UNIVERSITY HEALTH SYSTEM

ADULT AMINOGLYCOSIDE DOSING GUIDELINES

(SHOULD NOT BE USED IN CHILDREN LESS THAN 12 YEARS OF AGE)

Steps 1 - 3 are the same for either "traditional" or "once-daily" dosing of aminoglycosides.

STEP 1: Determine ideal body weight (IBW) (kg):

Male	Height	Female
36.2	4'6"	31.2
38.5	4'7"	33.5
40.8	4'8"	35.8
43.1	4'9"	38.1
45.4	4'10"	40.4
47.7	4'11"	42.7
50.0	5'0"	45.0
52.3	5'1"	47.3
54.6	5'2"	49.6
56.9	5'3"	51.9
59.2	5'4"	54.2
61.5	5'5"	56.5
63.8	5'6"	58.8
66.1	5'7"	61.1
68.4	5'8"	63.4
70.7	5'9"	65.7
73.0	5'10"	68.0
75.3	5'11"	70.3
77.6	6'0"	72.6
79.9	6'1"	74.9
82.2	6'2"	77.2
84.5	6'3"	79.5
86.8	6'4"	81.8
89.1	6'5"	84.1
91.4	6'6"	86.4

If the actual body weight (ABW) is less than the IBW then use ABW.

This table is based on the following formula: (Weight is in kg)

IBW (male) = 50 + (2.3)(inches over 5')

IBW (female) = 45 + (2.3)(inches over 5')

STEP 2: Estimate the creatinine clearance (CrCl):

$$CrCl = \frac{(140 - Age) \times (IBW) \times F^{\#}}{72 \times SCr^{*}}$$

#F = 1.0 for males; 0.85 for females

*In an emaciated patient: if SCr < 1.0, then use 1.0; otherwise use actual SCr.

NOTE: The following conditions or disease states limit the accuracy of this method of estimating the CrCl as well as this method of estimating the clearance of aminoglycosides:

Liver disease
Crush injuries
Burn injuries
Severe renal failure and/or dialysis
Unstable renal function
Emaciation
Ascites or edema
Pregnancy

STEP 3: Calculate the dosing weight (DW):

$$DW = (ABW - IBW) \times (0.4) + IBW$$

If the actual body weight (ABW) is less than the ideal body weight (IBW) then use the actual body weight as the dosing weight.

STEP 4 for "once daily" dosing, skip to end of "traditional" dosing section.

STEP 4 for "traditional" dosing: Calculate the loading dose (LD) based on the desired peak serum level, condition, and the calculated dosing weight (DW):

LOADING DOSE (use kg of DW calculated in Step 3)	Condition	Recommended Peak levels for Gentamicin/Tobramycin (mcg/ml)	Recommended Peak Levels for Amikacin (mcg/ml)
FOR GENTAMICIN & TOBRAMYCIN: 2 mg/ kg For AMIKACIN: 7.5 mg / kg	Cystic fibrosis	8-12	25-40
	Pneumonia, Biliary tract infection, Peritonitis, Sepsis	7-10	28-35
	FUO with neutropenia, Cellulitis, Diverticulitis, Pyelonephritis, Wound infection	6-8	24-32
FOR GENTAMICIN & TOBRAMYCIN: 1.5 mg/ kg For AMIKACIN: 5 mg / kg	Endocarditis (synergy), Cystitis-UTI	4-6	15-24

STEP 5 for "traditional" dosing: Determine the maintenance dose (MD) and the dosing interval from the CrCl and LD using the following table:

CrCl	Half-Life(hr)	MD = %LD
≥90	3.1	84% q 8 hours
80	3.4	91% q 12 hours
70	3.9	88% q 12 hours
60	4.5	84% q 12 hours
50	5.3	79% q 12 hours
40	6.5	72% q 12 hours
30	8.4	92% q 24 hours
25	9.9	86% q 24 hours
20	11.9	81% q 24 hours

For patients with CrCl < 20ml/min, go to Step 6. Consider alternate therapy for patients in acute renal failure.

Step 6 for "traditional" dosing: Order trough and peak serum levels <u>only if anticipated length of therapy is > 72</u> hours.

Appropriate times for serum sampling are as follows:

- For q8h & q12h intervals, obtain levels at the 3rd dose or 4th dose whichever is closest to 12N. The sample must be in the lab by 1pm because levels are run daily at 1pm.
- For a q 24h interval, and for patients with a CrCL <20, draw two levels after the loading dose:
  1st level -- 30 minutes after the infusion of the loading dose;
  2nd level -- approximately 18-24 hours later.
  This is done to obtain kinetics information as soon as possible, and to make adjustments. Steady-state may not yet be achieved, but it is recommended to obtain levels at this time to avoid toxicity.

<u>Trough levels</u> should be drawn immediately before the dose.
<u>Peak levels</u> should be drawn 30" after a 30" infusion.

If dosage adjustments are made, draw serum levels following the above recommendations. If therapy is unchanged draw additional levels every 5-7 days.

STEP 7 for "traditional" dosing: Adjust doses if necessary.

If serum levels are drawn appropriately and are within normal limits, then no adjustment is necessary unless the disease state or the patient's condition warrants a change.

Therapeutic ranges for University Hospital are as follows:

GENTAMICIN/TOBRAMYCIN	PEAK 4-8 mcg/ml TROUGH < 2 mcg/ml
AMIKACIN	PEAK 15-30 mcg/ml TROUGH < 10 mcg/ml

When adjusting doses, use the following <u>general</u> hints:

a) If the PEAK is too low or too high, adjust the DOSE.
b) If the TROUGH is too low or too high, adjust the INTERVAL.

