ORIGINAL ARTICLE

# Vancomycin administration: the impact of multidisciplinary interventions

**R K Crowley, F Fitzpatrick, D Solanki, S FitzGerald, H Humphreys, E G Smyth**

*J Clin Pathol* 2007;**60**:1155–1159. doi: 10.1136/jcp.2006.044727

See end of article for authors' affiliations

Correspondence to: Dr Rachel Crowley, Beaumont Hospital, Beaumont Road, Dublin 9, Ireland; rachelcrowley@beaumont.ie

Accepted 4 January 2007
**Published Online First 5 February 2007**

**Background:** The clinical microbiology team observed that patients were not receiving all prescribed doses of vancomycin. Ward staff was confused about ordering and interpreting vancomycin therapeutic drug monitoring (TDM) levels.
**Aim:** To audit the incidence of vancomycin dose omission. To implement a series of interventions to improve vancomycin dose administration, and to repeat the audit process to assess these interventions.
**Methods:** Three prospective audits were conducted to assess the impact of vancomycin TDM on administration of vancomycin. After the first audit, a number of changes in the TDM process were undertaken. After review of the second audit, a senior pharmacist coordinated ward-based pharmacists in assisting staff to interpret levels, and TDM interpretative charts were designed for drug charts. Following the third audit, feedback to hospital management and a plan for ongoing education were undertaken.
**Results:** There was a significant reduction in the number of vancomycin doses held inappropriately in the third (10% (78/782) of prescribed doses) when compared to the first audit (16% (161/1007) of doses) ($p<0.01$). Of doses that were held inappropriately, there was a significant decrease in doses held for no apparent reason in audit 3 (16% (27/170) of prescribed doses) when compared to audit 1 (25% (69/282) of doses) ($p<0.05$).
**Conclusions:** The interventions resulted in a 37.5% reduction in inappropriately held vancomycin doses over a one-year period; 10% of doses are still being held inappropriately. This study highlights the difficulties in identifying barriers to change and changing healthcare worker behaviour.

Monitoring blood levels of vancomycin (therapeutic drug monitoring (TDM)) is standard care for patients receiving vancomycin in our institution. We recommend that adults with normal renal function receive 15 mg/kg twice daily of intravenous vancomycin and use TDM to adjust dosages. In July 2003, the clinical microbiology team observed that patients were not receiving all prescribed doses of vancomycin. It became apparent that failure to administer prescribed vancomycin was secondary to confusion among staff about the indication for performing vancomycin TDM levels. We performed three prospective audits to assess the impact of vancomycin TDM and systems-based interventions on vancomycin administration.

## METHODS

Beaumont Hospital, Dublin is a 650-bed tertiary referral teaching hospital, containing the renal transplantation and neurosurgical units for the Republic of Ireland, a general intensive care unit (ICU) and a neurosurgical ICU. The clinical microbiology team conducts daily ward and ICU rounds.

### Previous vancomycin TDM policy

Prior to the first audit, vancomycin TDM levels were performed as ''trough'', ''peak'' or ''random'' levels. Non-consultant hospital doctors performed TDM phlebotomy at 9 am. TDM levels were analysed using the Innofluor Vancomycin Assay System (Seradyn) on the Abbott TDx system. The clinical microbiology team reviewed TDM results daily and added interpretative comments by 4 pm. Ward staff members were dependent on these interpretative comments, when the decision to administer a vancomycin dose was made.

### Patients

Adult in-patients prescribed intravenous vancomycin were surveyed. A different administration protocol exists for patients receiving renal replacement therapy, hence these were excluded.[1] Eligible patients were identified from microbiology consultations, laboratory records of vancomycin assays and pharmacy records. A single member of the clinical microbiology team reviewed patients daily.

