



Short report

Broad-spectrum antibiotic prescriptions are discontinued unevenly throughout the week

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SUMMARY

In order to investigate prescribing patterns of in-hospital broad-spectrum antibiotics (antimeticillin-resistant *Staphylococcus aureus* drugs, carbapenems and piperacillin/tazobactam), data on the distribution of antibiotic initiation and discontinuation throughout the week were analysed at Osaka University Hospital, Japan. No significant differences in the number of initiations were found between weekdays. However, broad-spectrum antibiotics were disproportionately discontinued on Tuesdays or on the second day after a holiday. This study suggests that broad-spectrum antibiotics tend to be continued over weekends or holidays and discontinued thereafter; this is likely to be due to behavioural factors beyond medical indications, and needs to be addressed in future antimicrobial stewardship initiatives.

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Introduction

Antimicrobial resistance (AMR) is a growing concern for global public health that undermines medical systems. Excessive and inappropriate use of existing antibiotics has resulted in the emergence of highly drug-resistant bacteria [1], and rational use of antibiotics is key to countering the rapidly escalating threat of AMR. Following endorsement of the AMR Global Action Plan by the World Health Organization in May 2015 [2], the promotion of antimicrobial stewardship programmes (ASPs) is strongly recommended.

At weekends, hospital functionality is reduced compared with weekdays; fewer medical and laboratory staff are available. Several reports have linked day of the week with the outcomes of healthcare services. For example, the management and mortality of myocardial infarction and cerebral stroke in patients admitted at weekends can be worse than in patients admitted on weekdays [3,4]. In terms of antibiotic prescribing, inappropriate or excessive use may increase at weekends in emergency centres [5] and primary care settings [6,7], which cannot be explained simply by disease prevalence or morbidity. Social or situational factors such as limited staff, rather than medical indications alone, may have influenced the antibiotic prescribing behaviour observed in these studies. To the best of the authors' knowledge, this is the first study to investigate the 'weekend effect' of in-hospital use of broad-spectrum antibiotics. On the basis of the authors' clinical experience, it was hypothesized that antibiotics are discontinued less frequently at weekends due to non-medical or

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non-pathophysiological factors. This study aimed to determine inconsistency in the use of broad-spectrum antibiotics throughout the week in order to encourage and guide antimicrobial stewardship.

Methods

A single-centre observational study on in-hospital use of broad-spectrum antibiotics was undertaken at Osaka University Hospital, a 1086-bed tertiary academic hospital in Japan. This hospital has 21 general wards (1037 beds) and two intensive care units (ICU) [ICU and trauma and critical care unit (TCU), 49 beds]. The average number of patients hospitalized per day and the average length of hospital stay in 2015 were 921.6 patients and 15.6 days, respectively. In the study hospital, pre-prescription authorization is unnecessary to initiate antibiotic treatment, and both attending doctors and residents can process orders for antibiotics. However, they must submit a notification form to the Division of Infection Control and Prevention when ordering any broad-spectrum antibiotics. An infection control team executes hospital ASP activities on weekdays by performing a prospective audit and feedback, but this is not undertaken at weekends. The study period was from April 2016 to March 2017. The two longer national holidays in Japan (28 April–6 May 2016 and 28 December 2016–4 January 2017) were excluded from the study as the antibiotic prescribing patterns could have differed over these periods compared with regular weekdays and weekends. All hospitalized patients who were administered broad-spectrum antibiotics during the study period were included in this study. Broad-spectrum antibiotics were defined as: antimeticillin-resistant *Staphylococcus aureus* (anti-MRSA) drugs, including vancomycin, teicoplanin, linezolid, daptomycin and arbekacin; and antipseudomonal drugs, such as carbapenems (meropenem, imipenem, doripenem and biapenem) and piperacillin/tazobactam (PIPC/TAZ). Informed consent was waived as the data were collected as part of the ASP without the use of any personal identifiers or the application of any intervention.

Weekdays were defined as Monday to Friday, and weekends were defined as Saturday and Sunday. Holidays were defined as national holidays. Routine care was usually provided on weekdays. Hospital staff functionality, both numerically and qualitatively, was reduced at weekends and during national holidays, but not during weekdays. On the general wards, there are no patient handovers between attending doctors. The patterns of antibiotic prescribing on each day of the week were analysed. In addition, the patterns of antibiotic prescribing on the days following national holidays were analysed in order to evaluate the influence of holidays on antibiotic discontinuation.

