

## Aminoglycoside Adult and Pediatric Once-Daily Initial Dosing Guidelines

### HSHS St. John's Hospital, Springfield, IL

#### ADULTS ONCE-DAILY DOSING:

##### I. PATIENT SELECTION

- a. Pharmacy will be automatically consulted for all patients receiving aminoglycosides.
- b. **Inclusion** criteria:
  - i. Patients with no documented allergies to the drug
  - ii. Those with suspected or confirmed infection caused by Gram-negative bacteria
- c. **Exclusion** criteria → Use conventional dosing for the following patient populations:
  - i. Pregnancy
  - ii. Patients with ascities or burns
  - iii. Patients on dialysis or those with severe renal dysfunction (CrCl < 30mL/min)
  - iv. Synergy for gram positive infections
  - v. Endocarditis

##### II. CALCULATE DOSE

- a. Use **Actual Body Weight** for dosing calculation unless the patient is obese (BMI ≥ 30 kg/m<sup>2</sup>). Use Adjusted Body Weight if obese.
- b. Extended interval dosing base on **Hartford Nomogram**
  - i. **Gentamicin / Tobramycin**: 7 mg/kg (may use 5 mg/kg for UTI)
  - ii. **Amikacin**: 15 mg/kg
- c. **NOTE**: the above doses were specifically studied for the Hartford Nomogram and the use of other doses is not recommended.
- d. **NOTE**: Amikacin recommended for infections caused by *Pseudomonas aeruginosa*

##### III. CALCULATE INTERVAL

| Dosing Intervals |                         |
|------------------|-------------------------|
| Estimated CrCl   | Initial Dosing Interval |
| > 60 mL/min      | q24h                    |
| 40 – 59 mL/min   | q36h                    |
| 20 – 39 mL/min   | q48h                    |
| < 20 mL/min      | Not recommended         |

##### IV. ADMINISTRATION

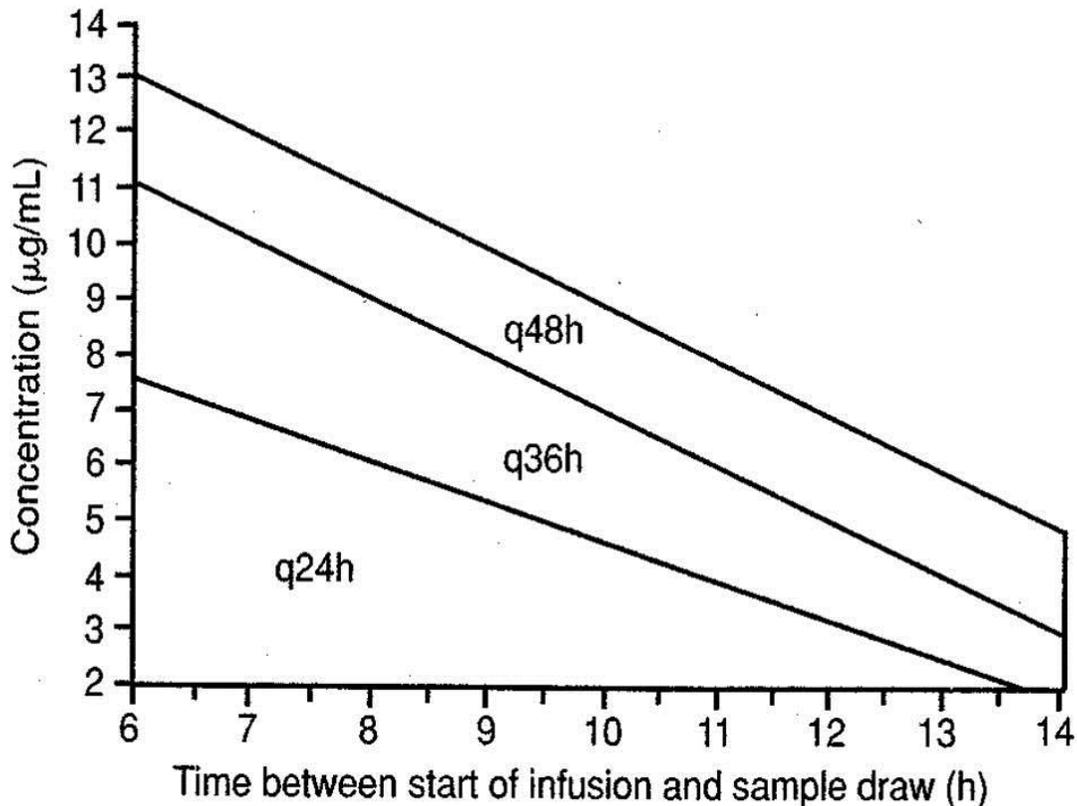
- a. To minimize the possibility of neuromuscular blockade, doses should be infused over at least 30 minutes.

