Title: Reducing inappropriate third-generation cephalosporin use in community-acquired pneumonia in a small Australian emergency department.

Running Title: Reducing 3GC use for CAP in a small Australian ED.

Authors:

1. **Mr Sean Alcorn** BPharm GradDipEd MPS MSHP
Clinical Facilitator/Lecturer
School of Pharmacy, Griffith University
Gold Coast campus, Griffith University, QLD 4222, Australia
Telephone (07) 555 27791 Facsimile (07) 555 28804
Email Address s.alcorn@griffith.edu.au
ORCID ID: 0000-0002-3533-6554
2. **Ms Janette Van Der Hoek** RN, BN, MAdvPrac
Acting Clinical Nurse Consultant
Infection Prevention & Control Services
Northern New South Wales Local Health District
3. **Professor Ramon Z. Shaban^{A,B}** CICP-E RN PhD FFCENA FACN
Clinical Chair of Infection Prevention and Control
 - a. The University of Sydney Susan Wakil School of Nursing and Midwifery & The Marie Bashir Institute for Infectious Diseases and Biosecurity, University of Sydney, 88 Mallet Street, Camperdown, NSW 2050.
Ph: +61 478 312 668
Email: ramon.shaban@sydney.edu.au
ORCID ID: 0000-0002-5203-0557
 - b. Nursing, Midwifery and Clinical Governance Directorate
Western Sydney Local Health District
c/- 176 Hawkesbury Rd, Westmead. NSW 2145

Corresponding Author: Sean Alcorn

ABSTRACT

Objectives: Antimicrobial stewardship is a key component of hospital accreditation in Australia and contributes to the prevention and containment of antimicrobial resistance. The *Second Australian Report on Antimicrobial Use and Resistance in Human Health* (AURA Report) 2017 calls for greater participation by small hospitals in antimicrobial stewardship activities. Community acquired pneumonia (CAP) and third generation cephalosporin (3GCs) use is a known target for intervention. This paper reports the results of an educational intervention for reducing inappropriate prescribing of 3GCs in the empiric treatment of CAP.

Methods: The intervention was based on a leadership and education campaign in an Emergency Department (ED) in a 96 bed acute rural hospital in New South Wales, Australia. A two-point retrospective audit within (April – June 2010, April – June 2011) was conducted comparing pre-intervention and post-intervention antibiotic prescribing trends for CAP from ED presentations. Data was collected via audit tool and appropriateness was assessed against endorsed guidelines. The main outcome measures were improved prescribing appropriateness and decreased utilisation.

Results: Whilst statistically insignificant, a reduction (6.4%) in inappropriate prescribing and a reduction in 3GC utilisation (16.7%) was demonstrated via increased utilisation of Benzylpenicillin.

Conclusions: Small hospitals have active contributions to make to prevent and contain antimicrobial resistance via antimicrobial stewardship (AMS). Our results suggest change can occur in antibiotic prescribing. The challenge is collecting this data for national data sets whilst instituting local benefits in the context of limited resources. Studies such as this model a targeted strategy for resource poor facilities to contribute to national antimicrobial utilisation data sets whilst instituting local AMS change.

INTRODUCTION

Antimicrobial Stewardship (AMS) has become a key component of hospital accreditation in the Australian health care sector as part of the National Safety and Quality Health Service Standards established by the Australian Commission on Safety and Quality in Health Care.⁽¹⁾ In particular *Standard 3 – Preventing and Controlling Healthcare Associated Infections* prescribes that all hospitals must have in place an AMS system that governs and measures local antimicrobial use.⁽²⁾ Strategies for monitoring antimicrobial usage included point prevalence surveys and contribution of data to state-wide or national usage programs.⁽²⁾ Implementing such a system presents a unique challenge for small rural hospitals with limited specialist skills and resources in this area.

