J Infect Chemother xxx (2017) 1–7

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic

Original Article

Sustained improvement in vancomycin dosing and monitoring post-implementation of guidelines: Results of a three-year follow-up after a multifaceted intervention in an Australian teaching hospital☆

Cameron J. Phillips [a, b, c, *], Ross A. McKinnon [c, d], Richard J. Woodman [e], David L. Gordon [b, f, g]

[a] SA Pharmacy, Flinders Medical Centre, Bedford Park, SA, 5042, Australia
[b] Department of Microbiology and Infectious Diseases, School of Medicine, Flinders University, Adelaide, SA, 5000, Australia
[c] School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, SA, 5000, Australia
[d] Flinders Centre for Innovation in Cancer, Flinders University, Adelaide, SA, 5000, Australia
[e] Flinders Centre for Epidemiology and Biostatistics, School of Medicine, Flinders University, Adelaide, SA, 5000, Australia
[f] SA Pathology, Microbiology and Infectious Diseases, Flinders Medical Centre, Bedford Park, SA 5042, Australia
[g] Division of Medicine, Flinders Medical Centre, Bedford Park, SA, 5042, Australia

ARTICLE INFO

Article history:
Received 19 June 2017
Received in revised form
14 August 2017
Accepted 19 September 2017
Available online xxx

Keywords:
Education
Guideline
Intervention
Therapeutic drug monitoring
Vancomycin

ABSTRACT

Introduction: Despite vancomycin being in use for over half-a-century, it is still not dosed or monitored appropriately in many centers around the world. The objective of this study was to determine the effectiveness of a multifaceted intervention to implement a vancomycin dosing and monitoring guideline across multiple medical and surgical units over time.

Methods: This was an observational before-and-after interventional cohort study. The pre-intervention period was August to December 2010–2011 and the post-intervention period was September to November 2012–2014. The implementation strategy comprised: face-to-face education, online continuing medical education, dissemination of pocket guideline and email reminder. Outcome measures included: appropriate prescribing of loading and maintenance doses, therapeutic drug monitoring, time to attain target range and nephrotoxicity.

Results: Post-implementation prescribing of loading doses increased (10.4%–43.6%, P=<0.001), guideline adherent first maintenance dose (44%–68.4% $P = 0.04$), correct dose adjustment from (53.1%–72.2%, $P = 0.009$). Beneficial effects pre and post-implementation were observed for adherent timing of initial concentration (43.2%–51.9%, $P = 0.01$), concentrations in target range (32.6%–44.1%, $P = 0.001$), time to target range (median 6–4 days, P=<0.001), potentially nephrotoxic concentrations (30.7%–20.9%, P=<0.001) and nephrotoxicity (10.4%–6.8%, P=<0.001).

Conclusions: A multifaceted intervention to implement a vancomycin dosing and monitoring guideline significantly improved prescribing, monitoring, pharmacokinetic and safety outcomes for patients treated with vancomycin over an extended period. However, increased guideline adoption by clinicians is required to maximize and prolong the utility of this important agent.

Abbreviations: CME, continuing medical education; FMC, Flinders Medical Center; GIN, Guideline International Network; ICCU, Intensive and critical care unit; IOM, Institute of Medicine; JMO, junior medical officer; MRSA, methicillin-resistant *Staphylococcus aureus*; NHMRC, National Health and Medical Council; NICE, National Institute for Clinical Excellence; SIGN, Scottish Intercollegiate Guideline Network; VRE, vancomycin-resistant Enterococcus.

☆ All authors meet ICMJE authorship criteria.

* Corresponding author. SA Pharmacy, Room 288, E-Block, Flinders Medical Centre, 1 Flinders Drive, Bedford Park, SA, 5042, Australia.
E-mail addresses: cameron.phillips@sa.gov.au (C.J. Phillips), ross.mcKinnon@flinders.edu.au (R.A. McKinnon), richard.woodman@flinders.edu.au (R.J. Woodman), d.gordon@flinders.edu.au (D.L. Gordon).

https://doi.org/10.1016/j.jiac.2017.09.010
1341-321X/

1. Introduction

Vancomycin has been in use for over half a century however we still have difficulty prescribing and monitoring this agent [1,2]. Practice recommendations have changed over time [3].To address these changes in practice and promote contemporary clinical guidance, a number of a professional societies from various nations, notably the United States, Japan and recently, China, have published vancomycin guidelines in the medical literature [4–6]. These national guidelines are in addition to the plethora of institutional vancomycin guidelines that been described in a recent systematic review [7]. Significant financial and human resources are invested into the development of transparent evidence-based clinical practice guidelines, however there is very limited information supporting these documents reflecting which implementation strategies best promote the guideline adoption.