##### V. PATIENT MONITORING

- a. General Monitoring:
  - i. Daily: medication profile, signs for efficacy and toxicity, clinical status
  - ii. Every other day: renal function (SCr, BUN, Intake/Output's) – if rapidly changing, monitor daily
  - iii. Every 3 days: CBC w/differential
  - iv. Pharmacist may order CBC and BMP as clinically indicated to ensure appropriate monitoring.

AMINOGLYCOSIDE ONCE-DAILY DOSING GUIDELINE

- b. A serum aminoglycoside concentration at 6-14 hours (~10 hours) post-infusion after the **FIRST** dose should be drawn.
- c. Dosage adjustments should be made according to the Hartford Nomogram (see below)
  - i. If the level falls on the line choose the longer dosing interval
  - ii. If the level falls off the nomogram use conventional dosing
- d. Pharmacist may make dose adjustments based off of drug level results.
- e. Maintenance levels should be drawn at least once weekly
  - i. For patients with acute changes in renal function a trough level should be drawn 30 minutes prior to next dose
- f. If using **amikacin**, plot  $\frac{1}{2}$  of the serum concentration on the nomogram
- g. If using 5 mg/kg dose, the resulting level must be multiplied by a factor to equal 7 mg divided by the dose used
  - i. Example: If a patient is receiving 5mg/kg/day and the 10h post-dose level was 2 mcg/mL, you would multiply the level by 1.4 (7/5) to get a level of 2.8 mcg/mL. This adjusted level is the one you would plot on the Hartford Nomogram.



**VI. EQUATIONS**

- a. **IBW Males:**  $IBW = 50 \text{ kg} + (2.3 \text{ kg for each inch over 5 feet})$
- b. **IBW Females:**  $IBW = 45.5 \text{ kg} + (2.3 \text{ kg for each inch over 5 feet})$
- c. **Adjusted Body Weight** =  $IBW + 0.4(\text{actual weight} - IBW)$
- d. **CrCl:**  $[(140 - \text{age}) \times (\text{Wt in kg})] / (72 \times \text{Serum Cr}) \quad \times 0.85 \text{ if female}$

## INFANTS & CHILDREN (age > 30 days) ONCE-DAILY DOSING:

### I. PATIENT SELECTION

- a. Pharmacy will be automatically consulted for all patients receiving aminoglycosides.
- b. Once-daily dosing algorithm is preferred method of aminoglycoside dosing.
- c. Conventional dosing preferred for tularemia, gram positive synergy, endocarditis, hemodialysis, renal insufficiency, ascites, burns, pregnancy, and ages not included in the dosing chart.
- d. This guideline covers infants and children > 30 days old. For neonates: see Conventional Dosing Policy.

### II. CALCULATE DOSE & INTERVAL

- a. Use actual body weight
- b. **NOTE:** tobramycin recommended for infections in patients with cystic fibrosis

| Cystic Fibrosis                          |                  |
|--|------------------|
| Drug                                     | Daily Dose       |
| Gentamicin / Tobramycin<br>Age ≥ 1 month | 10 mg/kg IV q24h |
| Amikacin<br>Age ≥ 1 month                | 30 mg/kg IV q24h |

| Non-Cystic Fibrosis                                  |                   |
|--|-------------------|
| Drug   | Daily Dose        |
| Gentamicin / Tobramycin<br>Age 3 months to < 2 years | 9.5 mg/kg IV q24h |
| Age 2 years to < 8 years                             | 8.5 mg/kg IV q24h |
| Age ≥ 8 years  | 7 mg/kg IV q24h   |
| Amikacin<br>Age ≥ 1 month                            | 15 mg/kg IV q24h  |

| Urinary Tract Infection                             |                   |
|---|-------------------|
| Drug  | Daily Dose        |
| Gentamicin / Tobramycin<br>Age 1 month to < 5 years | 7.5 mg/kg IV q24h |
| Age 5 years to < 10 years                           | 6 mg/kg IV q24h   |
| Age ≥ 10 years                                      | 5 mg/kg IV q24h   |

### III. ADMINISTRATION

- a. To minimize the possibility of neuromuscular blockade, doses should be infused over at least 30 minutes.

### IV. PATIENT MONITORING

- a. Renal function (BUN, SCr, UOP) should be monitored in all patients on aminoglycosides.
  - i. BUN and SCr should be monitored twice weekly
  - ii. UOP should be monitored daily

**AMINOGLYCOSIDE ONCE-DAILY DOSING GUIDELINE**

- iii. Pharmacist may order CBC and BMP as clinically indicated to ensure appropriate monitoring.
- b. Peaks and troughs should be drawn if therapy continues for greater than 48 hours
  - i. Draw peak 60 minutes after start of infusion.
  - ii. Draw trough 30 minutes prior to next dose.
  - iii. Does not apply to inhaled aminoglycosides.
- c. Pharmacist may make dose adjustments based off of drug level results.
- d. For patients on prolonged IV aminoglycoside therapy, peaks and troughs should be drawn twice weekly.
- e. If patient on aminoglycoside for  $\geq 10$  days, obtain SCr 1 week after treatment complete. If patient is to be discharged before this time, remind consulting physician to order SCr at follow-up visit.
- f. If patient on aminoglycoside for  $\geq 2$  weeks, remind consulting physician to order audiology exam.

