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Is there any difference in quality of prescribing between antibacterials and antifungals? Results from the first global point prevalence study (Global PPS) of antimicrobial consumption and resistance from 53 countries

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Objectives: To compare the quality of antibacterial with antifungal prescribing in the world.

Methods: Data from the global point prevalence study (Global PPS) were used. The Global PPS took place on any one day between February and June 2015 in 335 participating hospitals from 53 countries. It collected demographic data on patients treated with antimicrobials and data on prescription characteristics of the antimicrobials. For the present study, the quality of antibiotic prescription was compared with antifungal prescription using logistic regression analysis. The following indicators were compared: the presence of the reason for prescription and stop/review date in notes, and compliance with a local guideline.

Results: There were 48565 antimicrobial prescriptions for 34731 patients [median age 63 years (range 0–106); 52.6% male] in the Global PPS. Among these antimicrobials, 43513 (89.6%) were antibacterials and 2062 were antifungals for systematic use, and these data were used in this study. Reasons for prescriptions [77.7% versus 71.8%, OR 1.4 (95% CI 1.2–1.5)] and stop/review dates [38.3% versus 31.9%, OR 1.3 (1.2–1.5)] were found more often in notes for antibacterials than for antifungals. Antibacterials were prescribed less often according to local guidelines than antifungals [57.0% versus 71.0%, OR 0.6 (0.5–0.6)].

Conclusions: There are differences in the quality of antibacterial and antifungal prescribing and we identified opportunities that can be used to improve the quality of antimicrobial prescribing.

Introduction

Inappropriate use of antibacterials and antifungals has resulted in the emergence of resistance of bacteria and fungi to antibacterials and antifungals, respectively.[1,2] Improving the quality of antimicrobial prescribing is therefore paramount. While many papers have been published on the quality of antibacterial prescription,[3–5] papers on the quality of antifungal prescription are difficult to find. To identify which opportunities of antimicrobial prescription can be improved, measurement of how antimicrobials are prescribed is needed; for example, whether the prescribed antimicrobials are correct according to the guidelines and whether the reasons for prescription are mentioned in the patient's medical notes. Another example is how often antimicrobials with high oral bioavailability are given by mouth in comparison with an intravenous route of administration. When such information is available, the quality of antimicrobial stewardship implementation can be assessed[6] and audit of correct antimicrobial use can be performed.

The global point prevalence study (Global PPS) collected data on antibacterials and antifungals in the world in 2015 using a standardized and validated web-based application. Its aim was to compare antimicrobial prescribing in hospitalized adults, children and neonates between regions of the world.

In the present study, we used the data from the Global PPS to compare the quality of prescription between antibacterials and antifungals.

Methods

Global PPS

The Global PPS was a point prevalence study of antimicrobial use in acute care hospitals all over the world based on a standardized study protocol in

neonates, children and adults. The protocols have been validated and used previously in other point prevalence studies.[7,8] Protocols of the study can be found at http://www.global-pps.com/. In short, the Global PPS collected demographic data (age, gender and body weight) on each patient treated with an antimicrobial. For each antimicrobial prescription, dose per administration, dosing frequency, route of administration, reasons for prescription and whether the targeted infection was community or hospital acquired were recorded. Further data collected were related to the quality of antimicrobial prescription: whether the reason for prescription and stop/review date were mentioned in notes, and whether the choice of antimicrobials was compliant with local guidelines. Participation was voluntary, and the study took place on any one day between February and June 2015. The degree of participation in 53 countries can be found in Table S1 (available as Supplementary data at *JAC* Online). The participating hospital was also asked to submit the denominator data at the ward level, i.e. the number of patients on the ward at 8 am, and the total number of beds by ward.

Ethics

Approval from ethics committees at participating hospitals was obtained when necessary.

Statistical analysis

We compared four indicators of prescribing quality between antibacterials and antifungals using logistic regression and calculated the odds ratios, i.e. the chance of the specific quality indicator being higher/lower in antibacterial in comparison with antifungal prescription. $P < 0.05$ was deemed statistically significant. As well as the three above-mentioned quality indicators, we also compared the proportion of administrations by the oral route for antibacterials (fluoroquinolones: ciprofloxacin, levofloxacin and moxifloxacin) and antifungals (azoles: fluconazole and voriconazole). These antimicrobials were chosen due to their high oral bioavailability.[9,10]

Comparisons of the quality of antimicrobial prescription were also made among world regions. The regions were classified as described by the United Nations Statistic Division[11] and can be found in Table S2. All analyses were performed using IBM SPSS Statistics for Windows version 23.0 (IBM Corp., Armonk, NY, USA).

