the questionnaire.

- 6) How the GP acts if a patient does not respond as expected to initial antibiotic treatment: add an additional antibiotic, substitute first choice antibiotic with another antibiotic, or choice of another action (please elaborate).

In addition, the following information was obtained about each of the participating GPs; gender (male/female), age (< 30, 30 – 39, 40 – 49, 50 – 59, 60 – 69, > 69) experience as a GP (< 5, 5-9, 10-19, 20-29, >29 years) and type of practice (partnership-, cooperation- or solo practice).

Analyses

Categorical data, such as GP characteristics and antibiotic prescription strategies were presented as numbers and percentages. Short-course antibiotic therapy was defined as up to five days, whilst long-course antibiotic therapy was defined as six to ten days.

Multivariable logistic regression was carried out to analyse the association between GP characteristics and duration of therapy. Hence, providing odds ratio (OR) and 95% confidence interval (CI) for choosing a short course of antibiotics over a longer course. A p-value < 0.05 was considered statistically significant. All analyses were performed in SPSS version 26.0 [18].

Ethics

The study was registered at the Center for General practice at Aalborg University (ID 96-4). All participating GPs provided informed consent. Ethical approval was not obtained as this is not a requirement in Danish legislation.

Results

A total of 298 GPs were invited to participate, of whom 108 completed the survey (response rate 36.2%). Table 1 shows characteristics of the participating GPs. Female GPs comprised the majority of respondents (63%) and most worked in partnership practices (75%).

Antibiotic prescribing for CAP

Penicillin V was reported as first line treatment for CAP by all GPs (Table 2). About half of the GPs (55.6%) prescribed 1 mill IE / 1.2 mill IE four times daily, while 43.5% recommended 1 mil. IE / 1.2 mill IE three times per day. One GP stated that he chose to prescribe penicillin V either three times daily or four times daily depending on the age of the patient and the clinical findings.

Treatment duration varied from five (54.6%) to ten days (8.3%), with about one third of GPs prescribing a seven-day course of antibiotics (34.3%). Most GPs (75.9%) replied that they would not prescribe antibiotics for a longer period than usual if symptoms were deemed as

severe. A total of 83.3% of the GPs answered that they preferred to switch to another type of antibiotics if patients did not respond to initial treatment. Often a macrolide was preferred as a second-choice antibiotic (55.5%), but also amoxicillin (12.9%), and amoxicillin with clavulanic acid (12.0%) was prescribed by some GPs.

Some GPs (16.7 %) stated that they preferred other actions than immediate switch of antibiotics, when initial treatment failed. Most often, a reassessment of the patient and additional testing were mentioned as options (Table 3).

The majority of GPs (88.9%) responded that they did not recommend patients to stop an antibiotic course when symptoms resolved.

GP characteristics and treatment duration

Table 4 demonstrates the association between GP characteristics and prescribing a short course (5 days) of antibiotics compared to a longer course (6-10 days) of antibiotics for adults diagnosed with CAP.

Male GPs were three times less likely than their female GP colleagues to issue a 5-day antibiotic course (OR 0.35, 95%CI 0.13 to 0.94; P = 0.036). In addition, GPs with five to nine years of experience within the field of general practice were found to be about five times more likely to prescribe a 5-day course of antibiotics (OR 5.03, 95%CI 1.09 to 23.21; P = 0.039) compared to the GPs with seniority of 10-19 years.

Discussion

Principal findings

Penicillin V was used as first line antibiotic treatment for adults diagnosed with CAP. Some variation existed in the length of treatment duration - from about half of the GPs prescribing a

5-day course to others prescribing antibiotics for either six, seven, eight or ten days.

Prescribing a 5-day course of antibiotics was associated with being a female GP and having five to nine years of experience within the field of general practice.

Strengths and limitations

More than a third of all GPs in the North Denmark Region participated in this study, providing a response rate of 36.2%. However, when interpreting the findings of this study, some limitations should be kept in mind.

Voluntary participation may have contributed to selection bias. Possibly, only GPs with a special interest in the management of patients with acute respiratory tract infections took the time to fill in the questionnaire. In order to minimise selection bias and to ensure a good response rate, the GPs were offered a financial compensation for the time used for filling in the questionnaire.

