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### Vancomycin Dosing by Weight

Vancomycin has been around for decades and as a drug of choice for the treatment of MRSA infections. While intravenous dosing recommendations are usually weight based, vancomycin often times are simply prescribed using a flat dose strategy of 1 g every 12 hours. So with the growing obesity epidemic, it's worthwhile to ask whether we are commonly underdosing our patients when we write for vancomycin using the conventional flat dose.

You are listening to ReachMD, The Channel for Medical Professionals. Welcome to Focus on Pharmacy. I am your host, Dr. Charles Turck, PharmD, and our guest is Dr. Ronald Hall, II, PharmD. A board certified pharmacotherapy specialist, Dr. Hall works at the North Texas VA Healthcare System and the University of Texas Southwestern Medical Center in Dallas. Dr. Hall also has an appointment at the Texas Tech University Health Sciences Center School of Pharmacy and he is the lead author of a multi-center evaluation of vancomycin dosing that was recently published in the American Journal of Medicine.

### DR. CHARLES TURCK:

Dr. Hall, welcome to the program. We are discussing vancomycin dosing in the obese and I would like to start off by asking why the appropriateness of vancomycin dosing is becoming an increasingly relevant question in healthcare?

### DR. RONALD HALL, II:

Oh it's becoming an increasingly relevant question for one because we now have alternate options available and folks are starting to ask is vancomycin still the best choice. In addition, we have MRSA output that are having increasing vancomycin MICs and those increasing vancomycin MICs have been associated with decreased survival rates or decreased clinical outcomes that are favorable for patient.

### DR. CHARLES TURCK:

How exactly should vancomycin be dosed according to current treatment guidelines and past literature?

### DR. RONALD HALL, II:

Treatment guidelines have basically recommended the 15 mg/kg type of dosing strategies, trough concentration goals have ranged from 10-20 mcg/mL.

**DR. CHARLES TURCK:**

Which guidelines make those recommendations in particular?

**DR. RONALD HALL, II:**

The nosocomial pneumonia guidelines and the endocarditis guidelines which experts in the field usually refer to, also the bacteremia guidelines.

**DR. CHARLES TURCK:**

That's the empiric dose and then how do we adjust dosing typically?

**DR. RONALD HALL, II:**

Based on the trough concentration that we were just referring to 15-20 mcg/mL for nosocomial pneumonia and I believe the endocarditis is a little bit more general than that.

**DR. CHARLES TURCK:**

How exactly have healthcare professionals gotten stuck in the rut of prescribing 1 g IV every 12 hours when writing for vancomycin?

**DR. RONALD HALL, II:**

Well, I would say a couple of reasons, one is that the FDA has not changed the prescribing information for vancomycin in spite of multiple pharmacokinetic studies stating that actual body weight is the best descriptor to use when dosing vancomycin for obese patients, therefore clinical studies evaluating vancomycin against these newer competitors still use a 1 g q.12h. dose for everyone and then wait to a later to adjust dosing based on the local standard of care. Secondly, the advent of the premixed bag and along with the 1 g q.12h. being used in studies also facilitate folks being content with not increasing pharmacy time or coming up with the calculation of what the proper dose should be.

**DR. CHARLES TURCK:**

Even though we have talked about the flat dose potentially being inappropriate for several patients, is that dose ever appropriate?

**DR. RONALD HALL, II:**

It certainly is. For an average 70-kilo patient which is a phrase that's thrown around a fair bit, I don't think the average US patient is 70

kilos anymore, but for a patient who weighs 70 kilos if you do  $70 \times 15$  you come out with approximately 1 g per dose so in that way the patient or even slightly under 1 g dose is appropriate and patient that weigh dramatically under that or dramatically over that, you are either putting the patient at risk of adverse events if they weigh substantially under 70 kilograms or at further risk of suboptimal clinical outcome if they are being under dosed in the case of obese patients.

**DR. CHARLES TURCK:**

I have to imagine there are some healthcare professionals out there who are there just recently in medical school or who are perhaps in a ways removed from medical school may remember reading or hearing or learning something about toxicity associated with vancomycin and might be concerned about perhaps pushing the dose up to say may be 1.5 or 2 g of vancomycin per dose. Do you think that those concerns are well placed?

**DR. RONALD HALL, II:**

There have been a few papers recently describing increased nephrotoxicity rates with more aggressive vancomycin dosing scheme, and in particular, a paper by that looked at patients who received 4 g or more per day and found that those patients had an increased risk of kidney toxicity, however, only a few of those patients actually weighed more than 100 kg that received 4 per day and most of those patients, it appears actually received more than the recommended 30 mg/kg per day dose of vancomycin. So it may simply be a case of overdosing even beyond the clinical guidelines scenario than actual using the guideline recommended dose resulting in increased nephrotoxicity.

**DR. CHARLES TURCK:**

It's a nice to your study. As I had mentioned earlier, you had recently published a study in the American Journal of Medicine, what was the impetus for your study?

**DR. RONALD HALL, II:**

The impetus for our study was to determine for a drug such as vancomycin that has multiple studies telling us how to prescribe it in obese patients if those recommendations are actually being followed. My area of research is drug dosing in obesity, even though most of my studies that are ongoing are pharmacokinetics and pharmacodynamic studies to identify doses of other agents for obese patients. This study actually was looking the other the way around, okay, the dose is already defined how good a job or how bad a job are we doing of actually following those recommendations.

**DR. CHARLES TURCK:**

How was your study conducted then?

