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Short communication

Title:

Management of early infection with *Pseudomonas aeruginosa* in adults with bronchiectasis : a survey of French pulmonologist's practices.

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To the Editor,

Bronchiectasis is a chronic respiratory disease characterized by recurrent episodes of airway infections associated with acute exacerbations. Chronic airway infection, especially with *Pseudomonas aeruginosa* (PA), is associated with increased frequency of acute exacerbations, lowered quality of life and increased mortality in adults with bronchiectasis (1). The management of early PA infection in patients with bronchiectasis was historically derived from the experience acquired in people with cystic fibrosis (CF), but even in the CF population the management of PA infection remains debated (2). In 2017, a Task Force from the European Respiratory Society (ERS) provided guidelines for the management of adult bronchiectasis, with general directions on the management of early PA infection (3).

Because PA infection management in bronchiectasis is based on moderate to very low quality evidence, and as clinical practices may differ between countries, we aimed at describing the current practices of French pulmonologists, with a special focus on early PA infection. For this purpose, we elaborated an online self-administered questionnaire (*Lime survey*), and submitted it to the members of the Respiratory Infectious Research and Teaching Group (GREPI), a working group of the Société de Pneumologie de Langue Française (SPLF). The questionnaire, available from July 1st to September 30th 2019, included 17 questions related to the management of early PA infection in adults with bronchiectasis.

Thirty-five French pulmonologists filled the survey. They were working in a general (n=19; 54%) or a university (n=14; 40%) hospital, with four of them affiliated to a CF center, or were liberal practitioners (n=2; 9%). 25 (71%) declared to treat more than five bronchiectasis patients with a first isolation of PA per year.

In the context of a first PA isolation, 27 respondents (77%) declared to prescribe anti-PA antibiotics after obtaining a single PA-positive respiratory sample (“above the

significance threshold”, which was not specified) in case of acute exacerbation (4), whereas 15 (43%) do it in the absence of criteria for an acute exacerbation, and 12 (34%) if culture also reveals another pathogen and/or if PA is below the significance threshold.

In case of PA treatment decision, 30 respondents (86%) systematically propose systemic antibiotic therapy for 14 days. Clinicians’ preferences of antibiotic regimens (first choice and favourite alternative), duration of bitherapy and choice of molecules, according to PA phenotype (susceptible or still undetermined), are depicted in Figure 1.

Respondents’ adherence to potential reasons supporting the use of antibiotic regimens including an oral fluoroquinolone, alone or in combination, was as follows: facilitation of ambulatory management (n=34, 97%), acceptable safety profile (n=28, 80%), excellent oral biodisponibility (n=27, 77%), good tissular diffusion (n=25, 71%) and no need for biological surveillance (n=23, 66%).

Most reported reasons to prefer the combination of an anti-PA betalactamin to an aminoglycoside, instead of betalactamin + fluoroquinolone, were : a contraindication to fluoroquinolones without any to aminoglycosides (n=27, 77%), the presence of clinical or radiological signs of severity (n=22, 63%), a still unknown susceptibility of the PA strain to fluoroquinolones (n=16, 46%), or because they consider aminoglycosides more efficient than fluoroquinolones, even for fluoroquinolone-sensible PA strains (n=9, 26%).

28 respondents (80%) considered the use of a fluoroquinolone alone as non reasonable due to the lack of evidence supporting such choice, 17 (49%) considered that a fluoroquinolone is an acceptable alternative to a systemic bitherapy if the fluroroquinolone is combined to an inhaled antibiotic, whereas only 3 (9%) if not. However, only nine (26%) considered that the association of a fluoroquinolone with an inhaled antibiotic may be as efficient as a systemic bitherapy, whereas only four (11%) think that betalactamin + fluoroquinolone is less efficient than betalactamin + aminoglycoside.

15 respondents (43%) declared they systematically hospitalize patients to start an eradication treatment, 18 (51%) do it in case of clinical signs of severity, 12 (34%) in case of radiological or clinical signs of pneumonia, 11 (31%) if the phenotype of the strain is still unknown and the treatment is considered urgent, and 11 (31%) answered that it depends on the choice of antibiotic regimen.