The *Second Australian Report on Antimicrobial Use and Resistance in Human Health* (2017 AURA Report) references two main data sources for information on antimicrobial use in the Australian acute hospital context. The volume of antimicrobial use (AU) in Australia is predominately collated by the National Antimicrobial Utilisation Surveillance Program (NAUSP), and the appropriateness of antimicrobial prescribing via the National Antimicrobial Prescribing Survey (NAPS).⁽³⁾ Both data sets are obtained via voluntary audit and submission from participating hospitals. The 2016 AURA report highlights significant gaps in the representation of national AU from these systems due to minimal participation of small public hospitals and private hospitals.⁽⁴⁾ Although improved participation from hospitals was noted in AURA 2017.⁽³⁾ NAUSP data in particular was noted to be heavily weighted towards principal referral and large public hospitals where AMS activity is well established in both reports.^(3,4) NAPS data has had steady increases in participation but is heavily reliant on clinical pharmacist resources with 60.8% of NAPS auditors being pharmacists and inter-rater reliability indicating that appropriateness assessments are best conducted by AMS teams or this pharmacist group.⁽⁵⁾ In addition NAPS methodology of whole hospital point prevalence surveys is not well suited to small hospital bed numbers and the required repeated point prevalence (continued survey to meet a minimum 30 antimicrobial prescriptions) is noted by this study's authors of being onerous on limited resources in the small rural hospital setting.⁽⁵⁾ This statement is supported by feedback collated by the NAPS team indicating that regional and remote hospitals required more than a week to complete the survey and greater than 20% of participants required greater than a month to complete the patient survey due to participant numbers.⁽⁵⁾

This study describes a practice change initiative initiated in a small rural hospital emergency department (ED) that was deemed achievable in the context of limited AMS resources and lack of specialist AMS clinicians. At the time of this study NAPS was still in the pilot phase and NAUSP was unable to accommodate small rural hospitals in their data collection or benchmarking. Greater resourcing has now allowed for enhanced participation in NAUSP reporting from smaller hospitals in response to the findings from AURA 2016.⁽³⁾ A targeted educational intervention against a known broad spectrum group (third generation cephalosporins (3GCs)), for a well-defined presentation (community acquired pneumonia (CAP)) was determined to be an appropriate place to invest limited clinical pharmacy and infection control resources.

STUDY AIM

This study aimed to measure the impact of a small scale educational intervention on antibiotic prescribing. The goal of the intervention was to reduce the inappropriate prescribing of 3GCs in CAP for patients presenting to the ED.

METHODS

Setting

The study was conducted in a 97 bed acute rural hospital located in northern New South Wales, Australia. In 2010 there were 7,697 ED triaged presentations in the 7 bed department. The ED is staffed 24/7 with medical staff directed by a Fellow of the Australian College of Emergency Medicine (FACEM). Most admitted patients are cared for medically by visiting medical officers (VMO) and locum doctors. Antimicrobial formulary is non-restrictive, any credentialed doctor can prescribe a formulary antimicrobial. Previous unpublished studies in the facility had revealed only slight improvements in relation to the prescribing of Antimicrobials for the diagnosis of CAP.

Inclusion and exclusion criteria

Study cohorts were drawn retrospectively within two time-frames (April – June 2010 & April- June 2011) from ED presentations pre and post intervention. Medical records with a diagnosis of CAP were extracted using ‘The International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM)’ codes for all primary and secondary

pneumonias.⁽⁶⁾ The extracted code range was from J12.0 to J18.9. Exclusion criteria were applied, being: children (age <18yrs); transfers from other facilities; chest x-rays not supporting the diagnosis; antibiotics not initiated in ED; hospital acquired pneumonia and self-discharge prior to treatment.

Intervention

The intervention comprised two main elements, commencing in July 2010 post pre-intervention data collection (April – June 2010) and continued up to the post intervention data collection (April- June 2011);

(i) Leaders and Champions

A clinical pharmacist, supported by the clinical nurse consultant (CNC) infection control was designated as the positions responsible for leading this AMS change initiative. Management support came from the Director of Medical Services (DMS) and FACEM. Departmental change was facilitated by an ED nurse representative from the infection prevention and control committee.

(ii) Educational Campaign

An educational campaign designed to increase prescribers and the supporting clinical group's awareness and understanding of the project was initiated. The consequences of antimicrobial resistance, appropriate use of antimicrobial agents and the adopted antibiotic use guideline was the focus of this inexpensive and easy to implement intervention.⁽⁷⁾ The design and delivery of the campaign was shared between the Clinical Pharmacist, ED Nurse representative, FACEM, DMS and Infection Prevention and Control CNC.