Results

There were 48565 antimicrobial prescriptions for 34731 patients [median age 63 years (range 0–106), 52.6% male] in the Global PPS. Among these antimicrobials, 43513 (89.6%) were antibacterials (ATC code J01) and 2062 (4.3%) were antifungals (ATC code J02) for systematic use.

For about three-quarters (77.4%) of the antimicrobial prescriptions, the reason for prescribing was mentioned in the patient's notes. Compared with antifungal prescription, the reason for antibacterial prescription was more often mentioned in the patient's notes [77.7% versus 71.8%, OR 1.4 (95% CI 1.2–1.5)].

Only 57.6% of the antimicrobial prescriptions were according to the local guidelines, and for 19.9% of the prescriptions there was no guideline available. The choice of antibacterial was less often according to the local guidelines than the choice of antifungal [57.0% versus 71.0%, OR 0.6 (95% CI 0.5–0.6)].

The proportion of prescriptions with stop/review dates in the notes was low, i.e. 37.9%, but was higher for antibacterial prescription than antifungal prescription [38.3% versus 31.9%, OR 1.3 (95% CI 1.2–1.5)].

There were 4573 fluoroquinolones (9.4% among all antibacterials) and 1434 azoles (69.5% among all antifungals) prescribed. Both were given mostly as empirical therapy (75.8% of the fluoroquinolone prescriptions and 71.6% of the azole prescriptions). More azoles were given as prophylaxis than fluoroquinolones (45.6% versus 17.2%). Fifty-six percent of antimicrobials with high oral bioavailability in this study (fluoroquinolones and azoles) were prescribed for oral administration. The proportion of oral administration was higher for azole antifungals than fluoroquinolone antibacterials (73.1% versus 55.2%).

In all quality indicators, there were differences across regions in the world (Table 1).

Discussion

This study compared the quality of antibacterial and antifungal prescribing using simple quality indicators obtained from the Global PPS data. We found that, overall, the reason for an antibacterial prescription was more often mentioned in patient's notes than for an antifungal prescription. We can only speculate that this difference is caused by the observation that antifungals were given much more often according to a guideline than antibacterials; the reason for antifungal prescriptions was perhaps so obvious for the prescribers that it was not mentioned in the patient's notes. Yet the practice of giving any antimicrobials with no mention in the patient's notes for antimicrobial stewardship practice is not ideal. The observation that reasons were more often present for antibacterial prescription than antifungal prescription in patients' notes reached a statistically significant level in North and West Europe, East and South Asia, and Australia and New Zealand. As an exception, in South Europe the reason for an antifungal prescription was more often mentioned in patients' notes than the reason for an antibacterial prescription. Perhaps this difference can be explained by local regulation and reimbursement policy on antibacterials and antifungals; for example, whether a policy exists that antibacterials can only be released when the reason for prescription is mentioned in the patient's notes.

Overall, the choice of an antifungal was more often correct according to local guidelines than the choice of antibacterials. This difference was consistent among all regions of the world. There are at least three possible explanations for this difference. Firstly, the number of indications for antifungal prescription is more limited than that for antibacterial prescription. The smaller the number of indications and guidelines the fewer the options that someone needs to choose from. Secondly, the diagnosis of fungal infections is generally more difficult than that of bacterial infections. Consequently, to evaluate whether an antifungal is prescribed correctly according to guidelines a detailed review of the clinical files is necessary, and there is a limited number of medical specialists who prescribe antifungals, while antibacterials are prescribed by almost all medical specialists. This observation implies that the quality of antibacterial prescription can be improved by improving the training of antibacterial prescribers. Thirdly, antifungals are in general more expensive than antibacterials. Prescribers, like people in general, tend to make informed decisions when they need to deal with high cost. It is intriguing to know whether increasing the price of antibacterials would lead to more prescriptions according to guidelines.

Mentioning stop/review dates in the notes was, overall, more often performed for antibacterials than for antifungals. This difference can be explained by the fact that the duration of antibacterial

Table 1. Comparison of quality of antibacterial and antifungal prescription across world regions