### Audit 1

The first audit took place over one month during August–September 2003. Demographic details and vancomycin therapy were recorded on a database (Microsoft Excel). Appropriate therapy was defined as: treatment of a relevant isolate, for example meticillin-resistant *Staphylococcus aureus* (MRSA), involvement of the clinical microbiology team in the prescription, or if empiric, prescribed according to hospital guidelines. Prescribed vancomycin doses were considered to be ''inappropriately withheld'' if they were not given because staff waited for TDM results, unless the previous TDM result was too high.

### Interventions after audit 1

After review of the results, the clinical microbiology team assessed the process of vancomycin TDM. A number of processes that confused ward staff were identified.

- Staff were unsure which category of TDM level (''peak'', ''trough'' or ''random'') to order.
- Staff were excessively concerned about toxicity (confusing vancomycin with gentamicin) and were withholding vancomycin while awaiting TDM results.
- Non-consultant hospital doctors performed TDM phlebotomy; due to work commitments, phlebotomy was not performed on time.

**Abbreviation:** TDM, therapeutic drug monitoring

**Box 1: New computer ''pop-up'' screen**

**Vancomycin pre-dose level**
**Pre-dose level MUST be taken just before dose.
**Do NOT withhold next dose pending level unless:

(1) Previous level was toxic
(2) Renal impairment

Please let us know why the patient is on vancomycin. Enter this information in the ''order comment'' field.
Is vancomycin still indicated? Consider whether it can now safely be discontinued.
Please provide:

(1) Dose
(2) Timing of dose
(3) Most recent level and renal function (creatinine) in order to facilitate us in advising next dose.

- Laboratory staff waited to register sample arrival on the computer until TDM analysis each afternoon. Ward staff often interpreted unregistered samples as failure to send the sample, and a second sample was drawn from the patient that day.
- Interpretation comments by the clinical microbiology team were not ''user-friendly'' for ward staff.

The following interventions were undertaken:

- ''Peak'', ''trough'' and ''random'' levels were replaced by a single computer order for ''pre-dose'' vancomycin level, to be taken before the morning dose.
- A computer ''pop-up'' window appeared before completion of vancomycin TDM requests (box 1).
- The phlebotomy service agreed to take TDM samples at 9 am to ensure that the morning dose was not dependent on non-consultant hospital doctors.
- The laboratory undertook to register TDM sample arrival immediately, to allow ward staff to confirm sample receipt.
- The clinical microbiology team devised new interpretative comments (table 1).

Audit results were reported at hospital-wide multidisciplinary meetings. Members of the clinical microbiology team gave ward-based educational sessions on each ward.

## Audit 2

A second audit was conducted in February 2004.

### Interventions after audit 2

After review, we identified that confusion still existed regarding interpretation of vancomycin TDM levels, and we implemented further interventions.

- A senior pharmacist led ward-based pharmacists in improving staff interpretation of TDM levels, and reporting failure to administer prescribed vancomycin.
- Results of vancomycin TDM levels were distributed in the pharmacy department before pharmacist ward rounds.
- Pharmacists attached stickers of TDM interpretative charts to the drug charts of patients receiving intravenous vancomycin (table 1).
- TDM interpretative charts were displayed in each ward dispensing area.

**Table 1** Interpretative comments added to vancomycin pre-dose therapeutic drug monitoring levels by the clinical microbiology team prior to authorisation of results, and printed on stickers for drug charts

| Vancomycin pre-dose level result (mg/ml) | Interpretative comment added |
|---|---|
| 0–5 | This is a low pre-dose level<br>Is vancomycin therapy still indicated?<br>Check if vancomycin doses are being inappropriately held |
| 5–10 | Is vancomycin therapy still indicated?<br>If so, it is safe to re-dose<br>Repeat level in 2–3 days |
| 10–15 | Level appears to be re-accumulating<br>Suggest re-dose if vancomycin therapy is still indicated and re-check level in 24–48 hours<br>Bleep microbiology/pharmacy if concerned |
| >15 | High level. Result phoned<br>Please hold dose unless otherwise advised by clinical microbiology<br>Repeat level the following day |

The clinical microbiology team and senior pharmacist undertook further multidisciplinary audit feedback sessions.