Education was rolled out to stakeholders in July 2010. The FACEM and clinical pharmacist focused on the ED doctors and medical students, discussing didactic and case based use of the SMART-COP tool.⁽⁸⁾ A researched tool for stratifying pneumonia therapy via clinical criteria (referenced in the acronym) that is endorsed by the therapeutic guidelines. The tool was put into a poster format on the ED doctor's desk. The DMS focused on other prescribers at the medical staff council meetings and via memorandums. The ED nurse educated the nursing group in the ED via department meetings, one on one sessions, and familiarised all clinical ED staff with the SMART-COP tool. Education of all clinical staff was critical,

as a large proportion of ED prescribers were identified as locum doctors that required educational encouragement from permanent nursing staff on prescribing culture during their shifts. The CNC educated via committees/presentations/conversations at all other clinical settings in the facility and conducted short (20 minute) education sessions throughout the patient based units. Engaging not just the ED staff, but also the clinical staff across a range of units and disciplines was a pivotal part of the initiative.

An adjunct to the education campaign was a constant focus on positive feedback discussions at all levels about past auditing results in the facility. This was a deliberate strategy to engage clinicians in an AMS initiative as a positive rather than negative audit process in a hope to foster positive peer reinforcement.⁽⁹⁻

¹¹⁾ This feedback also occurred when the quality project was tabled at the facilities quality committee meeting, and also included at other facility meetings such as the department heads, medical council, and infection prevention and control meetings.

Data Collection

A facility designed data collection sheet was used to annotate the patient's demographics and an assessment of the record was made to confirm diagnosis of CAP utilising SMART-COP pneumonia severity assessment measures.⁽⁸⁾ A researched pneumonia categorisation tool with sensitivity of 92% and specificity of 62% for predicting IVRS in the Australian context for scores ≥ 3 .⁽¹²⁾

Demographic data was collected on patient age at admission and length of stay. Duration of antimicrobial therapy and measures of clinical outcomes were not collected in this study.

Guideline Compliance

Antimicrobials prescribed at admission were recorded for assessment against prescribing guidelines. The therapeutic guidelines utilises SMART-COP scores to stratify the use of 3GCs. Hospitalised patients with scores less than 5 are recommended Benzylpenicillin in combination with Doxycycline or Clarithromycin and those greater than 5 3GCs and Azithromycin.⁽¹³⁾ The SMART-COP diagnostic algorithm was utilised on all eligible patient record information in order to gauge the severity of the CAP. SMART-COP analysis was calculated to give a score by the study auditor independent of the prescribing physician. Scores were stratified into 4 different treatment guides: 0-2 points – low risk of

needing intensive respiratory or vasopressor support (IRVS); 3-4 moderate risk (1 in 8) of needing IRVS; 5-6 points – high risk (1 in 3) of needing IRVS; and 7+ - very high risk (2-3) of needing IRVS. Severe CAP = a SMART-COP score of 5 or more points.^(8, 13) Laboratory and clinical findings were not analysed for patterns or trends within the SMART-COP system. SMART-COP assessment of pneumonia severity was combined with information regarding adverse drug reaction status to determine compliance with the Therapeutic Guidelines Antibiotic Version 14 2010 for antimicrobial appropriateness in accordance with fig. 1.⁽¹³⁾

Figure 1: SMART-COP score and appropriateness of third-generation cephalosporin therapy developed from Therapeutic Guidelines Antibiotic Version 14 2010 Abbreviations ADR (adverse drug reaction) CAP (community acquired pneumonia)

Statistical Analysis

All data was analysed using IBM SPSS Statistics. Demographic statistics are presented as medians (interquartile range) and SMART-COP scores are presented as nominal counts n (%) with a mean (95% confidence interval). Cohort analysis is presented as nominal counts n (%) with two sided P values calculated using Fischer's Exact Test.

Outcomes

The primary outcome was appropriate prescribing of 3GCs. Secondary outcomes included the percentage of patients receiving 3GCs as a measure of exposure.

RESULTS

Demographics of included patients

Figure 2: Flow diagram of study inclusion Abbreviations ED (Emergency Department) CAP (community acquired pneumonia)

Characteristics of included patients

Initially 24 patients were identified in the pre-intervention and 37 patients were identified for inclusion in the post intervention. Six patients were excluded from the pre-intervention and 16 patients were excluded

from the post intervention as detailed (Fig. 2). The captured patient medical records for this period was n=18, n=21 for the pre-intervention and post-intervention groups respectively.

The median age in the pre-intervention was 81 years. Post-intervention patients were of similar ages with a median age of 69 years. The median length of stay (LOS) in the pre-intervention was 8.5 days vs 3.86 in the post-intervention.