To address guideline implementation, organisations involved with knowledge translation and guideline development including the National Institute for Health and Clinical Excellence (NICE), UK, the Scottish Intercollegiate Guideline Network (SIGN), the Australian National Health and Medical Research Council (NHMRC), the United States Institute of Medicine (IOM) and Guidelines International Network (G-I-N) provide general advice on guideline implementation [8–12]. This is important as there are numerous accounts in the literature of poor adoption of guidelines by clinicians [13–16]. Most of the peak organisations advocate for multifaceted interventions when implementing guidelines. Commonly recommended interventions by these organisations are: educational sessions [17], academic detailing [18–20], continuing medical education (CME) [21,22], provision of printed educational material [23], use of opinion leaders to endorse guidelines [24], and engaging target populations who will use the guideline [25]. However, the magnitude of effect from these interventions varies considerably and the impact these interventions have specifically when employed to implement vancomycin guidelines is unknown.

In a pilot study we implemented a vancomycin dosing and monitoring guideline, we elected to use interventions involving face-to-face education and the provision of a pocket guideline as these had limited cost implications. Despite low statistical power, the pilot produce favourable results, increasing prescribing of loading doses from 5 to 65% ($P = \leq 0.001$), adherent first maintenance dosages from 43 to 75% ($P = 0.04$), more concentrations in target range from 27% to 43.8% ($P = 0.04$), and non-significant reductions in potentially toxic concentrations, reduced nephrotoxicity and a trend to more patients attaining target ranger sooner [26]. However, as that pilot was conducted in a single surgical unit, it was unclear if the results of the intervention would be reproducible and sustainable. Thus the objectives of the current study were to determine the effectiveness of a multifaceted intervention to implement a vancomycin dosing and monitoring guideline across multiple units over time.

2. Patients and methods

2.1. Study setting and design

The study was an observational cohort before-and-after interventional design. The study was conducted at Flinders Medical Centre (FMC), a 580 bed government university teaching hospital in Adelaide, Australia. The interventional cohort was all adult patients treated with vancomycin during the months, September to November over three years 2012–2014. This interval is defined as the follow-up period. A pre-implementation comparator group included all patients treated with vancomycin during the months August to December over two years 2010–2011. Ethical approval for the study granted by the Southern Adelaide Clinical Human Research Ethics Committee, Australia (approval number 123.12).

2.2. Patients

Admitted patients ≥18 years receiving vancomycin who had ≥1 vancomycin concentration result were included in the study. Patients were identified from the daily therapeutic drug monitoring report generated by the biochemistry department. Patients were excluded if they commenced treatment in the intensive and critical care unit (ICCU), receiving hemo- or peritoneal dialysis, this was due to both units having dedicated vancomycin dosing protocols.

2.3. Serum creatinine measurement and creatinine clearance calculation

Serum creatinine (S_{Cr}) concentrations were measured using Roche (Basel, Switzerland) C702 enzymatic method. Calculation of creatinine clearance (CrCl) was performed using the Cockcroft-Gault equation,

$$\text{CrCl (mL/min)} = \{[(140 - \text{age years}) \times \text{body weight kg}] / (72 \times S_{Cr}\ \text{mg/dL})\} \times 0.85\ \text{(if female)}$$ [27].

2.4. Vancomycin guideline

The vancomycin dosing and monitoring guideline for adults used in this study was based on a guideline developed for a single unit pilot study in our institution [26], later used in a broader proof of concept study across medical and surgical units [28]. The guideline largely reflected the North American consensus recommendations adapted with Australian Therapeutic Guidelines content on vancomycin [29,30]. The current study guideline was endorsed with input from institutional leaders in infectious diseases, clinical pharmacology and pharmacy, refined in early 2012 and uploaded to the institutions intranet in August 2012. *Key prescribing features were*: a loading dose of 25 mg/kg at discretion of prescriber and maintenance dosing determined by CrCl (>90 mL/min 1.5 g 12-hourly; 60–90 mL/min 1 g 12-hourly; 20–59 mL/min 1 g 24-hourly; <20 mL/min 1 g every 2–7 days with vancomycin TDM 48-hourly). *Key monitoring features were*: timing of initial trough blood sample for concentration measurement was determined by CrCl (>60 mL/min required blood to be taken prior to the fourth dose; 20–59 mL/min before the third dose and <20 mL every 48-hourly until target (15–20 mg/L) attainment) (Supplementary file 1). In the pre-implementation period there was no institutional guidance on vancomycin dosing and monitoring except for a comment on pathology result record or electronic report of a target range 15–20 mg/L. This comment remained in effect for the follow-up period.

2.5. Target audience

The principal target audience of the implementation strategy was junior medical officers (postgraduate years 1 and 2) as they perform the majority of prescribing and pathology test ordering in our and many other institutions [31]. However, all medical, pharmacy and nursing staff were potential end-users of the guideline.

2.6. Interventions

There were four components to the multifaceted intervention to support the release of the guideline: 1) educational session, 2) an online continuing education module on vancomycin with knowledge assessment, 3) dissemination of printed material and 4) email reminder alert.

Please cite this article in press as: Phillips CJ, et al., Sustained improvement in vancomycin dosing and monitoring post-implementation of guidelines: Results of a three-year follow-up after a multifaceted intervention in an Australian teaching hospital, J Infect Chemother (2017), https://doi.org/10.1016/j.jiac.2017.09.010