Concerning the use of inhaled antibiotics for 3 months in this context, 13 respondents (37%) declared they never prescribe it in first-intention, whereas 11 (31%) systematically do it following a systemic bitherapy, and 15 (43%) might use it to replace one antibiotic of the initially prescribed systemic bitherapy. *A contrario*, 12 (34%) only use inhaled antibiotics after eradication treatment failed.

Finally, most of the respondents declared following the recommendations of the ERS Task Force most of the time (n=16, 46%) or sometimes (n=11, 31%), whereas five (14%) confessed not knowing them, and three (9%) preferred not to express themselves.

The results of this survey show that the practices of French Pulmonologists are heterogeneous, especially when considering microbiological and clinical criteria for anti-PA eradication treatment decision, choice of antibiotic regimen and molecules, duration of bitherapy and adjunction of inhaled antibiotics in bronchiectasis patients with early PA infection. When looking at the proposition of the ERS Task Force on possible and alternative PA-eradication treatment (3), French Pulmonologists seem reluctant to prescribe a fluoroquinolone as first line therapy, especially without the adjunction of an inhaled antibiotic. This may be explained by the lack of data on the efficacy of fluoroquinolone monotherapy out of the CF field (2), and the fear to select fluoroquinolones-resistant PA strain. However, prescription of nebulized antibiotics for 3 months is not systematic among French pulmonologists, although previous studies have suggested a significant benefit of

nebulized antibiotics adjunct for PA eradication in adults with bronchiectasis (5,6). The absence of drug marketing approval for this specific population, the cost of inhaled therapy or the imperfect adherence of patients to inhaled antibiotics might further explain it. Finally, the relative complexity of the proposed organigram for the choice of PA eradication treatment might also explain the mitigated adherence of French pulmonologists to ERS Task Force proposals. The main limitations of our work are a potential declarative bias and the limited number of respondents. However, respondents in this survey can be considered as a good representative panel of French pulmonologists involved in the management of adult patients with bronchiectasis since they have been participating actively in the research and teaching national group.

To conclude, the management of early PA infection in adults with bronchiectasis by French pulmonologists is not consensual. Randomized clinical trials are needed to precise which therapeutic options are likely to achieve the best eradication rate, and further optimize bronchiectasis patients' management and prognosis.