Occasionally there are instances when both the dose and the interval may need to be adjusted (e.g. - if peak is low and trough is high).

STEP 8 for "traditional" dosing: Monitor the following parameters:

In addition to serum drug levels (every 5-7 days), BUN and SCr should be monitored at least every 3 days. In patients with pre-existing renal, auditory or vestibular impairment, or in patients who receive prolonged, high-dose therapy, obtain baseline and weekly audiograms, and check for tinnitus or vertigo daily, if possible.

STEP 4 for "once daily" dosing: **Determine if your patient is a candidate.**

Although not included in the FDA labelling, "once daily" dosing may be as effective, less toxic, and less costly than "traditional" dosing. Once-daily dosing should be considered for all patients who require aminoglycoside therapy, <u>with the following exceptions:</u>

- Patients with CrCl < 60 ml/min and dialysis patients
- Pediatric patients
- Pregnant females
- Significant burn injury (> 20% BSA)
- Ascites
- Acute renal failure with unstable renal function
- Aminoglycoside used for gram-positive synergy (Enterococcus, Endocarditis)
- Aminoglycoside used for peri-procedure or peri-operative prophylaxis

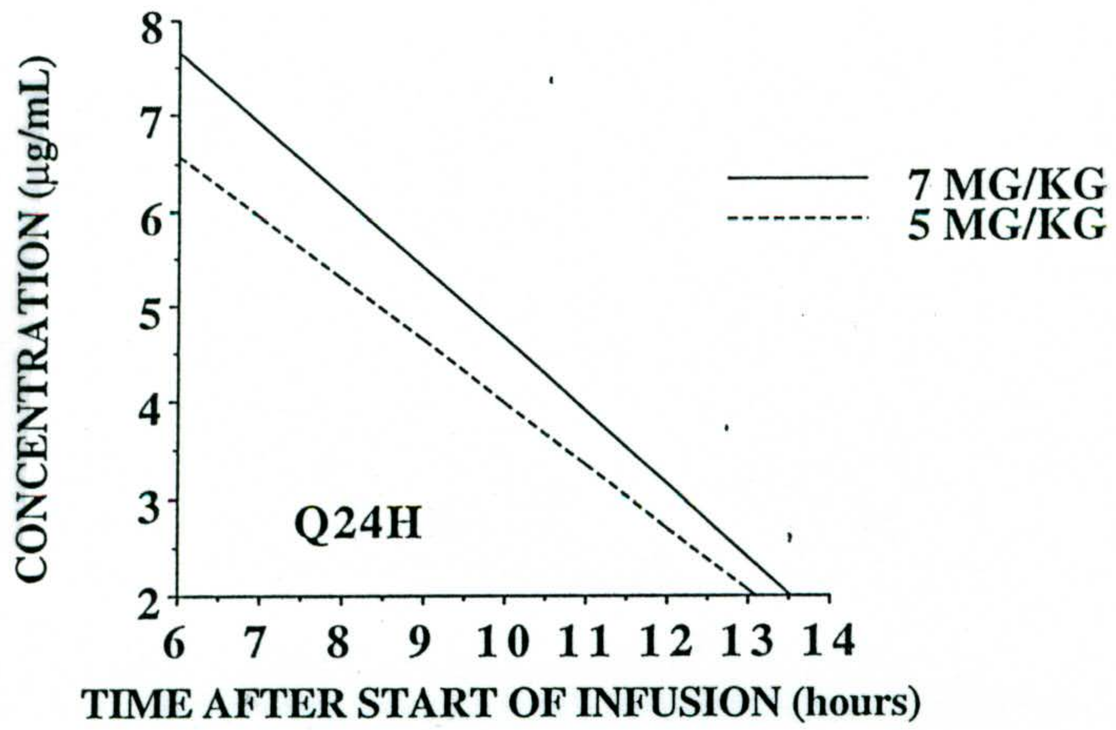
STEP 5 for "once daily" dosing: Order dose. Remember to use the dosing weight (DW) calculated in Step 3.

Initial dose:
5 to 7 mg/kg (DW) for gentamicin or tobramycin;
15 mg/kg (DW) for amikacin.
Dose is diluted in 50 to 100 ml of NS and administered IVPB over 60 minutes.

STEP 6 for "once daily" dosing: **Draw a random level 6 to 12 hours after initial infusion and assess with the following nomogram.**

Results of the random level is evaluated using the following nomogram to determine safety and continued dosing.
Compare the level with the area under the appropriate line (depends on the dose used). For amikacin, divide the observed serum concentration by 2, then use the nomogram.

AMINOGLYCOSIDE NOMOGRAM



If level does not fall below the line, this "once daily" dosing method should not be used. The "traditional" dosing method, as outlined above, should be the method used. If level does fall below the line, continue to Step 7.

STEP 7 for "once daily" dosing: Determine length of therapy.
The average length of therapy in the cited study was 3-5 days. Safety of "once daily" aminoglycoside for longer lengths of therapy has not been determined.

STEP 8 for "once daily" dosing: Monitor patient's BUN & serum creatinine at least every 72 hours. If an increase is seen, take another random level, and assess as before. In patients with pre-existing renal, auditory or vestibular impairment, or in patients who receive prolonged, high-dose therapy, obtain baseline and weekly audiograms, and check for tinnitus or vertigo daily, if possible.

For further information in calculating loading, maintenance and adjustment doses. Contact the decentralized pharmacist, or call extension 2890.

REFERENCES:

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Nicolau DP, Freeman CD, Belliveau PP, et al. Experience with once-daily aminoglycoside program administered to 2,184 adult patients. *Antimicrob Agents Chemother* 1995; 39(3):650-5.

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