For treatment initiation, the monthly numbers of antibiotic prescriptions started on each day of the week were compared. For treatment discontinuation, the percentages of discontinuation on each day of the week and on the days after a holiday, calculated by dividing the number of discontinued antibiotics by the total number of antibiotics prescribed on each weekday, were calculated. The data were also analysed separately for anti-MRSA drugs and antipseudomonal drugs, and between general wards and ICUs. The Kruskal–Wallis test and the Mann–Whitney U-test with Bonferroni's correction as a post-hoc procedure were used for comparison of continuous variables.

Pearson's Chi-squared test was used to compare the percentages of discontinuation. Analyses were performed using the EZR software based on R Version 3.3.2 [8]. Statistical significance was set at $P < 0.05$.

Results

During the study period, there were 16,609 (83.5%) and 3274 (16.5%) scheduled and emergent admissions, respectively. Almost all of the scheduled admissions occurred on weekdays ($N = 16,434$, 98.9%), with very few cases at weekends ($N = 175$, 1.1%). Emergency admissions were also more frequent on weekdays ($N = 2712$, 82.8%) than at weekends ($N = 562$, 17.2%). In total, 2318 patients commenced treatment with broad-spectrum antibiotics: 1742 patients in the general wards and 576 patients in the ICUs. Discontinuation of these drugs was observed in 2296 patients: 1739 patients in the general wards and 557 patients in the ICUs. The numbers of initiations and discontinuations differed because the two long national holiday periods were excluded from the analysis. The numbers of patients newly administered carbapenems, PIPC/TAZ and anti-MRSA drugs were 851, 761 and 791, respectively. The total numbers of days of administration were 7860, 6345 and 7183 days for carbapenems, PIPC/TAZ and anti-MRSA drugs, respectively. The number of patients admitted did not differ significantly between weekdays (data not shown).

The numbers of broad-spectrum antibiotic initiations on each day of the week are shown in [Figure 1](#). Over a weekly period, there were generally fewer antibiotic initiations on Saturdays and Sundays than on weekdays. However, there were no significant differences in antibiotic initiations between weekdays ($P = 0.42$). A similar pattern was observed in the subanalysis for the anti-MRSA and antipseudomonal drugs ([Figure S1](#), see online supplementary material). This trend was seen in general wards, with significantly fewer antibiotic initiations observed on Saturdays and Sundays, but there were no significant differences between weekdays ($P = 0.49$). Conversely, in the ICUs, the number of broad-spectrum antibiotic initiations did not change throughout the entire week ($P = 0.94$) or between individual weekdays ($P = 0.86$) ([Figure S2](#), see online supplementary material).

The percentages of discontinuation on each day of the week and on the days after a holiday are shown in [Figure 2](#). There were evidently fewer discontinuations on Sundays. Broad-spectrum antibiotics were disproportionately discontinued on Tuesdays ($P < 0.001$ between Tuesday and Monday, $P = 0.001$ between Tuesday and Wednesday, $P = 0.004$ between Tuesday and Thursday, $P = 0.004$ between Tuesday and Friday) ([Figure 2A](#)). Moreover, the proportion of discontinuation was significantly higher on the second day after a holiday ($P < 0.001$ between Days 1 and 2, $P < 0.001$ between Days 2 and 3, $P = 0.005$ between Days 2 and 4, $P = 0.008$ between Days 2 and 5) ([Figure 2B](#)). Similar patterns were found in the subanalysis for antibiotic categories ([Figure S3](#), see online supplementary material). A stratified analysis of data from the general wards showed that the disproportionately high frequency of discontinuation on Tuesdays was significant, especially in comparison with Mondays ($P = 0.003$) and Wednesdays ($P = 0.04$), whereas there were no significant differences between the weekdays in the ICUs ([Figure S4](#), see online supplementary material).

