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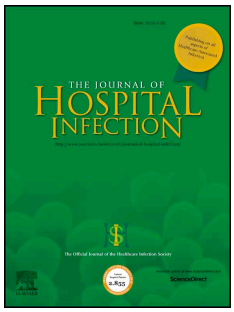

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The impact of penicillin allergy records on carbapenem prescribing: an observational retrospective cohort study.

Meropenem prescribing associated with penicillin allergy records

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Abstract

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 (age, sex, co-morbidity).

Of the 21,272 patients with no penicillin allergy 225 (1.06%) were prescribed meropenem, whereas of the 3443 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 English 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 use of carbapenems. If 90 percent of patients with a label of penicillin allergy are not truly allergic to penicillin when formally assessed as much literature 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

NHS ethics 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. The patient data were used in accordance with local NHS Hospital Policy.

Design

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, controls, were those patients without such a record. The first

patient spell, for both cases and controls, were included with all subsequent spells excluded if the patient had multiple inpatient spells, to avoid double counting of patients.

Setting

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

Participants

Inclusion criteria: 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. Exclusion criteria, children less than 1 year of age and adults over 100 years of age 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). Variables included: age, sex, co-morbidity (International Statistical Classification of Diseases and Related Health Problems 10th Revision[8] (ICD-10) administrative code, see supplementary material for codes used), name of antibiotic(s), whether the patients had a penicillin allergy record, whether the patient had a penicillin sensitivity recorded (combined to give one penicillin allergy record). Patient allergy and sensitivity status is manually entered to the patient's EPMA record, this information is retained within the EPMA system between inpatient spells. The planned outcome measure was at least one prescription for a carbapenem.

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: age, gender, and co-morbidities.

Results

There were 24,715 patient first 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 maximise statistical power.

Of the 21,272 patients with no penicillin allergy 225 (1.06%) were prescribed meropenem, whereas of the 3443 with penicillin allergy 240 (6.97%) were prescribed meropenem. The results of multivariable analysis of factors affecting meropenem prescribing are shown in Table 1. 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 whereas 129/3443 (3.7%) patients with a record of penicillin allergy were prescribed amoxicillin.

Variable	**OR**	**Lower - Upper**	**P value**
Penicillin allergy or sensitivity record	6.70	5.53 - 8.12	<0.001
Gender Female	1.36	1.12 - 1.66	0.002
Age on discharge	1.01	1.01 - 1.02	<0.001
Comorbidities			
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	1.40	1.10 - 1.78	0.007
COPD	0.47	0.23 - 0.98	0.043
Pulmonary	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	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

Table 1. Coefficients for logistic regression assessing independent risk factors for meropenem prescribing. 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

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, gender, and comorbidities; because prescription rates were below 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 removing those labels will likely reduce the use of second line antibiotics such as meropenem in hospitals.

Meropenem is recommended in our local antibiotic prescribing guidelines for sepsis and neutropenic sepsis in patients with a history of non-severe penicillin allergy history and as such we would expect to see increased prescribing of meropenem in those with a history of penicillin allergy.

Among the cohort of patients prescribed antibiotics, COPD patients were less likely to be given meropenem, while cancer patients, renal patients, respiratory patients, diabetic patients, peripheral vascular disease patients and liver patients were more likely to receive meropenem. We hypothesise 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 a 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 previously identified as a risk factor for urinary tract infections (UTI) due to ESBL-producing *E. coli* or *Klebsiella*

sp[9] and carbapenem antibiotics are the usual antibiotic choice for ESBL UTI, so this might explain some of the increase in meropenem prescribing we have seen in diabetic patients. Cancer patients are more likely to receive fluoroquinolones as part of their chemotherapy regimen,[11] which also increases risk of extended spectrum beta-lactamase producing bacterial carriage and infection.[9]

Limitations

This study is based on electronic data records, which are dependent on the quality of data entry. The data we have used however, are what is used in clinical practice and what drives prescribing. We expect gender, date of birth and antibiotic prescription to be accurate. Co-morbidities, identified by ICD-10 codes, rely on accurate hand written 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.

We have not differentiated allergy from sensitivity or further categorised 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. We have found that combined the allergy / sensitivity record has a profound effect on meropenem prescribing.

Conclusion

Meropenem prescribing is being 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.

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None. These data were generated as part of routine work within the organisation.

Transparency declarations

None to declare.

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