ISSUES & ANSWERS
FROM THE DESK OF
LAUREN A. TREPANIER, DVM, PhD, DACVIM, DACVCP

Is it ever safe to administer aminoglycosides?

Despite the intrinsic toxicity of aminoglycosides, several key management points can optimize their safe and effective use.

ISSUE
AMINOGLYCOSIDES HAVE EXCELLENT GRAM-NEGATIVE SPECTRUM but poor activity against anaerobes and in abscesses. The main limitations of aminoglycoside use are dose-dependent nephrotoxicity and ototoxicity, which are caused by the local generation of superoxide and other free radicals.

ANSWERS
AMINOGLYCOSIDES ARE STILL INDICATED for human patients with acute pyelonephritis, intraabdominal infections, osteomyelitis, and pneumonias associated with cystic fibrosis.

In dogs and cats, aminoglycosides are often the most cost-effective and convenient option for resistant isolates of Escherichia coli, Pseudomonas spp. and methicillin-resistant Staphylococcus spp. Despite the intrinsic toxicity of aminoglycosides, several key management points can optimize their safe and effective use.

GENERAL
Use once-a-day dosing
Aminoglycosides should be given once a day, which is more convenient than and (at least) as effective as administering 3 times a day.

- Once-a-day dosing may also be associated with less risk for nephrotoxicity.
  - Lower trough urinary concentrations may result in less overall uptake into renal tubular cells.
- Gentamicin sulfate: 6-8 mg/kg IV, IM, or SC (less painful) once a day
- Amikacin: 10-15 mg/kg IV, IM, or SC (less painful) once a day
  - May show lower minimum inhibitory concentrations (MICs) than gentamicin does against some gram-negative and mycobacterial isolates

Monitor patient status
- Make sure the patient is hydrated.
  - Consider concurrent IV or SC fluids.
- Monitor urine sediment.
  - Monitor for tubular damage via daily examination of fresh urine sediment for granular casts.
Minimize treatment duration
• Limit aminoglycoside therapy to 5 or fewer days\textsuperscript{10} when possible.

Avoid toxic drug interactions

Furosemide
• Systemic aminoglycosides should be avoided in patients being treated with furosemide, as the combination can increase nephrotoxicity and ototoxicity.\textsuperscript{11}

Cisplatin
• Aminoglycosides should be avoided in cancer patients being treated with cisplatin.\textsuperscript{12}
  —Cisplatin also can lead to dose-dependent nephrotoxicity and ototoxicity.

Consider other potential measures to prevent toxicity
• Silymarin (20 mg/kg PO once a day) and vitamin E (25 mg/kg PO once a day) can decrease aminoglycoside nephrotoxicity in dogs experimentally.\textsuperscript{13}
  —Needs to be assessed in clinical patients
• Melatonin, which has antioxidant properties, has been shown to decrease glycineaminopropylglutathione nephrotoxicity in rodents.\textsuperscript{14,15}
  —Has not been evaluated in dogs or cats

SPECIFICS

Use extra caution in patients with renal failure
• In patients with renal insufficiency, choose other agents when possible.
  —Ask for susceptibilities to additional agents (e.g., ticarcillin, cefotetan, aztreonam, meropenem).
• When aminoglycosides are necessary for patients with preexisting renal failure, extend the dosing interval\textsuperscript{16} (e.g., to every other day).
  —To minimize toxicity, aim for a serum trough level <2 µg/mL.\textsuperscript{17}
• Always rehydrate the patient and use concurrent fluid therapy (IV or SC).

REFERENCES

MORE on page 23 ▶