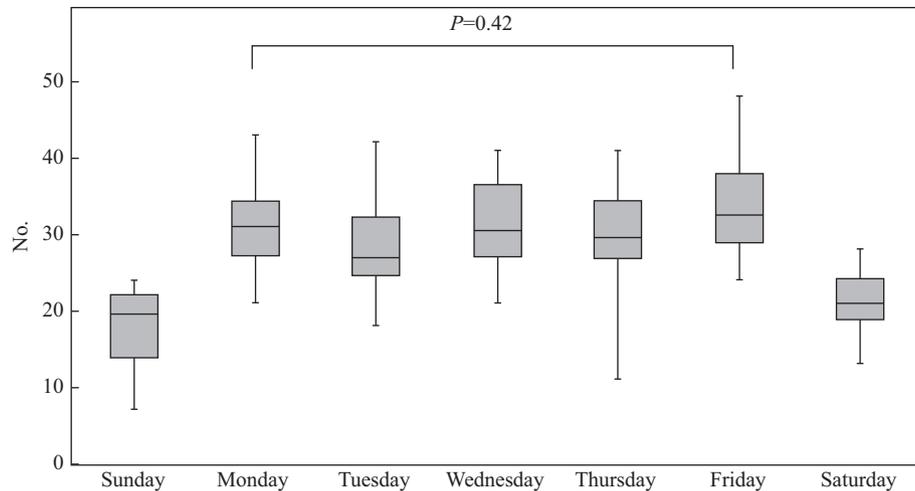
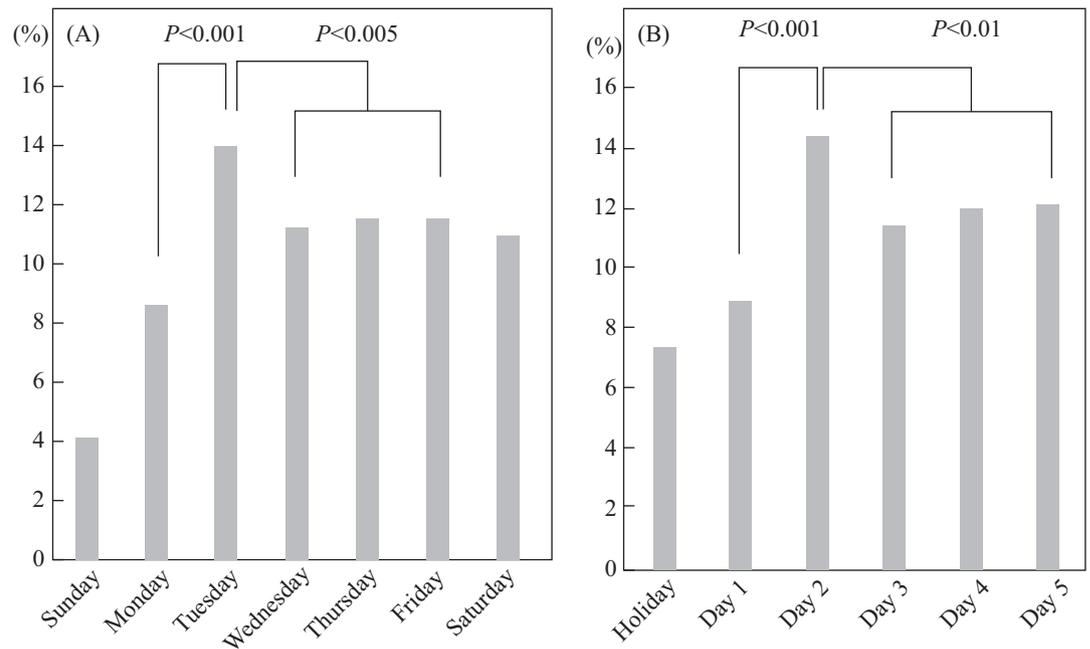


Figure 1. Number of broad-spectrum antibiotic initiations on each day of the week (hospital-wide scale). Monthly data are shown as median and box (interquartile range)-and-whisker (minimum–maximum) plots. The Kruskal–Wallis test was used to determine differences between the values for weekdays.



Antibiotic prescribing

Total number	3016	3249	3290	3145	3122	3224	3133	6778	3725	3366	2926	2789	2595
Number of discontinuations	125	280	460	354	360	372	345	500	330	486	334	333	313

Figure 2. Percentages of antibiotic discontinuation on each day of the week (A) and on the days after a holiday (B). Percentage of discontinuation was calculated by dividing the number of discontinued antibiotics by the total number of antibiotics prescribed on each day. The Pearson’s Chi-squared test was used to determine differences in discontinuation between days.

