Institution: University of Strathclyde

Unit of Assessment: 3

Title of case study: Improved patient care through new guidelines for antibiotic dosing and monitoring.

1. Summary of the impact (indicative maximum 100 words)

This research has improved the clinical use of powerful antibiotics. New guidelines for vancomycin use in adults have been adopted by the NHS throughout Scotland and in other parts of the UK. New neonatal vancomycin guidelines have decreased the time to achieve optimal antibiotic concentrations and reduced patient trauma and staff workload. These guidelines are used routinely in the Greater Glasgow area and other parts of the UK. Tobramycin guidelines improved the management of infection in patients with cystic fibrosis in the Glasgow and Edinburgh areas. Additional studies, which investigated guideline implementation across NHS Scotland, resulted in nationally supported resources designed to improve the quality of patient care when vancomycin or gentamicin is used.

2. Underpinning research (indicative maximum 500 words)

Context

The incidence of life-threatening infection with the "superbugs" MRSA and MSSA was between 0.4 and 0.5 per 1000 occupied bed days in Scotland during 2008. Vancomycin is one of the few antibiotics that is active against MRSA; gentamicin is used for infections caused by other life-threatening pathogens and tobramycin for recurrent respiratory infections in patients with cystic fibrosis (CF). There are around 9000 people with CF in the UK. Successful use of these antibiotics is challenging because (i) therapeutic doses are similar to those that cause toxicity, (ii) dose requirements vary widely among patients and (iii) complex guidelines are required. Consequently, gentamicin and vancomycin consistently appear in the top 10 list of medicines associated with dosing errors. In 2008, a Scotland-wide audit found that vancomycin dosage regimes used in routine clinical practice were unfit for purpose (Reference 1).

The principal methodology used in the research was population pharmacokinetic modelling of the sparse antibiotic concentration measurements that are routinely generated when vancomycin and tobramycin are prescribed. The models arising from this research were used to develop new dosage guidelines to achieve target antibiotic concentrations. Qualitative and quantitative studies were then conducted to identify which resources were needed to support the implementation of these new guidelines.

Key research findings

The clinical factors that determine vancomycin dose requirements in adults were identified by population pharmacokinetic analysis of vancomycin concentration data from 399 patients in Glasgow and Bristol. The population model arising from this work was used to create new guidelines for vancomycin dosing and monitoring in adult patients (Reference 2).

Factors that influence vancomycin dose requirements in neonates and young infants were used to create guidelines for vancomycin administration by intermittent infusion (Reference 3). Simulations based on this and other population models led to new guidelines that were designed to achieve target vancomycin concentrations using a continuous infusion approach to vancomycin therapy (Reference 4).

Population pharmacokinetic analysis of tobramycin concentration data collected from 51 patients with cystic fibrosis led to new dosage guidelines that were designed to achieve target concentrations more efficiently than standard approaches (Reference 5). These studies all began as MSc projects at Strathclyde University.

Barriers to implementation of gentamicin and vancomycin antibiotic dosage guidelines in clinical practice were investigated in a series of quantitative and qualitative improvement studies across NHS Scotland (2010-2012). These studies identified issues relating to calculation of initial dosage

regimens, accurate documentation of therapy, interpretation of antibiotic concentration measurements, communication of patient needs, and education of staff and resulted in the development of new resources to address these issues.

Key researchers at Strathclyde
From 1991 to 2005 Dr Alison Thomson held a full-time NHS post and a concurrent honorary lectureship at the University of Strathclyde, where her research was focussed, and she led the research underpinning Refs 3 and 5 (1999). She was appointed as Senior Lecturer in the School of Pharmacy and Biomedical Sciences in 2005, and conducted the pharmacokinetic and the quality improvement studies following her appointment (Refs 1, 2 and 4 below).

3. References to the research (indicative maximum of six references)

1. Helgason K, Thomson A, Ferguson C. A review of vancomycin therapeutic drug monitoring recommendations in Scotland, J. Antimicrob. Chemother., 61:1398-1399, 2008.
   Notes on quality: This manuscript was published in a high quality, peer-reviewed journal.

2. Thomson AH, Staatz, CE, Tobin C, Gall M, Lovering AM. Development and evaluation of vancomycin dosage guidelines designed to achieve new target concentrations. J. Antimicrob. Chemother., 63:1050-1057, 2009.
   Notes on quality: This manuscript was published in a high quality, peer-reviewed journal and is included in the REF2 (outputs) element of the submission. Publication of this manuscript contributed to the award of three grants to Dr Thomson and Professor Bennie from the Healthcare Associated Infection Task Force (£56,693 in 2010, £56,693 in 2011 and £19,915 in 2012).

