



# The clinical impact of *Pseudomonas aeruginosa* eradication in bronchiectasis in a Dutch referral centre

To the Editor:

About one-third of the patients with bronchiectasis is likely to develop a chronic infection with *Pseudomonas aeruginosa* [1, 2]. The available evidence to date suggest that *P. aeruginosa* colonisation in bronchiectasis may be associated with poorer outcome in terms of hospital admissions, exacerbation frequency and mortality [3–5]. The place of *Pseudomonas* eradication regimens is well defined in cystic fibrosis and supported by a Cochrane review, which showed that early detection of *P. aeruginosa* and subsequent early eradication treatment, consisting of nebulised antibiotics with or without oral antibiotics, could reduce the risk of chronic *P. aeruginosa* infection [6]. Recently published guidelines by the European Respiratory Society (ERS) suggested that adults with bronchiectasis and a new isolation of *P. aeruginosa* should also be offered eradication antibiotic treatment [7]. The aim of this study was to investigate the effectiveness of different *P. aeruginosa* eradication strategies and the clinical outcome after eradication.

This was a single-centre, retrospective cohort study using a bronchiectasis database from the Dept of Pulmonary Medicine of the Erasmus University Medical Center, Rotterdam, the Netherlands. The efficacy and success rate of different treatment eradication regimes after first *P. aeruginosa* isolation from sputum was determined. Exacerbation frequency and hospital admission rate were reviewed in the 12 months pre-eradication treatment and 12 months post-eradication treatment. Exacerbations were defined as events that led a care provider to prescribe antibiotics or events that led to hospitalisation (severe exacerbations). Treatment success was defined as when all sputum cultures were negative for a period of 6 months after eradication. In our clinic, sputum samples were obtained during regular outpatient clinic visits (most often, every 3 months) or during hospital admissions.

211 patients were identified from our bronchiectasis database between January 2012 to December 2016. 78 (37%) patients had sputum cultures positive for *P. aeruginosa*. 60 patients received an eradication regimen because of a new sputum isolation of *P. aeruginosa*. The other 18 patients were already colonised with *P. aeruginosa* before referral to our centre. The cohort analysis showed that 54% of the patients were female (n=32) and that the median (interquartile range) age was 57 (18) years. In the majority of cases, the cause of bronchiectasis was attributed to idiopathic and post-infectious diseases: in 31% and 20%, respectively.

The duration between *Pseudomonas* isolation and eradication treatment varied from 1 day to a maximum of 31 days. The most frequently used eradication regime consisted of nebulised tobramycin (1–3 months) combined with a 3-week course of oral ciprofloxacin, which has been prescribed to 23 (38%) out of the 60 patients, 13% of the patients received a combination of nebulised tobramycin and 2 weeks of oral ciprofloxacin, a combination of intravenous antibiotics and inhaled tobramycin was prescribed in 30% of the patients, and 8% received only ciprofloxacin for 2 weeks without inhalation antibiotics. We noticed success of eradication at 6 months in 44 (73%) out of the 60 patients who had a first sputum culture positive for *P. aeruginosa*. Of these patients, 36 (60%) remained *P. aeruginosa* free for  $\geq 1$  year. In total, 25 (42%) out of 60 patients remained *P. aeruginosa* free in the median follow-up period of 36 months. There was no significant difference in treatment outcome between the different antibiotic regimens. After eradication treatment, there was a significantly reduced exacerbation frequency in the 12 months after eradication compared to 12 months before eradication ( $p=0.011$ ). Thereby, lung function and hospital

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**An antibiotic approach directed at eradication of a new isolate of *Pseudomonas aeruginosa* can result in a significant reduction in exacerbation frequency in bronchiectasis patients** <http://ow.ly/L1Zl30nv1WS>

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TABLE 1 Clinical outcome of *Pseudomonas aeruginosa* eradication

	Pre-eradication	Post-eradication	p-value <sup>#</sup>
<b>FEV<sub>1</sub> % predicted median (range)</b>	68 [54–82]	74 [59–89]	0.549
<b>Exacerbation frequency</b>			<b>0.011</b>
No exacerbations	6 (10%)	16 (27%)	
One exacerbation	19 (32%)	17 (28%)	
Two or more exacerbations	35 (58%)	27 (45%)	
<b>Hospital admissions</b>			1.000
No exacerbations	40 (67%)	40 (67%)	
One or more exacerbation(s)	20 (33%)	20 (33%)	

FEV<sub>1</sub>: forced expiratory volume in 1 s. <sup>#</sup>: 12 months pre-eradication *versus* 12 months post-eradication, analysed with paired t-test for continuous variables and Chi-squared test for categorical variables. Bold indicates statistically significant p-values.

admission rates remained unchanged after eradication treatment, as is shown in table 1. Over a period of 6 months after eradication treatment, three patients had expectorated one sputum sample, 11 patients had expectorated two sputum samples and we collected three sputum samples from 46 patients. Overall, 49 patients used tobramycin inhalation, of whom 39 (80%) patients had received tobramycin inhalation solution and 10 (20%) patients, dry-powder tobramycin. There was no significant difference in eradication success between these two groups ( $p=0.711$ ).

Up to now, only three studies have been performed investigating *P. aeruginosa* eradication therapy in patients with bronchiectasis [8–10]. Two of these studies suggested that strategies that combined nebulised antibiotics and oral or *i.v.* antibiotics were more efficient compared to systemic antibiotics alone [8, 9]. We noticed in our study that eradication therapy might result in clinical benefits, with a significant reduction in the number of exacerbations in the year post-eradication compared to the year pre-eradication; however, without influencing the numbers of hospitalisation. In the study by ORRIOLS *et al.* [8], the number of exacerbations and the number and days of hospital admissions were significantly lower in the tobramycin inhalation than in the placebo group. In addition, in the study by WHITE *et al.* [10], exacerbation frequency was significantly reduced after an eradication approach, without affecting the number of hospitalisations.

The bronchiectasis guideline from the ERS suggests starting with eradication antibiotic treatment in case of a new sputum isolation of *P. aeruginosa* [7]. Several regimens are recommended by the ERS, varying from an oral fluoroquinolone course to inhalation antibiotics plus *i.v.* antibiotics. The studies described above differ in their antibiotic strategies. There is a tendency to start eradication treatment with an inhalation antibiotic (*e.g.* tobramycin or colistin). Furthermore, VALLIÈRES *et al.* [9] showed that an oral ciprofloxacin course of  $\geq 3$  weeks was just as efficient as a course of shorter duration, both in combination with nebulised colistin.

To conclude, different antibiotic regimes resulted in a *P. aeruginosa* eradication rate at 6 months of 73%, with a significant reduction in exacerbation frequency. However, up to now, there are few data concerning the effectiveness of different eradication strategies. In our opinion, a prospective randomised study comparing an oral or *i.v.* antibiotic course with inhaled antibiotics *versus* an oral or *i.v.* antibiotic course without inhaled antibiotics *versus* inhaled antibiotics only should be performed to determine the best antibiotic strategy for eradication of *P. aeruginosa*.

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