| <b>Gentamicin / Tobramycin</b> |                  |                    |
|--------------------------------|------------------|--------------------|
|                                | <b>Goal peak</b> | <b>Goal trough</b> |
| Cystic fibrosis                | 20 – 35 mcg/mL   | < 1 mcg/mL         |
| Non-cystic fibrosis            | 20 – 35 mcg/mL   | < 1 mcg/mL         |
| UTI                            | 12 – 20 mcg/mL   | < 1 mcg/mL         |

| <b>Amikacin</b>     |                  |                    |
|---------------------|------------------|--------------------|
|                     | <b>Goal peak</b> | <b>Goal trough</b> |
| Cystic fibrosis     | 25 – 35 mcg/mL   | < 3 mcg/mL         |
| Non-cystic fibrosis | 25 – 35 mcg/mL   | < 1 mcg/mL         |

- g. For patients with more serious infections (i.e. CF exacerbation, meningitis), a peak closer to 30 or 35 mcg/mL is preferred. For less severe infections (i.e. gram negative bacteremia), a peak closer to 20 or 25 mcg/mL is acceptable.

**V. EQUATIONS**

- a. **Schwartz equation:**  $eGFR \text{ (mL/min)} = (k \times \text{length in cm}) / (\text{SCr in mg/dL})$

| <b>Age</b>                     | <b>K</b> |
|--------------------------------|----------|
| Low birth weight $\leq 1$ year | 0.33     |
| Full term $\leq 1$ year        | 0.45     |
| >1 year – 12 years             | 0.55     |
| > 12 years female              | 0.55     |
| > 12 years male                | 0.7      |

- b. **Bedside Schwartz equation:**  $eGFR \text{ (mL/min)} = (0.413 \times \text{Ht in cm}) / (\text{SCr in mg/dL})$ 
  - i. Preferred in patients age 1 – 16 years
- c. **Cockcroft – Gault CrCl:**  $[(140 - \text{age}) \times (\text{Wt in kg})] / (72 \times \text{Serum Cr}) \times 0.85$  if female
  - i. Consider for adult-sized adolescents or teenagers
- d. **IBW in kg (males)** =  $50 + (2.3 \times \text{inches over } 60)$
- e. **IBW in kg (females)** =  $45.5 + (2.3 \times \text{inches over } 60)$

## References

1. Gilbert DN, Leggett JE. Aminoglycosides. In: Mandell GL, Bennett JE, Dolin R. Principles and practice of infectious diseases. 8<sup>th</sup> ed. Philadelphia: Churchill Livingstone Elsevier; 2015: 310-321.
2. Pai MP, Cottrell ML, Kashuba ADM, Bertino Jr JS.. Pharmacokinetics and pharmacodynamics of anti-infective agents. In: Dipiro JT, Talbert RL, Yee GC, et al. Pharmacotherapy: A pathophysiologic approach. 8<sup>th</sup> Edition. New York: McGraw Hill; 2015: 252-262.
3. Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Accessed May 26, 2017.
4. Freeman CD, Nicolau DP, Belliveau PP, Nightingale CH. Once daily dosing of aminoglycosides: review and recommendations for clinical practice. *J Antimicrob Chemother.* 1997;39: 677-686
5. Nicolau DP, Freeman CD, Belliveau PP, Nightingale CH, Ross JW, Quintiliani R. Experience with a once-daily aminoglycoside program administered to 2,184 adult patients. *Antimicrob Agents Chemother.* Mar 1995;39(3):650-655.
6. Pediatric & Neonatal Lexi-Drugs Online [Internet Database]. Hudson, OH: Lexi-Comp, Inc. Accessed July 6, 2017.
7. Siberry GK. Amikacin. Johns Hopkins Antibiotic Guide. Updated January 30, 2017. Accessed July 6, 2017.
8. Siberry GK. Gentamicin. Johns Hopkins Antibiotic Guide. Updated April 5, 2017. Accessed July 6, 2017.
9. Siberry GK. Tobramycin. Johns Hopkins antibiotic Guide. Updated November 5, 2015. Accessed July 6, 2017.
10. McDade EJ, Wagner JL, Moffett BS, Palazzi DL. Once-daily gentamicin dosing in pediatric patients without cystic fibrosis. *Pharmacotherapy.* 2010;30(3):248-253.
11. Safi KH, Damiani JM, Sturza J, Nasr SZ. Extended-interval aminoglycoside use in cystic fibrosis exacerbation in children and young adults: a prospective quality improvement project. *Global Pediatric Health.* 2016;3:1-7.
12. Flume PA, Mogayzel PJ, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. *Am J Respir Crit Care Med.* 2009;180:802-808.
13. Carapetis JR, Jaquiere AL, BATTERY JP, et al. Randomized, controlled trial comparing once daily and three times daily gentamicin in children with urinary tract infections. *Pediatr Infect Dis J.* 2001;20:240-246.