3. Grimsley C, Thomson AH. Population pharmacokinetics of vancomycin in neonates and young infants. Arch. Dis. Child., 81:F221-F227, 1999.
   Notes on quality: This manuscript was published in a quality, peer-reviewed clinical journal.

4. Patel AD, Anand D, Lucas C, Thomson AH. Continuous infusion of vancomycin in neonates. Arch. Dis. Child., 98:6478-47910, 2013.
   Notes on quality: This manuscript was published in a quality, peer- reviewed clinical journal. The work was selected for oral presentation at the UK Neonatal and Paediatric Pharmacy Group meeting in November 2011 and won the prize for the “Best Innovation”.

5. Campbell D, Thomson AH, Stack B. Population pharmacokinetics of aminoglycosides in patients with cystic fibrosis. Ther. Drug Monit., 21: 281-288, 1999.
   Notes on quality: This manuscript was published in the journal of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology, a quality, peer-reviewed journal.

4. Details of the impact (indicative maximum 750 words)
Process from research to impact
Tobramycin guidelines: In 1991 Dr Thomson held an NHS post in Glasgow that included responsibility for producing drug therapy guidelines; at this time she introduced a computer-based data analysis service to help individualise tobramycin therapy for patients treated by the Glasgow Cystic Fibrosis Unit (GCFU). Dosage guidelines, based on 12 hourly dosing, were generated from a population pharmacokinetic analysis of the data produced by this service (Reference 5) and were adopted for routine clinical use by the GCFU in 1999. In the Edinburgh Cystic Fibrosis Unit, traditional 8-hourly dosing regimens continued to be used. However, an audit of tobramycin therapy in this unit during 2008-10 identified major problems with this approach, and it was decided that a pilot study using the Glasgow guidelines should be conducted. The success of this pilot resulted in the GCFU guidelines being adopted for routine use in the Edinburgh Unit in 2011.

Vancomycin guidelines: NHS changes to target vancomycin concentration ranges prompted the adult vancomycin research, the results of which were incorporated into the 2008-9 “Prescribing

Guidance" booklet used within NHS Greater Glasgow and Clyde (NHS GGC) and edited by Dr Thomson. Around the same time, a national audit (Reference 1) demonstrated that the vancomycin guidelines used throughout Scotland were unfit for purpose. Following publication of the research in early 2009 (Reference 2), Dr Thomson was invited to present the rationale behind the NHS GGC vancomycin and gentamicin guidelines at the Scottish Antimicrobial Prescribing Group (SAPG) Antimicrobial Management Team Networking Event in June 2009. At that meeting, it was agreed to adopt the adult vancomycin guidelines for use throughout NHS Scotland and the gentamicin guidelines (also developed by Dr Thomson) as one of two options. These guidelines, together with online calculators created by Dr Thomson to facilitate accurate calculation of antibiotic doses, were published on the SAPG website in October 2009 (Source A).

Dr Thomson and Professor Marion Bennie were awarded a grant in 2010 from the Scottish Healthcare Acquired Infections (HAI) Task Force to evaluate the implementation of these national guidelines. Further grants were awarded in 2011 and 2012 to create new resources and educational material to support guideline implementation. These resources comprised specialised documentation for prescribing and monitoring gentamicin therapy, which was introduced within NHSGGC in 2012 and made available nationally in June 2013. New online dose "calculators" were created and released nationally in June 2013 and e-learning material was developed for use nationally through the "LearnPro®" platform.

The earlier neonatal vancomycin research (Reference 3) formed the basis of vancomycin guidelines previously used by neonatal intensive care units (NICUs) within Glasgow. In May 2009, Dr Thomson was asked by Professor Craig Williams, a consultant microbiologist from the Royal Hospital for Sick Children, Glasgow, to develop new, continuous infusion dosage regimens to solve underdosing and practical problems that were being experienced with the traditional, intermittent infusions. The new guidelines developed by Dr Thomson were tested in a pilot study in June 2011 and then adopted into routine clinical practice. Oral presentation of this work at the Neonatal Paediatric Pharmacists Group Meeting in 2011 prompted interest from other NICUs in the UK.