**DR. RONALD HALL, II:**

It was a retrospective chart review type of study and it was conducted at two centers, Presbyterian Hospital of Dallas and VA Medical Center in Dallas and neither one of those hospitals has a pharmacist guided dosing system for vancomycin, and basically we looked at

the dose of vancomycin and the frequency of vancomycin and evaluated the appropriateness both on a per dose and a per day basis.

If you are just joining us, you are listening to Focus on Pharmacy on ReachMD. I am your host, Dr. Charles Turck. Our guest is Dr. Ronald Hall, a board certified pharmacotherapy specialist at the Texas Tech University Health Sciences Center School of Pharmacy in Dallas. We are discussing a paper that he and others had published just recently in the American Journal of Medicine about IV vancomycin dosing in patients who are obese.

**DR. CHARLES TURCK:**

So, Dr. Hall, getting back to your study, what sort of patient population were you looking at?

**DR. RONALD HALL, II:**

The average age in our study I believe was 56, basically mid 50s, and these are patients with multiple comorbid medical conditions. However, we did only look at patients with what we considered normal renal function or creatinine clearance of at least 60 mL per minute as that's the creatinine clearance that our institutions use to start dose adjusting vancomycin.

**DR. CHARLES TURCK:**

Did you take duration of therapy into account when formulating the inclusion or exclusion criteria?

**DR. RONALD HALL, II:**

We did not for this study, this was actually a cursory look to see if it was even a problem at all and we are following that study up to look at folks specifically with MRSA bacteremia and will be looking at duration of therapy and following up some of these other studies that have reported effects on nephrotoxicity as well to see of the case in our population.

**DR. CHARLES TURCK:**

In your study, what sort of endpoints were you looking at?

**DR. RONALD HALL, II:**

In the study in the American Journal of Medicine, it was purely did the patients get an appropriate dose or not and from a pharmacy standpoint we also looked at did the dose get changed within a 24-hour period which was rather disappointing only 4 patients out of over 100 were inappropriately dosed received a dose change within the 24-hour period, so it is definitely not one discipline issue, it's a multidisciplinary problem.

**DR. CHARLES TURCK:**

Your primary outcome was whether or not a patient was empirically treated with 10 mg/kg for each of the different body mass index cohorts that you had defined in your study, why 10 mg/kg rather than 15?

**DR. RONALD HALL, II:**

That's a great question and we have got that question from other folks as well. The guidelines routinely recommend 15 mg/kg, but since vancomycin is usually dosed on a 250 mg or rounded to a 250 mg increment, we decided to be a little bit lax with our primary endpoint and to try to get folks the benefit of the doubt and then also look at the 15 mg/kg as a secondary measure.

**DR. CHARLES TURCK:**

So in terms of your studies results, what did you find as far as a correct dosing was concerned for each of the different body mass index cohorts?

**DR. RONALD HALL, II:**

For underweight patients, regardless of the dosing measure we utilized, we found that they received at least an adequate dose. Then with the normal weight patients when we used the lenient measure of 10 mg/kg, virtually all of them received an adequate dose, but when you went through the 15 mg/kg, only half of those patients received inadequate dose. The overweight population over 90% received 10 mg/kg dose, but only one patient in that group received at least 15 mg/kg per dose.

**DR. CHARLES TURCK:**

That was one patient out of how many?

**DR. RONALD HALL, II:**

Out of 99.

**DR. CHARLES TURCK:**

Wow! Okay, so 1% of patients was appropriately dosed with vancomycin empirically anyway.

**DR. RONALD HALL, II:**

Right, and we haven't even got to the obese patients yet. The obese patients only 28% received a 10 mg/kg dose and only 1 out of the 155 patients received a 15 mg/kg dose.

**DR. CHARLES TURCK:**

Were you surprised by these findings?

**DR. RONALD HALL, II:**

I would like to say yes, but unfortunately no. Like I say with the preponderance of FDA approval studies still utilizing a 1 g q.12h. flat dosing regimen for all patients and no sub analyses of that information to see the effect of obesity on patient outcomes, that's the way many folks are taught in the pharmacokinetic data even though it's made it into the guidelines on a mg/kg basis, it really hasn't translated into clinical practice.

**DR. CHARLES TURCK:**

You had also been a little critical too of not simply the medical professionals who had been dosing vancomycin, but also the role that pharmacy had played. Why was that again?

**DR. RONALD HALL, II:**

Well as pharmacist, we are supposed to be the medication or the drug experts and if we are not going to use the medication correctly that needs to be doses on a mg/kg basis, then we need to move on to a drug that we can use correctly.

**DR. CHARLES TURCK:**

What do you think the implications of your study are?

**DR. RONALD HALL, II:**

I would say the biggest implication is that we really need to reinforce to all disciplines involved in dosing vancomycin that it is based on actual body weight and that if we are concerned about nephrotoxicity or giving too high dose, there are alternate agents now available that you can use, so basically if we are going to use the medication, use it correctly and if there are other alternatives out there, use them if you are not going to dose vancomycin correctly.

**DR. CHARLES TURCK:**

We have been talking with Dr. Ronald Hall about how good job we are doing dosing IV vancomycin in the obese. Dr. Hall, thank you so much for joining us.

**DR. RONALD HALL, II:**

Absolutely, thanks for having me.

I am Dr. Charles Turck. You have been listening to Focus on Pharmacy on ReachMD, The Channel for Medical Professionals. Be sure to visit our website at [www.reachmd.com](http://www.reachmd.com) featuring on-demand podcasts of our entire library and thank you for listening.