## Audit 3

A third audit was conducted in September 2004.

The same member of the clinical microbiology team conducted all three audits and the same methods were applied throughout.

Personnel involved included one microbiologist who conducted the audit, another who provided education, and a senior pharmacist. All ward phlebotomists and pharmacists were involved after audit 1.

## Statistical analysis

Statistical significance for changes in dose omissions was calculated using the $\chi^2$ test.

# RESULTS

Table 2 outlines patient demographics, details of vancomycin therapy, and microbiology laboratory results. There were less surgical patients included in the third (30% (15/50) of patients) than the first audit (61% (33/54)) ($p<0.01$), possibly due to interventions by the clinical microbiology team during concurrent audit of surgical prescriptions. There were significantly more patients with pneumonia (42% (24/57)) included in the second audit (18.5% (10/54) in audit 1 ($p<0.01$) and 22% (11/50) in audit 3 ($p<0.05$)), possibly due to seasonality, with increased hospital occupancy and nosocomial infections during winter. The majority of vancomycin prescriptions were appropriate. The clinical microbiology team were less involved in the decision to prescribe vancomycin in the third audit (56% (28/50) of prescriptions) in comparison to the first (85% (46/54)) ($p<0.01$) (table 2).

There was a decrease in vancomycin doses prescribed over the study period (table 3). Results of the first audit indicated that 28% (282/1007) of prescribed vancomycin doses were not given, 16% (161/1007) of which were withheld inappropriately. In audit 2, there was a decrease in doses inappropriately withheld while staff waited for TDM results (6% (65/1161 prescribed doses) (table 3). By audit 3, there was a significant reduction in the overall number of doses held inappropriately:

**Table 2** Patient demographics, indications for and appropriateness of vancomycin therapy, and microbiology results over the three audit periods

| | Audit 1 | Audit 2 | Audit 3 |
|---|---|---|---|
| Patients and speciality | | | |
| Total | 54 | 57 | 50 |
| Medical | 14 (26%) | 21 (37%) | 24 (48%) |
| Surgical | 33 (61%) | 26 (46%) | 15 (30%) |
| Haematology and oncology | 7 (13%) | 10 (17%) | 11 (22%) |
| Reason for vancomycin prescription | | | |
| Empiric therapy* | 9 (16.5%) | 2 (3.5%) | 4 (8%) |
| Pneumonia | 10 (18.5%) | 24 (42%) | 11 (22%) |
| Device-related infection | 5 (9%) | 2 (3.5%) | 5 (10%) |
| Skin/soft tissue infection | 7 (13%) | 13 (23%) | 3 (6%) |
| Catheter-related infection | 5 (9%) | 4 (7%) | 5 (10%) |
| Neutropenic sepsis | 5 (9%) | 5 (9%) | 5 (10%) |
| Other infection† | 4 (7.5%) | 6 (11%) | 6 (12%) |
| Positive blood culture | 9 (16.5%) | 1 (2%) | 11 (22%) |
| Vancomycin prescription appropriate | | | |
| Yes | 51 (94%) | 54 (95%) | 48 (96%) |
| No | 3 (6%) | 3 (5%) | 2 (4%) |
| Involvement of clinical microbiology service in decision to prescribe vancomycin | | | |
| Yes | 46 (85%) | 38 (67%) | 28 (56%) |
| No | 8 (15%) | 19 (33%) | 22 (44%) |
| Microbiological indication for vancomycin (relevant positive isolate) | | | |
| None | 22 (41%) | 32 (56%) | 22 (44%) |
| MRSA | 18 (33%) | 15 (26%) | 17 (34%) |
| MSSA | 3 (5.5%) | 1 (2%) | 4 (8%) |
| CoNS | 9 (17%) | 6 (10.5%) | 4 (8%) |
| Other organism‡ | 3 (5.5%) | 3 (5%) | 3 (6%) |