Table 1. *Clinical characteristics of pre-intervention and post-intervention groups*

The effect of the intervention on third-generation cephalosporin use

In the pre-intervention 9 (50%) of patients received 3GCs compared with 7 (33.3%) in the post-intervention, demonstrating a 16.7% reduction in 3GCs utilisation. In the pre-intervention of patients that received 3GCs 2 (22.2%) were appropriately prescribed and 2 (28.6%) were appropriately prescribed in the post-intervention. Neither the variance in 3GCs exposure nor the assessment of appropriateness was statistically significant between the groups.

Table 2. *Pre-intervention and post-intervention cohort 3GCs utilisation analysis.*

DISCUSSION

We believe the value of our study is the insight into the difficulty small rural facilities face in demonstrating significant data to their local clinicians without assistance to factor for limited resources. The results of this study demonstrated a small change (6.4% improvement) in the appropriateness of prescribing in patients that received 3GCs. However this was not significant and recruitment of sufficient patients to power studies such as this presents workload issues for poorly resourced facilities through broader recruitment timeframes. A higher proportion of patients with LOS >7 days was noted by investigators in the pre-intervention. Patient LOS did not appear to correlate with patient acuity, with SMART-COP scores similar across both groups despite differences in length of stay. Variance was seen in the percentage of patients with scores in the 3-4 range, possibly indicating more acute patients in the post-intervention. This should not have had an impact on the selection of antibiotic or the assessment of appropriateness with 3GCs only indicated in patients with SMART-COP scores ≥ 5 or patients with non-anaphylactic penicillin adverse drug reactions.⁽¹³⁾ Further studies to analyse this finding may be a future

avenue at this facility, however it wasn't within the scope of this study to link inappropriate prescribing of 3GCs to increased length of stay.

Achieving and sustaining change can be difficult, particularly with smaller sites with limited resources. Nonetheless, AMS should be incorporated as a process of cultural and system change in all levels of healthcare.⁽¹⁴⁾ The 2016 AURA report and 2017 AURA report highlighted the need to increase hospital participation and scope of surveillance via NAPS and NAUSP to enhance the validity of its data across all settings, in an effort to achieve a single trusted source of information.^(3, 4) Small rural hospitals such as this have been identified as under resourced for AMS and clinical pharmacy activity with AMS programs largely established in large hospital settings.⁽⁴⁾ NAPS reports identify significant burden in small hospital participation and the NAUSP program has been unable to accept small hospital data in the past.^(4, 5) The 2016 AURA report notes that effective surveillance systems should be more than just data collections and that reports need to be developed in a way that is valuable and useful at all levels.⁽⁴⁾ In order for under resourced facilities such as this to implement appropriate audit and feedback based on sound behavioural change theory assistance at the national level on creating timely, individual feedback reports is required to support local efforts in data collection.⁽¹⁵⁾ A smaller scope NAPS and NAUSP program targeted at identified clinical areas of highly inappropriate broad spectrum agent use and specific usage data on these agents may be a solution for engaging these under resourced facilities, whilst providing timely useful benchmarking data of clinical usefulness at the local level.⁽¹⁵⁾ A strategy to enable or assist facilities such as this needs to be devised to suit the level of resourcing available if a true picture of national AU is intended. Achieving this is a challenging process that raises complex issues, particularly in small healthcare facilities not only due to limited resources to run programs but confounded by small sample sizes insufficiently powered to demonstrate significant practice change when measured. The significant impact on workload that these studies can have in small low resourced settings,^(4, 6) may be minimised by technology assistive initiatives at the national level.

This study suggests that education and feedback may have a positive impact on changing behaviour even if statistical power limits generalisation. Assistance in designing and analysing a nationwide targeted clinical indication study may engage these small and private hospitals in the AURA data. A concurrently delivered education program may also assist small facilities in adding interventional approaches to their

surveillance activity to address the development of AMR at the local and national levels whilst providing a significant increase in power to assess the value of targeted education interventions in this context.^(4, 9, 10, 15) Selecting a similar target area such as CAP and 3GCs may provide significant impact. CAP and 3GCs have been identified as problem areas in NAPS reports. CAP is the highest non-surgical indication for antimicrobial use whilst also having high levels of inappropriate use. Ceftriaxone was the second highest utilised drug accounting for 9.1% of prescriptions with 30.6% of courses being prescribed inappropriately.^(4, 5) Inclusion of the ED as an audited unit may also have flow on effects to promoting AMS action in the primary and aged care sectors due to the large proportion of primary care GPs working as visiting and locum medical staff in rural EDs.⁽¹⁶⁾

