VANCOMYCIN DOSING UPDATE – *September 2018*

BACKGROUND:

In March we modified our Vancomycin dosing process to include a ***total*** body weight loading dose with doses up to 3 grams. This was in response to a review that demonstrated very low trough attainment rates for patients with indications necessitating troughs of 15-20 mcg/ml. No other changes were made to current dosing processes.

DATA REVIEW (PRE/POST LOADING DOSE MODIFICATIONS):

Overall data (obese & non-obese) - Overall rates of trough attainment (obese & non-obese patients) were slightly improved with lower incidence of troughs less than 10 mcg/ml (9.8% vs 13.1%) although the total percentage either exceeding 22 mcg/ml or less than 10 mcg/ml was largely unchanged (29.1% vs 29.4%).

Obese patients (BMI > 30)

Baseline Data (BMI > 30)

Range	Number	Average	Percentage
< 10	7	8.33	11%
10 - 14.9	28	12.55	46%
15-21	24	17.7	39%
≥ 22	2	26.6	3%
	61		

57% of patients with indications requiring troughs of 15-20 did not have initial therapeutic troughs

Follow-up Data (BMI > 30)

Range	Number	Average	Percentage
< 10	13	8.3	10%
10 - 14.9	35	12.4	26%
15-21	55	17.9	41%
≥ 22	31	27.8	23%
	134		

Follow-up data has shown that the rate of target achievement has not significantly increased with an increased incidence of elevated trough values

DISCUSSION POINTS RELATED TO ABOVE DATA:

The above data prompted a review of 205 patients (obese & non-obese) that were treated with vancomycin utilizing our increased loading dose strategy. The below are relevant discussion points and recommended process modifications based on this review.

Although the loading dose was the only change that was implemented, this additional review identified other opportunities for dosing process improvement in hopes of improving vancomycin dosing performance. It appears as though the more aggressive loading doses may have brought to the surface other dosing practices that are also contributing to some elevated trough values that were not as evident with the previous utilization of lower adjusted body weight loading doses.

RECOMMENDED DOSING STRATEGY CHANGES:

Modification to 20 mg/kg TOTAL body weight loading dose:

- We will lower our total body weight loading dose to 20 mg/kg instead of 25-30 mg/kg. A max dose of 3 grams will still be utilized along with split loading doses for 2.5 gm and 3 gm loads. The dosing calculator will reflect this change.

Q 8 hour dosing (patients > 60 years of age)

- The **overall** use of Q 8-hour dosing intervals was not seen as an area of concern (N = 42; 8 elevated troughs – 19%)
- Patients ≥ 60 years of age represented 50% of all elevated troughs among patients receiving Q 8-hour dosing
    - All involved situations in which patients had very low serum creatinine values (≤ 0.5) that may have resulted in over-estimations of actual clearance and Q 12-hour intervals would have been more appropriate
- **New process → Q 8-hour intervals will no longer be an option on the calculator for patients ≥ 60 years.**

Dosing intervals exceeding the patient's estimated half-life (example: dosing interval of Q 12 hours in patient with t ½ = 21 hours)

- Elevated trough values were commonly observed in patients with dosing intervals that exceeded the patient's estimated half-life. This was also observed in situations in which lower maintenance doses (< 10 mg/kg) were utilized along with dosing intervals that were more frequent than the estimated half-life.
- Most common among patients with half-life to trough ratios exceeding 1.15 (example: Q 12-hour interval in patient with half-life of ~ 14). Some patients had intervals far exceeding the patient's estimated half-life (Q 24-hour interval in patient with half-life of 36 hours, etc.).
- **New process → The dosing calculator will display a warning if your half-life to trough ratio exceeds 1.15**

Q 18-hour intervals

- While Q 18-hour intervals were not commonly utilized (n=16), they were frequently associated with elevated trough values (8/16; 50%). Three of these situations resulted in acute kidney injury.
- This dosing interval was very commonly utilized in patients with elevated baseline creatinine values with half-lives in the 14-18-hour range. Rather than scheduling a Q 18-hour dose, consideration should be given to either re-evaluate the dosing scheme following the next set of labs or consider Q 24-hour dosing as an alternative.
- Q 18-hour intervals can also create difficulties if patients are discharged to home or other facilities upon discharge.
- **New process → The dosing calculator will now utilize a drop-down menu for dosing intervals and Q 18 hours will not be an option**

Elevated baseline creatinine values

- The most commonly observed factor contributing to elevated trough values and AKI was maintenance dose calculations based on elevated baseline creatinine values.
- Patients with Scr values that exceed their baseline values may have very unpredictable clearance and pharmacokinetics. Caution should be exercised when determining post-loading dose dosing needs
- Depending on the time that the consult is received, waiting until the next set of labs may be the best option
- Daily reassessment of renal function and re-evaluation of current dosing needs is critical
- If a maintenance dose is scheduled for these patients we must re-evaluate and possibly change dosing schemes if renal function worsens or improves
- **New process → The dosing calculator will display a warning if the creatinine value is ≥ 1.5**
    - This is only a warning and we must use clinical judgment when assessing initial Scr values
    - Some patients may meet AKI definition and have Scr values < 1.5 (see below)
- **AKI Definition:**
    - Increase of ≥ 0.3 mg/dl within 48 hours
    - Increase of ≥ 1.5x baseline within 7 days or in comparison to baseline value

Patients with initial half-life exceeding 18 hours

- Like above, consideration should be given at times to defer maintenance dose scheduling until follow-up labs are available.
- This should particularly be considered for 2nd & 3rd shift if f/u labs are expected or ordered within the next ~ 12 hours
- Communication will be key! WE MUST COMMUNICATE TO OUR FELLOW PHARMACISTS SO THEY ARE AWARE THAT MAINTENANCE DOSES HAVE NOT BEEN SCHEDULED.

Minimize Vancomycin exposure by recommending discontinuation when appropriate

- **Utilize *Vancomycin Use Criteria* on Form Web**
  https://fparchives.com/memorial/documents/VancomycinUseCriteria.pdf

CONCLUSION:

Upon review of the post-loading dose modifications it is clear that the increased incidence of elevated troughs and AKI is multifactorial. The larger loading doses have certainly precipitated this trend although it appears that some of our dosing practices are also contributing to this trend. Previously, we struggled to achieve initial therapeutic vancomycin levels due to our smaller loading doses but we did have a high incidence of subsequent elevated levels following the initial identification of a sub-therapeutic level ("knee-jerk" reaction to low level).

While a slight reduction in our loading dose methodology may provide some degree of benefit we must remember that our Vancomycin calculator is simply a computer estimation of a patient's clearance based on **NUMBERS ONLY.**

FINAL POINTS TO REMEMBER:

- Do not ONLY rely on estimated results from the dosing calculator
- New warnings will provide additional cautions, but these are warnings only.
- We must critically evaluate baseline creatinine values and exercise caution when the values may not accurately represent a patient's true clearance
- Do not be shy about modifying a dose someone else started – especially if the clinical picture has changed
- We must critically evaluate each dosing scheme on a daily basis
- Communication: since we will be deferring maintenance dose calculations for some patients to the next shift/day we must clearly communicate these so patients do not miss doses or have delays
- **Your brain is the best calculator! Use the calculator to help *guide* and *assist* you in your dose estimations.**