MRSA, meticillin-resistant *S aureus*; MSSA, meticillin-sensitive *S aureus*; CoNS, coagulase-negative staphylococcus.
*Empiric therapy: vancomycin prescribed according to the hospital's antimicrobial prescribing guidelines, to patients in whom no source of sepsis could be identified.
†Other infection: cardiovascular infection (not including vascular prostheses), central nervous system infection, intra-abdominal collection or urosepsis, osteomyelitis/infected bone graft.
‡Other organism: ampicillin-resistant enterococcus (3) (audit 1); ampicillin-resistant enterococcus (3) (audit 2); ampicillin-resistant enterococcus (1), *Corynebacterium* spp (1), *Streptococcus bovis* (1) (audit 3).

10% (78/782) of doses compared to 16% (161/1007) in audit 1 ($p<0.01$). There was a significant reduction in doses held for no apparent reason in audit 3 (16% (27/170) of doses) when compared to audit 1 (25% (69/282)) ($p<0.05$). There was no significant reduction in doses incorrectly withheld pending results of vancomycin TDM levels between audit 1 (33% (92/282) of doses) and audit 3 (30% (51/170) of doses).

## DISCUSSION

Our audit highlights difficulties in changing healthcare worker behaviour despite multiple interventions. In an era of increasing antimicrobial resistance (including MRSA), appropriate antimicrobial prescribing assumes new importance.

We are reassured by the findings that vancomycin prescriptions were appropriate for the majority of patients, despite reducing input from our department. However, we are concerned that the number of vancomycin doses inappropriately withheld will lead to treatment failure and contribute to emergence of vancomycin-resistant organisms. Because vancomycin TDM appeared to influence vancomycin administration, we assessed the entire process of TDM in order to improve vancomycin administration. We successfully improved vancomycin administration by employing a multidisciplinary, education-based approach. Our interventions significantly reduced, but did not abolish, the proportion of prescribed doses that had been inappropriately withheld.

Ward staff confused the toxicity profile of vancomycin with that of gentamicin, which may explain the high percentage of vancomycin doses withheld. Excessive concern about vancomycin toxicity is not unique to our institution. Most clinicians believe vancomycin to be both nephrotoxic and ototoxic,[2] although vancomycin is safer than generally perceived.[3–5] We focused on continuous education of staff about vancomycin toxicity.

Why perform vancomycin TDM? We abolished peak vancomycin levels, which have always been controversial because it is difficult to be sure of accurate timing of phlebotomy and there is little evidence that peak vancomycin levels are a marker for toxicity.[6] We established a single vancomycin TDM level that we called ''pre-dose'', discontinuing ''peak'', ''trough'' and ''random'' levels. Reducing available choices was an attempt to reduce confusion and to facilitate interpretation of results. It has been shown that optimal dosing can be achieved using pre-dose levels alone, reducing costs and burden of phlebotomy for patients and staff alike.[7 8] In contrast, monitoring of pre-dose (trough) levels is justified when vancomycin and aminoglycosides are prescribed concurrently, in patients with multiple comorbidities and fluctuating renal function, and during long courses of vancomycin.[9] TDM for other antibiotics has provided cost savings by reducing duration of therapy and length of hospital stay.[10]

We had to determine what ''pre-dose'' level would be of greatest therapeutic benefit without toxicity. Trough vancomycin concentrations of 10 mg/l are considered therapeutic,[11] but in severe infections, higher concentrations are required.[12] We observed that vancomycin doses were withheld if TDM results were 10–12 mg/ml, a level considered to be therapeutic, and staff failed to increase the dose in patients with TDM levels less than 10 mg/ml. Such actions contribute to treatment failure and spread of resistant organisms such as vancomycin resistant enterococcus. We changed our interpretative comments (table 1) accordingly. A single TDM level has been shown to be sufficient for monitoring patients with normal renal function,[13] so we proposed that patients with normal renal

