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Short report

Impact of penicillin allergy records on carbapenem prescribing: an observational retrospective cohort study

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SUMMARY

Penicillin allergy labels have been associated with second-line antibiotic prescribing. This study measured the impact of penicillin allergy labels on meropenem prescribing. Rates of meropenem prescribing were compared between patients with a penicillin allergy record and patients without such a record. Potential confounders were also collected (i.e. age, sex and co-morbidities). Of the 21,272 patients with no penicillin allergy, 225 (1.06%) were prescribed meropenem, whereas of the 3443 patients with penicillin allergy, 240 (6.97%) were prescribed meropenem. Meropenem prescribing is associated with a patient's penicillin allergy record. Given that many penicillin allergy records are incorrect, addressing spurious penicillin allergy labels may reduce meropenem prescribing.

Introduction

Carbapenems are broad-spectrum antibiotics that are generally held in reserve and used to treat infections caused by antimicrobial-resistant (AMR) bacteria. Over recent years, the effectiveness of this valuable class of antibiotics has been threatened by the global emergence of bacteria that can produce carbapenemase enzymes which inactivate these antibiotics [1]. In order to reduce the selection pressure for the emergence and spread of multi-resistant bacteria, including those that produce carbapenemases, the UK Department of Health Commissioning for Quality and Innovation (CQUIN) framework has set targets for the reduction of carbapenem prescribing [2].

Patients with a record of penicillin allergy may be prescribed carbapenems more often than patients without a penicillin allergy record [3]. Carbapenems are used rather than cephalosporins or other broad-spectrum antibiotics when second- or third-line treatments are needed because of the low reported rates of allergic reactions to carbapenems in patients with a penicillin allergy record [4,5]. Penicillin allergy status may therefore be driving the use of carbapenems. If 90% of patients with a label of penicillin allergy are not truly allergic to penicillin when formally assessed, as much literature

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suggests [6], penicillin allergy records may be unnecessarily increasing the use of carbapenems. 'De-labelling' patients with false penicillin allergy records may therefore be a means of reducing unnecessary carbapenem use, and complying with the AMR CQUIN [2].

The aim of this study was to measure the impact of penicillin allergy status on meropenem prescribing, taking account of confounding factors.

Methods

This study was designed and reported using the STROBE statement [7].

Ethics

National Health Service (NHS) ethical approval was not required as the study did not meet the health research authority definition for research, or the requirements for NHS Research Ethics Committee approval. Patient data were used in accordance with local NHS hospital policy.

Design

This was a case–control study within a cohort of all patients who were prescribed antibiotics during the study period. Cases were considered to be patients with a penicillin allergy record in their electronic health records, and controls were those patients without such a record. The first inpatient spell, for both cases and controls, was included, with all subsequent inpatient spells excluded if the patient had multiple inpatient spells to avoid double counting of patients.

Setting

This study was conducted in a district general hospital in England with 750 inpatient beds. The hospital serves a local population of 430,000 people, and this figure can increase significantly during holiday seasons.

Participants

Any inpatient (adult or child) prescribed a systemic antibacterial agent(s) (British National Formulary Chapter 5.1) between April 2016 and April 2017 inclusive was eligible for inclusion in this study. Children aged <1 year and adults aged >100 years were excluded to reduce the risk of unintentional identification.

Data sources and variables

Data were extracted from the electronic prescribing and medication administration system (EPMA; JAC Computer Services, Basildon, UK). Variables included: age, sex, co-morbidity [International Statistical Classification of Diseases and Related Health Problems 10th Revision [8] (ICD-10) administrative code, see online supplementary material for codes used], name of antibiotic(s), if the patients had a penicillin allergy record, and if the patient had penicillin sensitivity recorded (combined to give one penicillin allergy record). Patient allergy and sensitivity status is entered manually into the patient's EPMA record, and this information is retained within the EPMA system between inpatient spells. The planned outcome measure was at least one prescription for a carbapenem.

Table I
Coefficients for logistic regression assessing independent risk factors for meropenem prescribing

Variable	OR	Lower–upper	*P*-value
Penicillin allergy or sensitivity record	6.70	5.53–8.12	<0.001
Female sex	1.36	1.12–1.66	0.002
Age at discharge	1.01	1.01–1.02	<0.001
Co-morbidities			
Asthma	0.57	0.27–1.19	0.136
Cancer	1.89	1.49–2.39	<0.001
CHD	0.68	0.43–1.07	0.097
Renal disease	1.40	1.10–1.78	0.007
COPD	0.47	0.23–0.98	0.043
Pulmonary disease	1.56	0.80–3.03	0.194
DM	1.31	1.02–1.67	0.033
Smoker	1.22	0.89–1.66	0.213
CVA	1.11	0.81–1.53	0.516
AMI	1.28	0.78–2.10	0.333
CHF	1.22	0.90–1.67	0.206
Connective tissue disease	1.06	0.65–1.73	0.817
Dementia	0.98	0.65–1.47	0.917
Liver disease	2.08	1.17–3.68	0.012
Peptic	1.72	0.67–4.46	0.258
PVD	1.75	1.22–2.52	0.002
Paraplegia	0.88	0.37–2.09	0.777

CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; CVA, cerebral vascular accident; AMI, acute myocardial infarction; CHF, congestive heart failure; PVD, peripheral vascular disease; OR, odds ratio.