Discussion

Overall, an uneven pattern of broad-spectrum antibiotic discontinuation was observed throughout the week; specifically, the numbers of antibiotics discontinued on Tuesdays and on the second day after a holiday were significantly higher compared with other days. This pattern was observed for both anti-MRSA drugs and antipseudomonal drugs, but was not

observed in the ICUs. Onset of infectious diseases should not be biased to certain days, so the termination of antibiotic administration should also be distributed evenly over the course of a week. However, the results showed fluctuation over the week, suggesting that there are contributing factors apart from medical indications. Multiple factors such as human resource shortages could influence antibiotic prescribing, as shown previously [5–7].

There are several explanations for the uneven discontinuation of antibiotics. Inappropriateness of antibiotic initiation at weekends, possibly as a result of the reduced number of medical staff, could be a reason. Antibiotics initiated on Saturdays or Sundays would tend to be de-escalated on Tuesdays because of the so-called '48–72-h timeout' for antibiotics. However, the number of antibiotic initiations appeared to be lower at weekends than on weekdays, not supporting this hypothesis. At the study hospital, the ASP team reviews the formulary of broad-spectrum antibiotics each weekday. Therefore, ASP activity would not influence the fluctuation in antibiotic discontinuation. It is reasonable to discontinue antibiotics on Mondays, the first day after a weekend, but the broad-spectrum antibiotics were disproportionately discontinued on Tuesdays and on the second day after a holiday. At academic medical facilities, young clinicians check laboratory data, discuss the test results with attending doctors, and finally decide whether to terminate or change antibiotic treatments; these steps require a whole day. It is speculated that this lengthy decision-making process, which can be observed at other medical facilities, is one of the reasons for the uneven discontinuation of antibiotics observed in this study.

Solutions for the disproportionate antibiotic prescribing should be discussed. Recent British literature concerning quality improvements in hospitals reported that it is valuable to implement a review of antibiotic administration before the weekend [9]. Leaving up-to-date notes on treatment for weekend staff can reduce their workload and make physicians responsible for decision-making. By evaluating patients properly on a daily basis, the authors believe that antibiotic use can be further optimized. An increase in hospital staff during national holidays might also ameliorate antibiotic usage, at a cost that might be worthwhile. Also, decisions regarding antibiotic prescribing can be affected by physicians' backgrounds, including their medical careers and specialty. These personal inclinations for antibiotic prescribing should be managed by ASP activities [10].

Several limitations should be noted. First, the data were derived from a single institution, and the findings may not be true for other facilities with different work cultures and protocols. Second, differences in hospital admission numbers between weekdays and weekends may have influenced the dates of antibiotic discontinuation. In the study hospital, nearly 85% of the cases were scheduled admissions and the admission rate at weekends was only 3.7%. This indicates that the majority of antibiotics were presumably administered for nosocomial infections. Thus, these results may not be applicable to other acute care hospitals with more emergent admissions, regardless of the day of the week. Third, this study was not designed to analyse patient outcomes, which are important in determining the effectiveness of ASP.

In summary, this study reports an inconsistent rate in the discontinuation of broad-spectrum antibiotics throughout the week at the study hospital, particularly in the general wards. Improvements in rational antibiotic use are increasingly required in this era of increasing AMR. There is a need to establish an ASP team that is available even on weekends and holidays in order to optimize antibiotic prescribing in hospitals,

particularly for antibiotics with broad-spectrum activity. However, this is not realistic at the majority of facilities due to a shortage of medical staff or specialists. In this context, the results of the present study indicate that the ASP could include a review system for antibiotic treatment prior to the weekend, ensuring optimal patient care throughout the weekend despite lower functioning capacity. This may reduce the number of patients treated with antibiotics over the weekend just in case. Differences in staffing between weekdays and weekends are common worldwide; thus, a similar phenomenon to that reported in this study is likely to be observed elsewhere. A multi-centre study would be needed for confirmation.

Conflict of interest statement

None declared.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhin.2018.11.004>.

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