Electronic prescribing: Reducing delay to first dose of antibiotics for patients in intensive care

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Abstract

Delays in antibiotic therapy in the context of severe sepsis are associated with increased mortality. One way to reduce such delays may be through modifications to electronic prescribing (EP) systems. The research team evaluated the role of one such EP system in reducing delays in antibiotic administration in an Intensive Care Unit (ICU). First, the delays in antibiotic administration in adult ICU patients was quantified. The EP system was then modified to remove deafult time settings for antibiotic doses, which ensured that all antibiotic doses were scheduled for administration within an hour of the prescription being generated. Enhanced training for clinicians and nurses was also implemented, focusing on the EP system and highlighting the importance of prompt antimicrobial prescribing and delivery to the patient. The antibiotic administration was re-audited, and a significant reduction in delays (p=0.002, Mann-Whitney U test) was found. This study demonstrates how prudent use of EP systems can help to reduce delays in antibiotic administration in an ICU setting, thus potentially contributing to reducing mortality in patients with sepsis.

Problem

Prompt administration of antibiotics in the context of sepsis has been highlighted over the past decade as part of a global effort to reduce deaths from infection. This has been spearheaded by the Surviving Sepsis campaign (www.survivingsepsis.org). Optimising electronic prescribing (EP) systems is likely to be an important part of a multi-faceted approach to reducing delays in antibiotic administration (1), but there are limited published data surrounding best practice for EP in Critical Care settings.

As part of an ongoing shift from paper-based prescribing to electronic systems, the role of EP in managing sepsis requires evaluation. There are many established benefits of EP in management of antimicrobial therapy, including reduction in prescribing errors, alerting the prescriber to safety issues (e.g. allergies, drug interactions), informing robust audit, and contributing to antibiotic stewardship (2, 3). However, there are also potential pitfalls or unintended consequences of such systems (2), and it is therefore crucial that systems are regularly evaluated to ensure optimum performance (4). The extent to which EP systems could contribute to reducing delays in antibiotic administration is uncertain.

Background

The Surviving Sepsis campaign advocates use of the 'resuscitation care bundle', a package of interventions that provides a structured approach to the management of sepsis (5, 6). 'Sepsis' is commonly defined as a systemic inflammatory response syndrome (SIRS) arising as a consequence of infection; this becomes 'severe sepsis' if associated with organ dysfunction, hypotension, or tissue hypoperfusion (6). One component of the resuscitation care bundle is the timely administration of appropriate antibiotics, based on

evidence that prompt initiation of antibiotics improves survival in septic shock (7). Surviving Sepsis guidelines recommend that the first antibiotic dose should be given within an hour of presentation to patients with severe sepsis (6).

The research team set out to evaluate the role of our EP system in administration of antibiotics to patients with severe sepsis in an Intensive Care Unit (ICU) environment. It was hypothesized that some delays in antibiotic administration might be attributable to the default dose timings implemented by the EP system, and that simple modifications to the EP protocol might therefore reduce such delays.

The team's performance in achieving antibiotic administration within an hour of the prescription being generated was audited, retrospectively reviewing cases before and after the implementation of EP modifications. Overall, this study aims to inform the introduction and ongoing use of EP for antibiotic prescriptions in critical care and emergency settings.

Baseline Measurement

The research team studied patients on two adult ICUs within Oxford University Hospitals NHS Trust, a large tertiary referral centre in the UK. These units admit patients from a broad range of general medical and surgical specialties, but exclude neurosurgical and cardiac patients.

EP is undertaken on our ICUs using IntelliVue Clinical Information Portfolio (ICIP Revision D.03; Philips, UK). Using ICIP, an electronic antibiotic prescription can be initiated in one of two ways:

1. A 'stat' (or once only) dose for immediate administration. This approach is used in line with local guidelines for gentamicin prescriptions for patients with severe sepsis.

2. A regular prescription, which defaults to set times (e.g. 0600, 1400 and 2200 for a three-times daily dose). This approach is more frequently adopted for other commonly used antibiotics. Unless combined with a stat dose, this default approach can cause delays in administration, (with the extent of delay dependent on the time at which the prescription is generated).

The research team's institution's guidelines recommend that patients with severe sepsis should be given a stat dose of gentamicin in combination with other broad-spectrum antimicrobial cover (preceding the availability of microbiology lab results to guide therapy). Electronic records were therefore searched in order to identify all episodes of stat gentamicin prescriptions. Using this as a marker of initiation or change of antimicrobial therapy in the context of severe sepsis, cases in which gentamicin was used as part of a planned or prophylactic antimicrobial strategy were then excluded (e.g. for removal of a urethral catheter or for surgical prophylaxis in theatre).