Types of Impact

- The research has had an impact on government (NHS) policy through the introduction of national guidelines for antibiotic use.
- The new guidelines improve the quality of patient care by decreasing the time to achieve therapeutic antibiotic concentrations, reducing patient trauma and reducing staff workload.
- Quality improvement studies identified barriers to effective implementation of therapeutic guidelines and developed resources to overcome these barriers.

The research has principally influenced healthcare in Scotland. Through publication of the work, the findings have also been implemented in other parts of the UK and attracted interest from healthcare practitioners in Europe and the USA.

Changes to NHS guidelines and resources for staff

There have been changes to antibiotic dose and monitoring guidelines used within the NHS.

- New vancomycin dosage guidelines for adult patients have been adopted throughout Scotland (Source A) and implemented locally in other parts of the UK (Sources B, C and D).
- Resources and guidelines developed through the Quality Improvement projects are recommended for use throughout NHS Scotland and can be accessed by NHS and other healthcare staff from outside Scotland to support the development of their local guidelines (Source A).
- Guidelines for vancomycin administration by continuous infusion in neonates won the "Best Innovation" prize at the UK Neonatal and Paediatric Pharmacists Group meeting in 2011. They have been adopted by NICUs in Glasgow and Cambridge (Source E and Source F).
- Guidelines for tobramycin administration have been adopted by the Edinburgh Cystic Fibrosis Unit, (Source G), and have been in use in the Glasgow unit prior to and since 2008. These two units cover the major population of Scotland.

Improvements to patient care

There has been an improvement in the quality of patient care through more efficient achievement of target concentrations.

- The adult vancomycin dosage guidelines increased the likelihood of achieving safe and effective concentrations within the first 4 days of therapy from 22% to 71% (Reference 2).
- The neonatal continuous vancomycin infusion guidelines increased the percentage of concentrations within target ranges from 46% to 82% (Source E and reference 4).
- Satisfactory peak concentrations of tobramycin in the Edinburgh Cystic Fibrosis Unit increased from 31% to 74% and satisfactory predose concentrations from 93% to 100% (Source G).

Patient trauma caused by repeated venepuncture and the workload of doctors, nurses and pharmacists have been reduced.

- The neonatal vancomycin guidelines reduced the need for additional venepuncture from 54% to 7% of blood samples and made the concentration measurements easier to interpret (Source E and Ref 4).
- The tobramycin guidelines reduced the mean number of dose adjustments per patient in Edinburgh from 1.4 to 0.45 and sets of blood samples per patient from 2.5 to 1.5 (Source G).

5. Sources to corroborate the impact (indicative maximum of 10 references)

A. http://www.scottishmedicines.org.uk/files/SAPG_Guidance_on_gentamicin_and_vancomycin_policies_revised.pdf will support the claim(s) that the adult vancomycin dosage guidelines have been adopted by NHS Scotland for routine clinical use. Gentamicin and vancomycin dosage calculators have been updated for use throughout Scotland. Documentation resources for gentamicin are available for use throughout Scotland

B. http://www.icid.salisbury.nhs.uk/MedicinesManagement/Guidance/AntimicrobialMedicine/Pages/VancomycinIntermittantInfusion.aspx will support the claim(s) that the vancomycin guidelines have been adopted into clinical use in other parts of the UK.

C. http://www.rdehospital.nhs.uk/docs/prof/antimicrobial/Vancomycin_EXETER__FINAL_2010_(3)1.pdf will support the claim(s) that the vancomycin guidelines have been adopted into clinical use in other parts of the UK.

D. http://www.srft.nhs.uk/EasysiteWeb/getresource.axd?AssetID=8263 will support the claim(s) that the vancomycin guidelines have been adopted into clinical use in other parts of the UK.

E. Consultant neonatologist, Neonatal Intensive Care Unit, Yorkhill Hospital, NHS Greater Glasgow & Clyde can be contacted to support the claim(s) that the new vancomycin guidelines for continuous infusion in neonates have been adopted for routine clinical use and improved patient care in Glasgow

F. Lead Pharmacist - Paediatrics, Cambridge University Hospitals NHS Foundation Trust can be contacted to support the claim(s) that the new vancomycin guidelines for continuous infusion in neonates have been adopted for routine clinical use and improved patient care in Cambridge.

G. http://www.sciencedirect.com/science/article/pii/S1569199313602313
Page S71, D. McCabe, H.C. Rodgers - will support the claim(s) that adoption of the Glasgow tobramycin dosing guidelines for patients with cystic fibrosis led to a significant improvement patient care in the Edinburgh Cystic Fibrosis unit.