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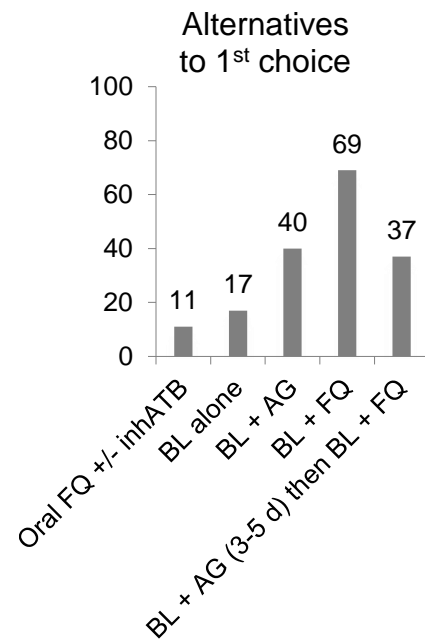
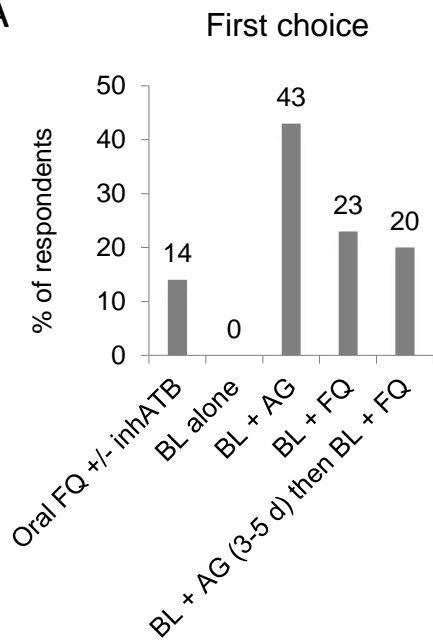
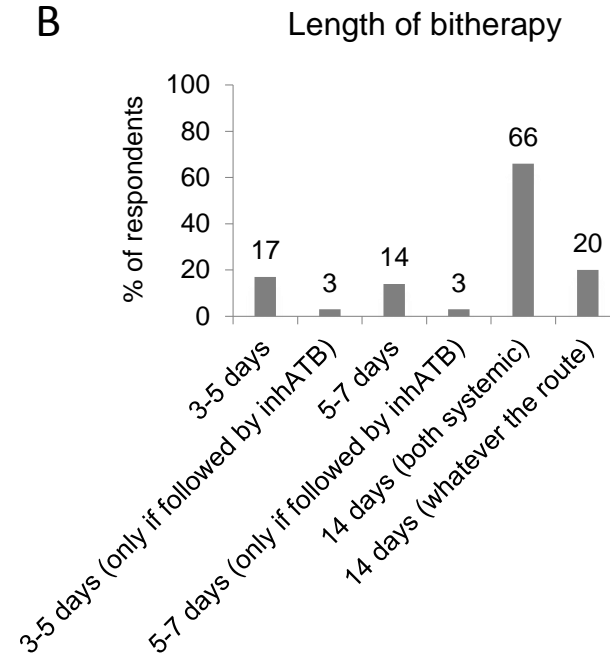
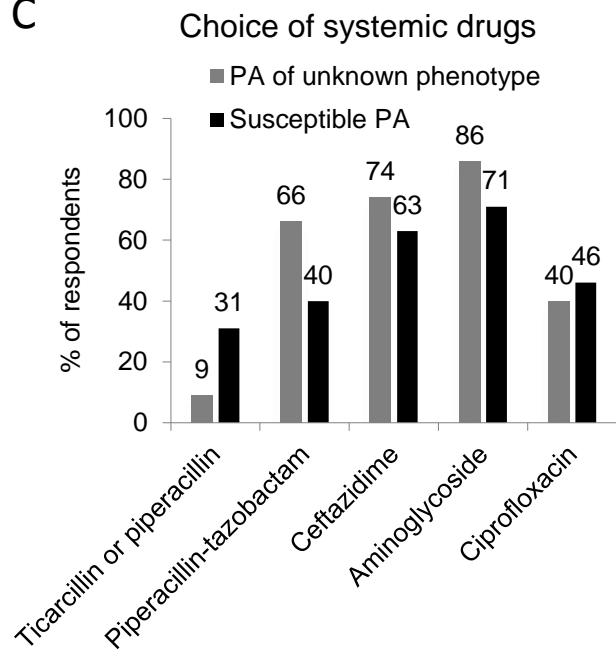
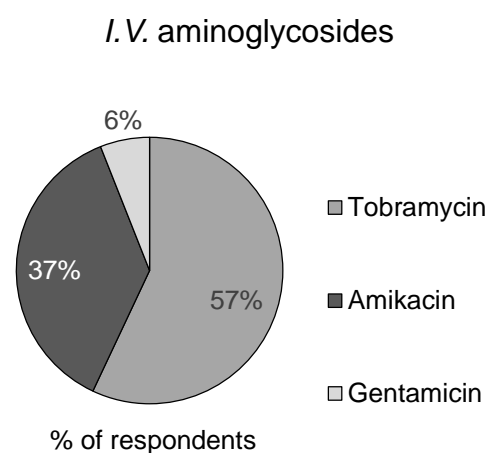
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Figure 1 – Clinicians choices concerning antibiotic therapy for *Pseudomonas aeruginosa* early infection in adults with bronchiectasis. A/ First choice (*left*, one single response per respondent), and favourite alternative to first choice (*right*, one or two responses per respondent), of antibiotics regimen for susceptible *Pseudomonas aeruginosa* (PA); B/ Length of bi-antibiotherapy (multiple answer possible); C/ Privileged choices of molecules (multiple answer possible) when the antibiogram of the strain is not yet available (unknown phenotype, grey bars) or in case of susceptible PA strain (black bars); D/ Privileged choice of *I.V.* aminoglycosides (one single response) when prescribed; E/ Inhaled antibiotics respondents may prescribe to treat PA infection in bronchiectasis patients (multiple choice). Every respondent answered to each of the questions.

Abbreviations : AG : aminoglycoside; BL : anti-PA betalactamin; d: days; FQ : fluoroquinolone; inhATB : inhaled antibiotics, *I.V.* : intravenous ; PA : *Pseudomonas aeruginosa*

A**B****C****D****E**