There are limitations of this study. The retrospective nature of our study presented difficulty estimating final cohorts in our study leading to small study participants post exclusion. Therefore, as the study cohorts were small the study was under powered to demonstrate statistical significance. A targeted educational intervention against a known broad-spectrum group, for a well-defined presentation was determined to be an appropriate place to invest limited resources. Small positive inroads in prescribing are occurring, assisting the positive feedback mechanism utilised in the project. Based on this, statistical significance was not thought to be a significant reason to not disseminate the results to local clinicians, as literature indicates moderately positive results can occur in changing healthcare workers behaviour by utilising audit and feedback processes.⁽¹⁷⁾ When considering the importance of reducing global exposure to antibiotics the 3GCs exposure reduction after intervention of 16.7% was thought to be an important culture change motivator to be fed back to clinicians,⁽¹¹⁾ as a positive incremental step forward on the previous data. Moreover, the significant impact on workload that these studies can have in small low resourced settings may be minimised by enabling prospective real time auditing data to be directly collected by unit rather than external staff via streamlined data collection and central or computerised analysis created at the national level. Significant planning and education resourced at the national level may allow for an increase in the audit periods to recruit more patients and therefore increase statistical power, whilst also improving feedback frameworks.⁽¹⁵⁾

CONCLUSION

The findings provide small rural hospitals and similar healthcare facilities with insight of how one small hospital successfully implemented an AMS initiative using data sets identified as necessary for improving future AURA reports. The findings can be utilised to guide the inclusion of small practice change initiatives to allow for resource poor facilities to contribute towards the National Antimicrobial Resistance Strategy. Quality improvement cycle and change theories can modulate small positive incremental changes in antimicrobial prescribing in a small rural hospital ED. Although not statistically significant we believe feedback of our results to clinicians was still a significant culture change initiative in our AMS program which was highly suitable to our low resourced setting. It provides an avenue for the AURA report authors to explore a targeted strategy for resource poor facilities to engage with NAUSP and NAPS programs allowing them to contribute to national AU data whilst instituting local AMS change.

AUTHORSHIP STATEMENT

All authors contributed to the study design. SA & JV conducted the experimental methods and SA prepared the manuscript. All authors read and revised the manuscript and approved the final version.

CONFLICTS OF INTEREST

Authors declare no conflicts of interest. RS has editorial affiliation with this journal and has not participated in decision making or peer review for this submission.

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ETHICS APPROVAL

Approval to conduct this quality assurance project and publish its findings with exemption from human research ethics approvals was granted by the Northern NSW Local Health District.

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Table 1. Clinical characteristics of pre-intervention and post-intervention groups		
Variable	Pre-intervention	Post-intervention
Patients Recruited	18	21
Demographics		
- Age (years)	81 (27)	69 (26.5)
- Length of stay (days)	8.5 (2.47-14.53)	3.86 (2.54-5.17)
Clinical Assessment at ED admission, n (%)		
SMART-COP (score) = 0 – 2 (low risk of IRVS)	13 (72.2)	12 (57.1)
SMART-COP (score) = 3 – 4 (moderate risk of IRVS 1 in 8)	3 (16.7)	8 (38.1)
SMART-COP (score) = 5 – 6 (high risk of IRVS 1 in 3)	1 (5.6)	1 (4.8)
SMART-COP (score) > 7 (very high risk of IRVS 2 in 3)	1 (5.6)	0 (0)
SMART-COP (mean)	2.11 (1.03-3.19)	2.38 (1.73-3.03)
Abbreviations: IRVS, intensive respiratory or vasopressor support.		

Table 2. Pre-intervention and post-intervention cohort 3GCs utilisation analysis.			
Variable	Pre-intervention	Post-intervention	P value
Patients Recruited	18	21	
3GCs Exposure (n, %)	9 (50%)	7 (33.3%)	0.342
3GCs Appropriateness (n, %)	2 (22.2%)	2 (28.6%)	0.999
Abbreviations: IRVS, intensive respiratory or vasopressor support.			