Prescribing preferences and availability of nebulisers and inhalers for inhaled medications in bronchiectasis: results of a specialist survey

Received: 29 Sept 2023
Accepted: 8 Nov 2023

To the Editor:

Bronchiectasis clinical practice guidelines advocate several medications to be prescribed by the inhaled route [1, 2]. Examples are inhaled saline (isotonic or 3–7% hypertonic) as a mucolytic and inhaled antibiotics for eradication of *Pseudomonas aeruginosa* or for maintenance treatment of people chronically infected with various organisms (mainly *P. aeruginosa*) [1]. In people with concomitant asthma or COPD, guidelines advocate inhaled corticosteroids, and patients with clinically significant breathlessness are recommended to receive long-acting β-agonists and/or muscarinic antagonists. Evidence supporting these recommendations is based on randomised controlled trials (RCTs) for inhaled antibiotics (reviewed by Laska *et al.* [3]) and for hypertonic saline [4]. The delivery of a nebulised drug to the bronchi has been estimated to vary 10-fold between nebuliser systems due to factors such as mean mass aerodynamic diameter, drug loss to the atmosphere and nebuliser, and nebulisation time [5]. Consequently, the European Respiratory Society (ERS) has published guidelines on the choice and care of nebulisers used for acute and chronic airway diseases, including cystic fibrosis and bronchiectasis [5].

In keeping with the ERS guidelines' [5] recommendations, RCTs of inhaled medication often administer the inhaled study medication through a uniform and protocol-specified nebuliser device, designed to optimise particle size and delivery as a drug–device combination. Examples are: the InnoSpire Deluxe air compressor (Philips Respironics), a jet nebuliser tested with inhaled tobramycin solution [6]; a vibrating-mesh nebuliser (VMN) for inhaled tobramycin solution [7]; I-Neb (Adaptive Aerosol Delivery VMN) for inhaled colistin [8]; PARI LC Sprint (a jet nebuliser) for inhaled ciprofloxacin [9]; and eFlow rapid VMN (PARI Pharma) for inhaled hypertonic saline [4]. These are specialised nebulisers powered by jet or vibrating mesh technologies, sometimes with adaptation to the patient's breathing pattern, designed to optimise particle size and, hence, drug delivery. To date, no drug has been licensed for bronchiectasis and inhaled antibiotics are frequently used off-label. A large number of different nebuliser and inhaled devices are available, and in the absence of licensed drug–device combinations, off-label treatments may be delivered with widely varying devices. The assurance of optimal drug delivery is therefore unknown.

Our aim in this study was to assess the preferences of specialists and the availability of devices used for inhaled medications in patients with bronchiectasis. To this aim, we conducted an online survey of prescribing preferences of inhaled medications and nebulisation devices, which was administered to respiratory health care professionals who treat patients with bronchiectasis. The survey was developed by members of the European Multicenter Bronchiectasis Research and Audit Collaboration (EMBARC) [10] and consisted of 11 items, which were open and multiple-choice questions of single and multiple selection. The survey was administered through e-mail to respiratory professionals caring for patients with bronchiectasis who were recruited from the EMBARC collaboration, and it was available from December 2019 to February 2020. Participation was anonymous and voluntary, and no ethical approval was required. SPSS Statistics 28.0 (IBM, New York, NY, USA) was used for statistical analyses. Descriptive analysis was used, and data are reported as frequencies and percentage of the total number of survey respondents. Normality was tested using the Kolmogorov–Smirnov test. ANOVA and t-tests were used to assess groups of parametric data. Statistical significance was set at $\alpha<0.05$.

Shareable abstract (@ERSpublications)
Specialists caring for people with bronchiectasis recommend specialised nebulisers for inhaled antibiotics, but are often limited by availability and cost of nebulisation devices https://bit.ly/40FvFdZ

Cite this article as: Shteinberg M, Spinou A, Goeminne P, *et al*. Prescribing preferences and availability of nebulisers and inhalers for inhaled medications in bronchiectasis: results of a specialist survey. *ERJ Open Res* 2024; 10: 00724-2023 [DOI: 10.1183/23120541.00724-2023].