ICU admissions within two separate 3-month periods, pre- and post-intervention (92 days in each case; Table 1) were retrospectively reviewed. The team also recorded other antibiotics started within 24 hours of the gentamicin, which are routinely included in an empiric broad-spectrum approach to severe sepsis (8).

For each antibiotic, the time delay between the prescription being generated and administration of the drug to the patient was calculated. The mortality and date of death (where applicable) was recorded retrospectively from the hospital electronic patient records.

See supplementary file: ds2058.docx - "Table 1"

Design

The research team adopted a pre-post-intervention ('quasi-experimental') study design (9) to investigate delays in antibiotic prescribing before and after making modifications to the EP system. The study protocol was conceived and designed in consultation with representatives from Intensive Care, Pharmacy and Infectious Diseases/Microbiology, and in collaboration with the Intensive Care Departmental Lead for the ICIP system.

After identifying substantial delays in antibiotic administration in the first time period audited (pre-intervention), the team made two interventions before re-auditing the second time period (post-intervention). First, the ICIP was altered in order to eliminate the default times setting for antibiotics. The scheduled time for the first dose instead became the nearest subsequent hour. A red flag icon is used on the electronic system to highlight new or modified prescriptions to reduce the risk of a new drug being overlooked. Second, additional training for new clinical staff on ICU was instituted . This took the form of reinforcing guidelines for the management of sepsis at the time of staff induction to ICU, and featured antibiotic prescribing as a specific component in the package of EP training.

Heightened awareness of timely antimicrobial prescriptions was

maintained by the ICU pharmacist, by a daily microbiology ward round on ICU, and by the regular rotation of Infectious Diseases trainees through the ICU. All of these measures will remain in place in the long term.

Statistical analysis using GraphPad Prism v.5.0a (2007) was performed and on-line tools at http://graphpad.com/quickcalcs/, using Fishers Exact Test and Mann-Whitney U Test to compare pre- and post-intervention cohorts. Institutional approval for the study was provided by our Clinical Audit Team which reports to the Care Quality Commission.

Strategy

The strategy for amending the EP protocol was designed in collaboration with the Lead Nurse for ICIP on Intensive Care. This was to ensure that the changes were technically feasible, while achieving the desired goal of avoiding delays of over an hour in antibiotic administration due to default settings within the ICIP software package.

Rather than amending default settings for the timing of antibiotic doses, the possibility of an electronic prompt to prescribers was also considered. This would act as a reminder to review the timings set for drug doses. However, the research team decided against this approach as it was felt to create additional workload for the prescriber, to result in a non-uniform approach to dose timings, and to risk 'user fatigue' (where prescribers are confronted by so many electronic reminders that they tend to ignore them).

The approach to the study and proposed changes to EP were discussed with all team members, including representatives from Intensive Care, Anaesthesia, Infectious Diseases, Microbiology and Pharmacy. In addition, the audit was presented at our institution's Departmental Infectious Diseases meeting, attended by clinical and laboratory microbiologists, Infectious Disease physicians, and antimicrobial pharmacists. The project was also summarised as a poster at the 2012 National Federation of Infection Societies Meeting (http://www.britishinfection.org), which allowed discussion with a wider audience.

Feedback from both these forums was positive, with pharmacists in particular highlighting concerns over the potential for default time settings to contribute to delays in drug administration. Our audiences agreed that modification to EP systems is a crucial component of reducing antibiotic delays. Staff from other institutions commented on the paucity of data from their own hospitals, acknowledging the importance of ongoing study and dissemination of results.

Induction sessions for new clinicians starting work on the Intensive Care Unit now feature substantially more time spent on EP, with specific detailed training on antimicrobial prescriptions, including a demonstration of how times are allocated for drug doses. The research team has also mandated documentation of indication for use which contributes to improved antimicrobial stewardship, and will also improve the ease of future similar audits.

Induction to ICU for nursing staff also includes discussion of timely antimicrobial prescribing and administration; nurses are encouraged to challenge instances in which delays might occur, and the red flag system is highlighted across disciplines.

Results

Overall, 100 episodes in which a stat gentamicin dose was prescribed were assessed. Patient characteristics in the pre- and post-intervention groups are shown in Table 1. The two groups were comparable in terms of gender and age (p=1 and p=0.1, respectively; Table 1). There was considerable heterogeneity of clinical diagnoses, reflecting the diverse case mix admitted to the ICUs; the numbers here were too small to permit meaningful statistical comparison between groups. More patients in the post-intervention group were given other antibiotics in combination with gentamicin (p=0.04; Table 1), suggesting that these patients may have been more unwell at baseline.