Participating GPs were more likely to be female and younger compared to the total Danish GP population [19]. Importantly, the GPs were self-reporting and perhaps prone to provide the answer perceived to be preferred. Social desirability bias can influence the answers given in a questionnaire study as a hypothetical scenario might not fully reflect daily practice.

However, several GPs provided answers (e.g. ten days of treatment) that are not in line with current guidelines for treatment of CAP, and the author team believes that the GPs to a large extent did report their own treatment decisions. One might consider complementing this questionnaire survey with a systematic data collection over time to ensure a genuine insight into the treatment regimens for CAP in general practice.

Comparison with other studies

Large discrepancies exist in the use of penicillin V – even within the European Union [20].

Some countries like Spain, Belgium and Lithuania hardly use any penicillin V, while in most Nordic countries, penicillin V comprises a quite large percentage of the total consumption of

penicillins (ATC J01) [20].

In the present study, all participating GPs stated that they used penicillin V as first line treatment for CAP. Contrarily, another Danish study published in 2017 by Aabenhus et al. found that only 44% of antibiotic prescriptions issued for treatment of pneumonia comprised penicillin V [21]. In the study by Aabenhus et al., macrolides comprised 27% of the scripts issued for pneumonia. In line with this finding, we found that most often a macrolide antibiotic was issued if the effect of penicillin V failed. Interestingly, none of the Danish guidelines specifically recommends the use of macrolides as second line treatment of CAP [8-11, 16, 17]. The Danish College of General Practitioners recommends a reassessment of the patient, in line with the response of 16.7% of the participating GPs. One might speculate that the substitution to a macrolide antibiotic is based on the assumption that treatment failure is most probably due to an atypical bacterial agent causing the infection, such as for example *mycoplasma pneumonia* [6,22].

This Danish questionnaire survey found that female GPs more often prescribed a 5-day antibiotic course for CAP than their male colleagues. The author team is not aware of any other studies exploring the association between GP gender and duration of antibiotic treatment. However, other studies have identified that practices with a higher proportion of male GPs tend to have a higher antibiotic prescription rate [23,24].

Implications

This questionnaire survey revealed a rather large variation (five to ten days) in the length of antibiotic treatment for patients diagnosed with CAP in Danish general practice. A previous literature review, including six studies, did find similar clinical success rates in CAP patients treated with either a short-course (5 days) or a longer course of antibiotics (7+ days) [25].

However, the evidence supporting the use of a short-course antibiotic therapy, e.g. five days, instead of a longer course is quite limited. The most recently published Cochrane systematic

review exploring the use of short-course versus long-course treatment of CAP, with the same type of antibiotics, did not find any eligible trials [12]. Consequently, more trials determining the effect and safety of shorter treatment regimens for CAP need to be performed to support the GPs' treatment decision.

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Conflict of interest

I declare that the corresponding author has collected and filed a conflict of interest form (the ICMJE form) from all authors of the manuscript and have nothing to disclose.

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Table 1: GP characteristics.

	General practitioners (n = 108)
Gender	
Woman	68 (63.0)
Man	40 (37.0)
Age	
30-39 years	17 (15.7)
40-49 years	50 (46.3)
50-59 years	23 (21.3)
60-69 years	15 (13.9)
>69 years	3 (2.8)
Practice type	
Partnership practice	81 (75.0)
Cooperation practice	10 (9.3)
Solo practice	17 (15.7)
Seniority	
<5 years	27 (25.0)
5-9 years	26 (24.1)
10-19 years	33 (30.6)
20-29 years	15 (13.9)
>29 years	7 (6.5)

Values presented as n (%).

Table 2: GP responses regarding prescription of antibiotic therapy of CAP.

