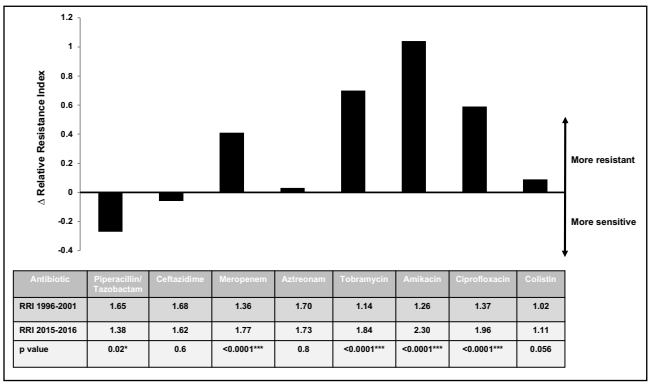
Increasing burden of antimicrobial resistance in pseudomonas aeruginosa from adult patients with cystic fibrosis (CF) in Northern Ireland: Then and now

Letters

INCREASING BURDEN OF ANTIMICROBIAL RESISTANCE IN *PSEUDOMONAS AERUGINOSA* FROM ADULT PATIENTS WITH CYSTIC FIBROSIS (CF) IN NORTHERN IRELAND: THEN AND NOW

Editor,

Cystic fibrosis (CF) is characterised by defective mucociliary clearance and chronic airway infection.[1] The most commonly isolated pathogen from CF airways is a Gram-negative bacterium, *Pseudomonas aeruginosa* (PA).[2] Chronic PA infection is associated with significant morbidity and mortality in CF patients[3] and necessitates multiple antibiotic courses.[2] Antimicrobial resistance (AMR) in PA may be driven by the exposure of bacterium to antibiotic, either in the acute setting or during anti-pseudomonal chronic suppressive therapy. We examined AMR from PA isolates from a single adult CF centre, by comparing antibiotic susceptibility from contemporary isolates with a collection from 13 years ago.



Antibiotic	Piperacillin/ Tazobactam	Ceftazidime	Meropenem	Aztreonam	Tobramycin	Amikacin	Ciprofloxacin	Colistin
RRI 1996-2001	1.65	1.68	1.36	1.70	1.14	1.26	1.37	1.02
RRI 2015-2016	1.38	1.62	1.77	1.73	1.84	2.30	1.96	1.11
p value	0.02*	0.6	<0.0001***	0.8	<0.0001***	<0.0001***	<0.0001***	0.056

Fig 1. Change in mean Relative Resistance Index [RRI] over a 13 year period with respect to Pseudomonas aeruginosa isolates (n=200) from the sputum of adult CF patients

Two collections of PA isolates were examined, each consisting of 100 non-duplicated organisms, which had isolated from the sputum of adult CF patients attending the Northern Ireland Adult Cystic Fibrosis Centre, Belfast City Hospital. Collection A was isolated during the period 1996-2001 and Collection B (2015-2016). Microbiological isolation of PA was performed from freshly expectorated sputum, by employment of selective culture for 24-48h, followed by biochemical confirmation with API20NE identication strips (Biomerieux Ltd, UK). Antibiotic susceptibility was performed on each isolate by standard disk diffusion assay and resulting zone sizes were interpreted against published CLSI criteria. Eight antibiotics from three classes of antibiotics were examined, including beta-lactams, fluoroquinolone and polymyxin, as detailed in Figure 1. Antibiotic susceptibility was quantified by employment of a novel marker, Relative Resistance Index [RRI], as recently described.[4] Briefly, qualitative "sensitive", "moderately resistant" and "resistant" data were converted into a quantitative RRI value, through employment of an algorithm.[4] An unpaired two-tailed t-test was used for comparison of trends between these two periods and a probability (p) value of less than 5% ($p<0.5$) was considered statistically significant. There were no differences in the microbiological isolation methodology nor with the antibiotic susceptibility methodology between these two collection periods.

A comparison of RRI scores between the two collection periods is shown (Figure 1). RRI and AMR increased significantly for ciprofloxacin ($p<0.0001$)***, aminoglycosides (both amikacin and tobramycin, $p<0.0001$)*** and meropenem ($p<0.0001$)*** for PA isolates from 1996-2001 to 2015-2016. There was reduction in AMR during this period with piperacillin/tazobactam and ceftazidime.

Overall, this study showed markedly greater resistance in the 2015-2016 PA cohort. Increase in AMR may reflect chronic exposure of PA to several classes of antibiotics used in the management of CF airways infection. Until now, it has been relatively difficult to perform comparative studies on AMR in CF, due to the reliance on generating largely qualitative data (S, I &R) from disk diffusion assay. However, RRI may help tracking changes in resistance patterns either at a population level or at an individual patient level, either with a single antibiotic agent, several agents within a single class or collectively between antibiotic classes.

This approach may be useful in helping to track emergence in AMR epidemiologically, those agents which display the greatest shift in AMR, as well as helping to guide antimicrobial stewardship practices and policies in CF.

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Andrea Gramegna[1,2,3*], John E. Moore[1,2,4,5], John McCaughan[1,2], B. Cherie Millar[1,2,5], Judith Ewing[2], J. Stuart Elborn[4,6], Francesco Blasi[3] and Damian G. Downey[2,4]

1 Department of Bacteriology, Belfast City Hospital, Belfast Health & Social Care Trust, Lisburn Road, BELFAST, BT9 7AD, Northern Ireland,

2 Regional Adult Cystic Fibrosis Centre, Belfast City Hospital, Belfast Health & Social Care Trust, Lisburn Road, BELFAST, BT9 7AD Northern Ireland,

3 Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Internal Medicine Department, Respiratory Unit and Regional Adult Cystic Fibrosis Center,IRCCS Fondazione Cà Granda Ospedale Maggiore Policlinico, Milan, Italy

4 Centre for Experimental Medicine, Queen's University Belfast, Northern Ireland,

5 School of Biomedical Sciences, Ulster University, Cromore Road, Coleraine, BT52 1SA, Northern Ireland.

6 Imperial College and Royal Brompton Hospital, London

Correspondence to: Dr. Andrea Gramegna,Department of Pathophysiology and Transplantation, Università degli Studi di Milano,Internal Medicine Department,Respiratory Unit and Regional

Adult Cystic Fibrosis Center, IRCCS Fondazione Cà Granda Ospedale Maggiore Policlinico, Milan, Italy.

gramegna.med@gmail.com

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