Patients received their gentamicin dose within an hour of prescription (as recommended by Surviving Sepsis guidelines (6)) in ≥75% of cases, with no difference between pre- and post-intervention groups (p=0.46; Table 1). This reflects local guidelines that recommend gentamicin should be prescribed and given as a stat dose as a component of broad-spectrum antibiotic therapy.

In contrast, other ('non-gentamicin') antibiotics were subject to much more significant delays, as these are not routinely prescribed as stat doses. In the pre-intervention group, these agents were given to the patient within an hour of prescription in only 40% of cases (Table 1). Post-intervention, this improved significantly, such that 67% of cases received their antibiotic dose within an hour of prescription (p=0.0018; Table 1, Figure 1).

Mortality in these patients was 34% overall. Comparing pre- and post-intervention groups, the team did not did not demonstrate an overall reduction in mortality (p=0.8 at 30 days; p=0.54 at 100 days; Table 1).

See supplementary file: ds2197.jpg - "Time delays figure with legend"

Lessons and Limitations

Overall, the study has demonstrated statistically significant reductions in delays in administration of antibiotics to patients with severe sepsis brought about by modifications to our EP system, combined with enhanced staff training. Delays in antibiotic administration in our ICUs overall compare favourably to those published in other series (10).

The research team did not intend or expect the interventions to change delays in gentamicin administration, as this antibiotic was prescribed as stat doses in both pre- and post-intervention cohorts, and our institution's sepsis protocol remained unchanged throughout. Rather, the changes that were implemented successfully brought other antibiotics into line with our routine

practice for gentamicin, resulting in much better compliance with Surviving Sepsis guidelines (6) (Fig. 1).

The data demonstrate how a routine and modifiable component of an EP system – the setting of default times for drug administration – can potentially contribute to detrimental outcomes for patients. Personnel responsible for implementing and managing EP systems should be aware of these unintended consequences of routine settings, and consider introducing modifications to minimise delays in drug administration. This type of modification is simple to implement, highly cost-effective, and easy to re-audit over time.

There was not a reduction in mortality between pre- and post-intervention groups. This is unsurprising given the team's small sample size, heterogeneity of case mix, and complexity of factors that predict mortality. In addition, the post-intervention group received more antibiotic agents, and may have been more unwell at baseline. The care bundle approach itself underlines the need for not just one, but a package of interventions that act together to impact on outcomes. Nevertheless, previous studies have shown that prompt antibiotic administration alone can reduce mortality (7), and therefore strategies to reduce time delays should be pursued aggressively.

There are certain caveats to the study design. Selecting patients based on a stat gentamicin dose only identifies a subset of those with severe sepsis, although (based on local guidelines) this approach should capture the majority of this patient group. This study focuses on just one component of overall time delays in antibiotic administration, namely the lag between generation of a prescription and the patient receiving the drug. Further studies would be required to assess preceding delays (e.g. between presentation of the patient and initiation of the antibiotic prescription). ICIP only captures limited information, and some of the antibiotic delays that were observed may have been intended or unavoidable. The time periods surveyed, pre- and post-intervention, are in different months of the year and therefore may not be directly comparable. This could partly explain the differing case mix.

Many patients presenting with sepsis are first assessed by the Emergency Department or on general hospital wards, rather than in ICU. However, the research team's approach of using stat gentamicin doses aimed to focus attention onto cases of sepsis arising de novo in an ICU environment (rather than incorporating patients who had already commenced treatment for sepsis). Although the findings are likely to be broadly applicable across different hospital settings, further studies would be required to investigate the extent to which the study's conclusions can be generalized.

Qualitative feedback based on the discussions and presentations for the study suggests widespread agreement that such EP modifications and training are vital tools in reducing antibiotic delays. In our units, nursing staff have commented on the positive impact of extra training and have recognised the increased use of stat antibiotic doses to minimise delays. Future audits will be important to monitor the progress and to identify any further areas

for improvement.

Despite current improvements, there are still delays in antibiotic administration beyond an hour in a proportion of cases and the team will continue to work on identifying and reducing such delays. In particular, ongoing education and training of clinical staff is likely to be paramount.

Conclusion

The project has demonstrated that simple modifications to an Electronic Prescribing system (in this case, ICIP), combined with enhanced training of users, can significantly reduce time delays in antibiotic administration. These data offer an important insight for staff working in a Critical Care environment, as well as informing those involved in the design and implementation of EP systems. Combining these interventions can increase compliance with international recommendations and potentially contribute to reducing patient mortality from sepsis (6, 7).

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Declaration of interests

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