Scottish Government Health Directorates Chief Scientist Office

The impact of antimicrobial exposure on subsequent antimicrobial resistance in patients with COPD and bronchiectasis (CZH/4/1145)

Researchers
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Aim
To investigate antimicrobial resistance (AMR) among patients with chronic respiratory disease and associations with prior exposure to antibiotics in the community in order to identify high risk patients and prescribing to inform clinical practice and prescribing policy at a local and national level.

Project Outline/Methodology
Sputum samples from patients with chronic lung conditions (COPD and bronchiectasis), who have registered with a research database were analysed, using standard culture and antibiotic susceptibility tests in the NHS microbiology lab. Feasibility testing of a type of test (PCR) for AMR detection in sputum was conducted in a research lab and existing PCR results for bacterial identification were made available. Lab results were linked to information about the patients' lung conditions from the research databases, and to demographic, primary care prescribing and hospital admissions datasets. Data were anonymised for analysis in the Health Informatics Centre (HIC) secure Safe Haven. Associations between previous antibiotic prescriptions, patient factors, and AMR, and associations with mortality, were evaluated using statistical tests (logistic regression).

Key Results
647 sputum samples from 331 patients were analysed. 50% of the patient cohort were male and the average age was 68 years. 137 (41%) patients had at least one positive (i.e. bacteria detected) sputum culture and 56 (41%) of these had a sample with antibiotic resistant bacteria. The most common bacteria identified was *Haemphilus influenzae* (15% of patients), 35% of these were resistant.

In logistic regression, there were trends suggesting increased likelihood of AMR with older age, male gender, decreased social deprivation, comorbidity, previous hospital admissions and increasing symptom severity, but the associations were not statistically significant.

130 (95%) of patients with positive sputum cultures had antibiotics in primary care in the year prior to first sample. There were trends towards increased AMR with cumulative antibiotic exposure over the previous year (odds ratio (OR)=1.02, 95%CI 0.9-1.13, for each additional 30 days of antibiotics), and with more recent antibiotic exposure (OR=0.93, 0.85-1.02, for each additional 30 days since most recent antibiotic exposure) but these were not statistically significant.

40 (12%) study patients died between sample date and end of follow up. Mortality rates were 9/56 patients (16%) with AMR and 31/275 (11%) in those without. Age, comorbidity, prior admissions and symptom severity were all significantly associated with increased mortality but AMR was not.

434 (67%) samples had PCR results for bacterial identification available, and up to 394 types per sample were identified. Using PCR to test for AMR on individual sputum samples was not technically feasible within this study, as other researchers have independently found over the same time period.

Conclusions
There were trends towards associations between cumulative antibiotic exposure and likelihood of AMR in this cohort of patients with chronic respiratory disease but the strength of findings was limited by the relatively small number of positive sputum samples and the high prevalence of prior antibiotic exposure.

What does this study add to the field?
The findings of this novel study, involving collaboration between the NHS, a research laboratory and epidemiology, add to current hypotheses about associations between antibiotic exposure and resistance at the at individual patient level. There are currently very few such studies in the literature.

Implications for Practice or Policy
An original aim was to generate data that informs specific antibiotic prescribing guidance, but the sample size prohinted specific recommnedations

Where to next?
We plan to link routinely generated NHS microbiology laboratory sample results to this rich dataset to increase the number of positive samples and improve statistical power. We will also be conducting a pilot study of using metagenomics in place of single sample PCR to detect AMR in sputum.

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