**Table 3** Details of vancomycin therapeutic drug monitoring (TDM) levels, prescriptions and reasons for prescribed doses not given

| | Audit 1 | Audit 2 | Audit 3 |
|---|---|---|---|
| Vancomycin TDM levels | | | |
| Total | 302 | 312 | 227 |
| Category of TDM level | | | |
| Peak | 56 | | |
| Trough | 168 | | |
| Random | 78 | | |
| Pre-dose | NA | 312 | 227 |
| Vancomycin doses | | | |
| Vancomycin doses prescribed | 1007 | 1161 | 782 |
| Vancomycin doses prescribed but not given | 282 (28%) | 254 (22%) | 170 (22%)** |
| Reason for prescribed vancomycin doses not given | | | |
| Ward staff waiting for result | 92 (9%) | 65 (6%) | 51 (6.5%) |
| Vancomycin TDM result >15 mg/l | 112 (11%) | 97 (8%) | 84 (11%) |
| No reason | 69 (7%)* | 85 (7%) | 27 (3.5%)* |
| No intravenous access | 9 (1%) | 6 (1%) | 8 (1%) |

NA, not applicable.
Percentages shown are expressed as percentages of overall prescribed doses of vancomycin.
*p<0.05, **p<0.01.

function—as defined by a creatinine <120 μmol/l or glomerular filtration rate >50 ml/min—should have twice weekly vancomycin TDM monitoring.

Similar interventions have been efficacious in other studies. The importance of pharmacy liaison has been shown previously.[14 15] Pre-printed chart stickers improve compliance with prophylactic antibiotic guidelines.[16] Abolition of peak levels, contacting clinicians, education and computer ''pop-up'' screens were used to optimise vancomycin TDM in Yale University, which succeeded with a 60% decrease in TDM requests, sustained at one year.[14] Unlike the Yale study, our main aim was to improve vancomycin administration, but there was also a decrease in our TDM requests (table 3). Our inclusion of TDM levels as part of the phlebotomy service, and laboratory registration of samples on arrival, also contributed to the reduction of levels requested (table 3). The decrease in TDM requests in the Yale study was greater than that shown in our study—potentially because they discouraged TDM altogether in patients with normal renal function. While we have elected to continue with vancomycin TDM for the reasons discussed, we plan continuous review of TDM and its effect on vancomycin administration.

Our measures to improve vancomycin administration focused on changes to the TDM process, to avoid generating a culture of blame among professional groups involved. Since it is established that audit and feedback have a small to moderate effect on practice,[17] we performed feedback and educational sessions at hospital, ward and team level. Many staff members are employed on a temporary basis and thus any improvement attributable to individual training would not be sustainable. Education needs to be ongoing in view of the continuous turnover of staff in our institution.

Regarding limitations of our study, we did not survey staff to identify areas of confusion. The practice changes made were based on observations, discussions with ward staff and suggestions made at departmental meetings. The three audits were prospective, therefore in the interest of patients any inappropriate prescription or omission was corrected. Prescribed and missed doses were reduced by this intervention, and it is likely that a retrospective audit would show a less favourable prescription profile. Although our interventions are comparable to, and more extensive than, those made in other studies,[14 15] we could not assess the impact of each individual intervention.

It appears that the practice of vancomycin TDM negatively impacts on the number of doses received by the patient. We attempted to address dosing failure with changes to the TDM process and staff education. However, as 10% of prescribed vancomycin doses are still being held inappropriately, this merits continued intervention.

It was important to find a solution to the challenge of improving vancomycin administration that would be of use to future staff. We have successfully established a system to ensure better dose administration, which is self-perpetuating and independent of individual staff members. We plan to continue monitoring this process and extend our audits to other antimicrobials. We achieved a significant improvement in vancomycin administration, but we recognise that this is an area requiring ongoing intervention and monitoring.