https://doi.org/10.1183/23120541.00724-2023

TABLE 1 Use of inhaled medications and preferred mode of delivery

	Choice of device for medication delivery					Type of nebuliser for nebulised medications				
Pharmacological class (patients using)	**Nebulisers**	**Metered-dose inhalers**	**Metered-dose inhalers with spacer**	**Dry-powder inhalers**	**Either metered-dose or dry-powder inhalers**	**Respondents**	**Any available nebuliser**	**Jet tested with the drug**	**Ultrasonic**	**Vibrating mesh**
Bronchodilators (n=115)	47 (41.2)	26 (22.8)	52 (45.6)	37 (32.5)	60 (51.8)	47	24 (51.1)	19 (40.4)	7 (14.9)	11 (23.4)
Inhaled corticosteroids[#] (n=106)	15 (14.2)	19 (17.9)	49 (46.2)	39 (36.8)	62 (58.5)	15	7 (46.7)	7 (46.7)	3 (20)	3 (20)
Isotonic saline (n=86)			NA			86	47 (55.3)	27 (31.8)	7 (8.2)	7 (8.2)
Hypertonic saline (n=108)			NA			108	48 (45.3)	38 (35.8)	11 (10.4)	10 (9.4)
Inhaled antibiotics (n=99)	76 (78.4)	NA	NA	5 (5.2)[¶]	NA	90	25 (27.8)***	46 (51.1)	8 (8.9)	25 (27.8)

Data are presented as n (%) unless otherwise stated. Respondents were asked whether they prescribe each of the pharmacological classes. For those answering "yes" or "sometimes", questions regarding mode of delivery and choice of nebulisers were available. For each pharmacological class, numbers indicate respondents who replied "yes" or "sometimes". Percentages do not sum to 100%, as respondents could select more than one answer. NA: not applicable. [#]: inhaled corticosteroids±long-acting β-agonists; [¶]: either nebuliser or dry-powder inhalers, 16.5%. ***: p<0.001 for comparisons between inhaled antibiotics and inhaled saline, both isotonic and hypertonic.

130 specialists answered the survey: 94 (72.3%) identified as respiratory physicians; the rest were nurses (23, 17.7%), physiotherapists (eight, 6.2%) and five (3.8%) from other professions. Respondents came from 25 countries (in and outside Europe) with the majority (53, 40.7%) from the UK, and 10 (7.7%) from France and from Germany.

Table 1 presents the prevalence of medication use, preferred delivery mode per type of medication and preferred nebuliser devices. For inhaled antibiotics, specialists were less likely to allow "any nebuliser" compared to when using other inhaled medications (27.8% *versus* 45.3–55.3%; $p<0.001$ for comparisons with inhaled saline, both isotonic and hypertonic). Specialists reported that they often recommend using a mouthpiece (77, 59.2%) when nebulising. The most important factors when choosing a nebuliser were suitability of prescribed medication (79, 60.8%), ease of use and cleaning (68, 52.3%), compliance with standards for particle size (56, 43.1%) and cost (49, 37.7%). There was no significant difference in the consideration for the choice of nebulisers between regions ($p>0.05$ for comparisons between regions: UK, Eastern Europe, Western Europe and non-Europe). In response to an open-ended question regarding the choice of nebulisers, availability and cost considerations were often limiting in the choice of nebulisers.

Availability of inhaled medications (isotonic/hypertonic saline or antibiotics) for people with bronchiectasis does not necessarily ensure the availability of the specialised nebuliser which was tested with the drug in a clinical trial. Our findings show that while specialists in bronchiectasis care have an appreciation of the importance of the quality and suitability of the nebuliser device, availability is often limited. However, no study, to our knowledge, has compared the efficacy of drug delivery or clinical outcomes of different nebulisers, and so the choice of a nebuliser device is largely driven by cost and availability. Therefore, patients use available devices (usually low-cost jet nebulisers), which may affect drug deposition into the airways as well as nebulisation time, and in turn may impair adherence and effectiveness. The use of simple jet nebulisers will become increasingly hard to justify when the evidence base for drug plus advanced device emerges. Our findings indicate that specialists place more importance on the nebuliser system when prescribing inhaled antibiotics than isotonic or hypertonic saline. The preference of many experts for pressurised metered-dose inhalers is surprising given the impact on carbon emission by propellants used in these inhalers [11] and the availability of dry-powder inhalers for most types of inhaled medication. Likewise, the heterogeneity of the responses regarding nebuliser choices may reflect both lack of standards but also could stem from inadequate knowledge of specialists regarding different nebulisers and their drug suitability. For example, the use of ultrasonic nebulisers may not comply with some antimicrobials due to excessive heating of the solution [12]; however, ultrasonic nebulisers were the chosen nebulisers for inhaled antibiotics among eight (8.9%) of the specialists.