Bias

Consecutive patients fulfilling the inclusion criteria were included to reduce the risk of bias (i.e. all raw data were analysed and there was no filtering of patients).

Study size

Pre-study sample size calculations were not undertaken because the study was a retrospective service evaluation.

Statistical methods

A pre-specified logistic regression model was used to investigate the relationship between penicillin allergy records and prescription of meropenem, taking account of potential confounders (i.e. age, sex and co-morbidities).

Results

There were 24,715 first inpatient spells where at least one antibiotic was prescribed. Thirty-two and 465 patients were prescribed ertapenem and meropenem, respectively. There was only one imipenem prescription, precluding meaningful

analysis. Subsequent analysis concentrated on meropenem to maximize statistical power.

Of the 21,272 patients with no penicillin allergy, 225 (1.06%) were prescribed meropenem, whereas of the 3443 patients with penicillin allergy, 240 (6.97%) were prescribed meropenem. The results of multi-variable analysis of factors affecting meropenem prescribing are shown in Table I. Increased meropenem prescribing was associated with penicillin allergy status, increasing age, female sex and selected co-morbidities (cancer, renal disease, peripheral vascular disease, diabetes and liver disease). Patients with chronic obstructive pulmonary disease (COPD) were less likely to be prescribed meropenem. Amoxicillin was prescribed for 7511/21,272 (35.3%) patients without a record of penicillin allergy, compared with 129/3443 (3.7%) patients with a record of penicillin allergy.

Discussion

Key findings

Patients with a penicillin allergy record were approximately six times more likely to be prescribed meropenem than patients without a penicillin allergy record, even after accounting for age, sex and co-morbidities; as prescription rates were <10%, the odds ratio approximates to the relative risk. Efforts to ensure allergy records are accurate [6], and to identify patients with incorrect penicillin allergy and sensitivity records and subsequent removal of those labels will likely reduce the use of second-line antibiotics such as meropenem in hospitals.

Meropenem is recommended in the local antibiotic prescribing guidelines for sepsis and neutropenic sepsis in patients with a history of non-severe penicillin allergy history. As such, increased meropenem prescribing would be expected in those with a history of penicillin allergy.

Among the cohort of patients prescribed antibiotics, patients with COPD were less likely to be given meropenem, while patients with cancer, renal disease, respiratory disease, diabetes, peripheral vascular disease and liver disease were more likely to receive meropenem. It is hypothesized that a perceived or actual risk of infection with multi-drug-resistant Gram-negative bacteria (MDR-GNB) may account for some of this increased risk of carbapenem prescription. Although these co-morbidities have not been specifically identified as risk factors for MDR-GNB in guidelines [9,10], previous antibiotic exposure is a risk and these groups tend to be high antibiotic users [10]. Diabetes has been identified previously as a risk factor for urinary tract infections (UTIs) due to extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* or *Klebsiella* spp. [9], and carbapenem antibiotics are the usual antibiotic choice for ESBL UTIs so this might explain some of the increase in meropenem prescribing seen in patients with diabetes. Patients with cancer are more likely to receive fluoroquinolones as part of their chemotherapy regimen [11], which also increases the risk of ESBL-producing bacterial carriage and infection [9].

Limitations

This study was based on electronic data records, which are dependent on the quality of data entry. However, the data used are those used in clinical practice and those which drive prescribing. It is anticipated that sex, date of birth and antibiotic prescription will be accurate. Co-morbidities, identified by ICD-10 codes, rely on accurate handwritten inpatient medical records, and therefore patient co-morbidity assignment errors may occur.

The large cohort size in this study is a strength, but the results may not be generalizable due to it being a single-centre study. Others have shown the association between meropenem prescribing and penicillin allergy [3], but further multi-site studies are needed to confirm this association.

This study did not differentiate allergy from sensitivity, or further categorize the recorded reactions that the patient experienced; in practice, these terms are often used interchangeably, and poor recording of reactions usually precludes a more detailed analysis. This study found that combining the allergy/sensitivity record had a profound effect on meropenem prescribing.

In conclusion, meropenem prescribing is driven by penicillin allergy records. Given that many penicillin allergy records are incorrect, addressing spurious penicillin allergy labels may be a way to reduce unnecessary meropenem prescribing.

Conflict of interest statement
None declared.

Funding sources
None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2018.11.020.

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