	Antibiotic therapy (n = 108)
Antibiotics	
Phenoxymethylpenicillin (Penicillin V)	108 (100.0)
Clarithromycin	0 (0.0)
Roxithromycin	0 (0.0)
Amoxicillin	0 (0.0)
Amoxicillin/clavulanic acid	0 (0.0)
Other	0 (0.0)
Penicillin V dosage	
1 mill. IE / 800 mg (1,2 mill IE) x 3 pr day	47 (43.5)
1 mill. IE / 800 mg (1,2 mill. IE) x 4 pr day	60 (55.6)
Other, dosage (xx mg and xx times pr day)	1 (0.9)
Days of therapy	
5	59 (54.6)
6	1 (0.9)
7	37 (34.3)
8	2 (1.9)
10	9 (8.3)
Days of therapy (grouped)	
Short-course antibiotic therapy (5 days)	59 (54.6)
Long-course antibiotic therapy (6 – 10 days)	49 (45.4)
Severe symptoms - longer therapy	
No	82 (75.9)
Yes	26 (24.1)
Severe symptoms - days of therapy	
7	7 (6.5)
8	2 (1.8)
10	17 (15.7)
Stop therapy - symptom stop	
No	96 (88.9)
Yes	12 (11.1)
No effect of therapy – action	
Add other antibiotics	0 (0.0)
Change of antibiotics	90 (83.3)
Other action	18 (16.7)
Change of antibiotics	
Macrolide	60 (55.5)
Amoxicillin	14 (12.9)
Amoxicillin/clavulanic acid	13 (12.0)
Other antibiotic	3 (2.7)

Values presented as n (%)

Table 3: GP written responses concerning action plan when initial therapy failed.

No effect of therapy - other action (written answer)

- *Depending on physical examination and paraclinical findings.*
 - *Sputum culture test for atypical pneumonia, possibly hospitalisation.*
 - *Sputum culture and resistance test.*
 - *Clinical reassessment and possibly change of antibiotics.*
 - *Additional tests: CRP, throat swab, sputum culture.*
 - *Roxithromycin.*
 - *Diagnose reassessment.*
 - *CRP test and white blood cell differential count a few days in a row. If increasing values then change to roxithromycin.*
 - *Reassesses the patient.*
 - *Hospitalisation of unwell patient.*
 - *Blood test for infection before changing antibiotic.*
 - *Reassess the diagnosis.*
 - *Clinical reassessment, possibly paraclinical tests.*
 - *Reevaluate indication and possibly change of antibiotics.*
 - *Clinical reassessment and blood test for infection to evaluate possible viral infection. If examinations suggest bacterial infection and there is no response to narrow spectrum antibiotics, then change to macrolide.*
 - *Clinical reassessment.*
 - *Depending on symptoms, but possibly change of antibiotics.*
 - *Hospitalisation if patient is unwell.*
-

Table 4: Association between GP characteristics and short-course (5 days)^a antibiotic therapy with regard to CAP.

	Short-course therapy N (%)	Univariable OR (95 % CI)	P-value	Multivariable OR (95 % CI)	P-value
Gender					
Woman	42 (62%)	(ref)		(ref)	
Man	17 (43%)	0.46 (0.21-1.01)	0.054	0.35 (0.13-0.94)	0.036
Age					
30-39 years	8 (47%)	0.46 (0.15-1.40)	0.171	0.73 (0.14-3.71)	0.705
40-49 years	33 (66%)	(ref)		(ref)	
50-59 years	10 (43%)	0.40 (0.14-1.09)	0.073	1.14 (0.26-4.92)	0.866
60-69 years	6 (40%)	0.34 (0.11-1.13)	0.078	1.27 (0.16-9.90)	0.820
>69 years	2 (67%)	1.03 (0.09-12.19)	0.981	10.16 (0.19-534.81)	0.252
Seniority					
<5 years	14 (52%)	1.14 (0.41-3.16)	0.795	1.41 (0.26-7.55)	0.690
5-9 years	20 (77%)	3.54 (1.13-11.07)	0.030	5.03 (1.09-23.21)	0.039
10-19 years	16 (49%)	(ref)		(ref)	
20-29 years	6 (40%)	0.71 (0.21-2.44)	0.585	0.77 (0.16-3.74)	0.745
>29 years	3 (43%)	0.80 (0.15-4.13)	0.787	0.51 (0.03-9.59)	0.653
Practice type					
Partnership practice	45 (56%)	(ref)		(ref)	
Cooperation practice	7 (70%)	1.87 (0.45-7.74)	0.390	0.98 (0.20-4.86)	0.983
Solo practice	7 (41%)	0.56 (0.19-1.62)	0.284	0.78 (0.23-2.64)	0.693

a. The reference category is: 6-10 days named long-course antibiotic therapy.

OR: odds ratio for choosing short-course (5 days) antibiotic therapy over long-course (6-10 days) antibiotic therapy.

CI: 95 % confidence interval.

Ref: value set as reference category.