### Take-home messages

- Physicians should be aware that not all prescribed doses of antimicrobials are administered.
- A multidisciplinary, systems-based approach can improve antimicrobial dose administration.


### Authors' affiliations

**R K Crowley, F Fitzpatrick, S FitzGerald, H Humphreys, E G Smyth,** Departments of Clinical Microbiology, Beaumont Hospital, Dublin, Ireland
**D Solanki,** Department of Pharmacy, Beaumont Hospital, Dublin, Ireland


Competing interests: None declared.

## REFERENCES


1 **Palmer-Toy DE**. Therapeutic monitoring of vancomycin. *Arch Pathol Lab Med* 2000;**124**:322–3.
2 **Finch RG**, Eliopoulos GM. Safety and efficacy of glycopeptide antibiotics. *J Antimicrob Chemother* 2005;**55**(Suppl 2):ii5–13.
3 **Eng RH**, Wynn L, Smith SM, *et al*. Effect of intravenous vancomycin on renal function. *Chemotherapy* 1989;**35**:320–5.
4 **Wilson AP**. Comparative safety of teicoplanin and vancomycin. *Int J Antimicrob Agents* 1998;**10**:143–52.
5 **Hammett-Stabler CA**, Johns T. Laboratory guidelines for monitoring of antimicrobial drugs. National Academy of Clinical Biochemistry. *Clin Chem* 1998;**44**:1129–40.
6 **Catchpole C**, Hastings JG. Measuring pre- and post-dose vancomycin levels—time for a change? *J Med Microbiol* 1995;**42**:309–11.
7 **Saunders NJ**. Why monitor peak vancomycin concentrations? *Lancet* 1994;**344**:1748–50.

8 **Tan WH**, Brown N, Kelsall AW, *et al*. Dose regimen for vancomycin not needing serum peak levels? *Arch Dis Child Fetal Neonatal Ed* 2002;**87**:F214–16.
9 **Pou L**, Rosell M, Lopez R, *et al*. Changes in vancomycin pharmacokinetics during treatment. *Ther Drug Monit* 1996;**18**:149–53.
10 **Crist KD**, Nahata MC, Ety J. Positive impact of a therapeutic drug-monitoring program on total aminoglycoside dose and cost of hospitalization. *Ther Drug Monit* 1987;**9**:306–10.
11 **Tobin CM**, Darville JM, Thomson AH, *et al*. Vancomycin therapeutic drug monitoring: is there a consensus view? The results of a UK National External Quality Assessment Scheme (UK NEQAS) for Antibiotic Assays questionnaire. *J Antimicrob Chemother* 2002;**50**:713–18.
12 **Wysocki M**, Thomas F, Wolff M. Why monitor peak vancomycin concentrations? *Lancet* 1995;**345**:646.
13 **Andres I**, Lopez R, Pou L, *et al*. Vancomycin monitoring: one or two serum levels? *Ther Drug Monit* 1997;**19**:614–19.
14 **Bates DW**, Soldin SJ, Rainey PM, *et al*. Strategies for physician education in therapeutic drug monitoring. *Clin Chem* 1998;**44**:401–7.
15 **Ansari F**, Gray K, Nathwani D, *et al*. Outcomes of an intervention to improve hospital antibiotic prescribing: interrupted time series with segmented regression analysis. *J Antimicrob Chemother* 2003;**52**:842–8.
16 **Ritchie S**, Scanlon N, Lewis M, *et al*. Use of a preprinted sticker to improve the prescribing of prophylactic antibiotics for hip fracture surgery. *Qual Saf Health Care* 2004;**13**:384–7.
17 **Jamtvedt G**, Young JM, Kristoffersen DT, *et al*. Audit and feedback: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev* 2003;(3):CD000259.