It is important to acknowledge and address the availability of specialised nebulisers in the future, when inhaled drugs are registered; currently, when prescribing inhaled antibiotics; and when assessing efficacy in "real life" studies.

Michal Shteinberg [1,2], Arietta Spinou [3,4], Pieter Goeminne[5], Megan Crichton[6], Charles Haworth[7] and James D. Chalmers[6]

[1]Pulmonology Institute and CF Center, Carmel Medical Center, Haifa, Israel. [2]The Technion – Israel institute of technology, The B. Rappaport Faculty of Medicine, Haifa, Israel. [3]School of Life Course and Population Sciences, Faculty of Life Sciences and Medicine, King's College London, London, UK. [4]King's Centre for Lung Health, King's College London, London, UK. [5]Department of Respiratory Diseases, AZ Nikolaas, Sint-Niklaas, Belgium. [6]Division of Molecular and Clinical Medicine, University of Dundee, Dundee, UK. [7]Cambridge Centre for Lung Infection, Royal Papworth Hospital and University of Cambridge, Cambridge, UK.

Corresponding author: Michal Shteinberg (michalsh@technion.ac.il)

Provenance: Submitted article, peer reviewed.

Conflict of interest: M. Shteinberg reports grants or contracts from GSK, Trudell Medical International and Tel Aviv League for Lung Diseases, outside the submitted work; personal payments for consultations from AstraZeneca, Boehringer Ingelheim, Dexcel, Kamada, Synchrony Medical, Trumed and Zambon, outside the submitted work; payment for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, Boehringer Ingelheim, Kamada, Sanofi and Insmed, outside the submitted work; support for attending meetings and/or travel from Boehringer Ingelheim Israel, Astra Zeneca Israel, Kamada, Rafa and GSK Israel,

outside the submitted work; participation on a data safety monitoring or advisory board for Bonus Biotherapeutics, Boehringer Ingelheim and AstraZeneca, outside the submitted work; is an *American Journal of Respiratory and Critical Care Medicine* Associate Editor, a management board member of the Israeli Pulmonology Society, the Israeli Society for Tuberculosis and Mycobacterial Diseases, and EMBARC, and editorial board member of the *European Respiratory Journal* and *Chest*, and a member of the European Respiratory Society task force on bronchiectasis guidelines, disclosures made outside the submitted work; and receipt of oPEP devices for clinical trial from Trudell medical international, outside the submitted work. A. Spinou has nothing to disclose. P. Goeminne reports lectures fees from Insmed, RMEI and GSK, outside the submitted work; support to attend conference from Chiesi outside the submitted work; and participation on a data safety monitoring board or advisory board for Boehringer, GSK and Pfizer, outside the submitted work. M. Crichton reports consulting fees from Boxer Capital LLC, outside the submitted work. C. Haworth reports consulting fees from 30 Technology, Aradigm, CSL Behring, Chiesi, Gilead, Grifols, GSK, Insmed, Janssen, LifeArc, Meiji, Mylan, Novartis, Pneumagen, Shionogi, Teva, Vertex and Zambon, outside the submitted work; and payment for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Chiesi and Insmed, outside the submitted work. J.D. Chalmers reports grants or contracts from AstraZeneca, Genentech, Gilead Sciences, GlaxoSmithKline, Insmed, Grifols, Novartis and Boehringer Ingelheim, outside the submitted work; consulting fees from AstraZeneca, Chiesi, GlaxoSmithKline, Insmed, Grifols, Novartis, Boehringer Ingelheim, Pfizer, Janssen, Antabio and Zambon, outside the submitted work; and is an associate editor of this journal.

Support statement: EMBARC3 is funded by the European Respiratory Society through the EMBARC3 clinical research collaboration. EMBARC3 is supported by project partners Armata, AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, Grifols, Insmed, Janssen, Lifearc and Zambon. J.D. Chalmers is supported by the GlaxoSmithKline/Asthma and Lung UK Chair of Respiratory Research.

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