	Reason for prescribing mentioned in patient notes			Prescriptions were according to local guidelines			Stop/review date mentioned in notes			Proportion of oral administration		
	Antibacterials	Antifungals	OR antibacterials versus antifungals (95% CI)	Antibacterials	Antifungals	OR antibacterials versus antifungals (95% CI)	Antibacterials	Antifungals	OR antibacterials versus antifungals (95% CI)	Antibacterials	Antifungals	OR antibacterials versus antifungals (95% CI)
Europe												
Northern	84.0	77.3	1.6 (1.1–2.2)[a]	74.0	77.8	0.8 (0.6–1.2)	51.6	48.9	1.1 (0.8–1.5)	55.7	81.8	0.3 (0.06–1.3)
Western	80.7	73.3	1.5 (1.3–1.9)[a]	62.2	69.0	0.8 (0.7–1.0)	40.2	30.6	1.5 (1.3–1.8)[a]	76.2	66.1	1.6 (0.9–2.9)
South	69.7	78.3	0.6 (0.5–0.8)[a]	42.5	73.0	0.3 (0.2–0.4)[a]	31.0	31.4	1.0 (0.8–1.3)	42.1	64.2	0.4 (0.1–1.2)
East	72.9	100.0	NA	75.7	97.6	0.1 (0.01–0.5)[a]	40.7	40.5	1.01 (0.5–1.9)	33.3	100.0	NA
America												
North	85.9	81.0	1.4 (1.0–2.1)	66.6	71.3	0.8 (0.6–1.1)	38.2	29.1	1.5 (1.1–2.1)[a]	47.6	84.0	0.2 (0.06–0.5)[a]
South	82.5	85.0	0.8 (0.5–1.4)	51.0	72.8	0.4 (0.3–0.6)[a]	40.2	50.1	0.6 (0.4–0.9)[a]	56.7 (171)	46.2 (13)	1.5 (0.5–4.7)
Asia												
East and South	75.3	56.6	2.3 (2.0–2.8)[a]	62.1	71.9	0.6 (0.5–0.8)[a]	45.2	28.5	2.1 (1.7–2.5)[a]	47.8 (790)	77.9 (86)	0.3 (0.2–0.4)[a]
West and Central	74.3	67.2	1.4 (0.8–2.5)	35.2	41.3	0.8 (0.5–1.3)	19.3	15.5	1.3 (0.6–2.7)	49.3 (215)	71.4 (14)	0.4 (0.1–1.3)
Australia and New Zealand	87.7	76.1	2.2 (1.1–4.5)[a]	59.6	78.2	0.4 (0.2–0.8)[a]	29.3	15.2	2.4 (1.1–5.4)[a]	87.5 (48)	85.7 (7)	1.2 (0.2–1.4)
Africa	72.1	76.2	0.8 (0.4–1.7)	38.8	40.4	0.9 (0.5–1.7)[a]	32.8	16.7	2.4 (1.1–5.5)[a]	46.4 (207)	0	NA

NA, cannot be calculated.
[a]Statistically significant at $P < 0.05$.

therapy, in general, is more established than the duration of antifungal therapy; for example, the duration of antibacterial therapy in pneumonia and in urinary tract infection.[12,13]

We also found that, overall, among all antimicrobials with excellent oral bioavailability, the proportion of antifungals that were prescribed orally was higher than the proportion of antibacterials that were prescribed orally. This difference was statistically significant in North America and South and East Asia. The difference is perhaps caused by the more frequent use of antifungals as prophylaxis than antibacterials. Antifungal prophylaxis is often recommended in patients with substantial risk of invasive fungal infections; for example in patients with allogeneic haematopoietic stem cell transplant or patients with chemotherapy for acute leukaemia,[14] or in patients with recent abdominal surgery with recurrent gastrointestinal perforations in an intensive care unit where fluconazole is recommended.[15] As prophylaxis, the oral route of administration is more convenient than the intravenous route. However, it should be borne in mind that, in many cases of targeted treatment, there are antimicrobials with excellent bioavailability that can still be given by mouth.[9]

All of the quality indicators in this study can be used to improve the quality of antimicrobial prescribing. For example, the proportion of the oral mode of administration can be increased among antibacterials with excellent bioavailability since oral therapy is easy to give and cheaper than intravenous therapy.[9] Moreover, the oral route of administration saves nursing time and does less harm to patients from device-related reactions. Another example is issuing antimicrobials by the pharmacist only if the reason for the prescription is documented in the patient's notes. This will increase awareness of the importance of correct indications among antimicrobial prescribers.

This point prevalence study gives the best estimates of antimicrobial treatment of around 35000 patients in the world on one day. However, an important limitation of this study is that participation was voluntary. Therefore there are constraints on the generalizability of our findings. Furthermore, this study may overestimate the quality of prescribing as hospitals with better antimicrobial stewardship programmes are probably more likely to take part.

In conclusion, we show that there are differences in quality of prescribing between antimicrobials and antifungals. The identified indicators, which are mostly already known, can be used to improve the quality of prescribing antimicrobials.

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Transparency declarations

None to declare.

Supplementary data

Tables S1 and S2 are available as Supplementary data at *JAC* Online.

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