AMINOGLYCOSIDES AND AKI IN GERIATRIC PATIENTS

PROVIDED BY: MONASH HEALTH LIBRARY **DATE:** 19 APRIL 2024

Please find following a summary of a literature search and relevant results. All articles can be provided in full - email library@monashhealth.org for a list of the articles you require.

QUESTION

In elderly patients does a single dose of aminoglycoside increase the risk of AKI compared to or non-geriatric patients?

RESULTS

ONLINE RESOURCES (GREY LITERATURE)

GUIDELINES

The Australian and New Zealand Society of Nephrology. (2021). **Do not give multiple daily doses of aminoglycoside antibiotics to patients with normal and stable kidney function as the risk of toxicity is less with a single daily dose**. Web link.

Stanford Health Care. (2021). **Aminoglycoside Dosing Guideline.** Web link.

Queensland Department of Health. (2018). **Aminoglycoside Dosing in Adults**. Web link.

KDIGO. (2012). **Clinical Practice Guideline for Acute Kidney Injury**. Web link.

Chapter 3.8. Prevention of aminoglycoside- and amphotericin-related AKI

MEDICINE DATABASES

Australian Medicines Handbook. (2024). **Aminoglycosides**. Web link.

Martindale Medicines Complete. (2024). **Aminoglycoside toxicity.** Web link.

POINT OF CARE TOOLS

Merck Manual. (2022). **Aminoglycosides.** Web link.

UpToDate. (2023). **Pathogenesis and prevention of aminoglycoside nephrotoxicity and ototoxicity.** Web link.

Therapeutic Guidelines. (2024). **Principles of aminoglycoside use.** Web link.

PEER-REVIEWED LITERATURE – MOST RECENT FIRST

Articles are grouped by theme:

- Key Studies
- Emergency Department

- Intensive Care Unit
- Surgical Department

Each article summary contains excerpts from the abstract and an online link.

KEY STUDIES

Chinzowu, T., et al. (2021**). "Risk of antimicrobial-associated organ injury among the older adults: a systematic review and meta-analysis."** *BMC Geriatrics 21*(1): 617. Full text.
This systematic review and meta-analysis examined the relationship between antimicrobial exposure and organ injury in older adults. The overall absolute risks of acute kidney injury among older adults prescribed aminoglycosides, glycopeptides, and macrolides were 15.1% (95% CI: 12.8-17.3), 19.1% (95% CI: 15.4-22.7), and 0.3% (95% CI: 0.3-0.3), respectively. Older adults have a significantly higher risk of sustaining acute kidney injury when compared to the general adult population. Older adults prescribed aminoglycosides have a similar risk of acute kidney injury to the general adult population.

Paquette, F., et al. (2015). **"Acute Kidney Injury and Renal Recovery with the Use of Aminoglycosides: A Large Retrospective Study."** *Nephron 131*(3): 153-160. Full text.
Recent acute kidney injury (AKI) guidelines, based on studies performed a decade ago, recommend avoiding aminoglycosides (AGs) in patients at risk of AKI. We retrospectively identified adult patients who received gentamicin or tobramycin for >=5 days in 2 large university-affiliated centers, excluding critically ill and dialysis patients. AG administration has recently decreased but the risk of AKI remained unchanged and half of the patients did not recover. Vancomycin coadministration, high AG trough levels and heart failure independently predicted AKI.

EMERGENCY DEPARTMENT

Venturini, S., et al. (2021). **"Acute kidney injury and single-dose administration of aminoglycoside in the Emergency Department: a comparison through propensity score matching."** *Giornale italiano di nefrologia 38*(3). Full text.
The aim of this study has been to investigate whether a single shot of AG when septic patients present at the Emergency Department (ED) is associated with acute kidney injury (AKI). Our experience shows that a single-shot administration of gentamicin upon admission to the ED does not determine an increased incidence of AKI in septic patients.

Liljedahl Prytz, K., et al. (2020). **"Antibiotic treatment with one single dose of gentamicin at admittance in addition to a beta-lactam antibiotic in the treatment of community-acquired bloodstream infection with sepsis."** *PloS one 15*(7): e0236864. Full text.
This retrospective cohort study including patients with sepsis or septic shock aimed to investigate whether one single dose of gentamicin at admittance (SGA) added to beta-Lactam antibiotic could result in a lower risk of mortality than beta-Lactam monotherapy, without exposing the patient to the risk of nephrotoxicity. This retrospective observational study including patients with community-acquired sepsis or septic shock and positive blood cultures, who meet Sepsis-3 criteria, shows that the addition of one single dose of gentamicin to beta-lactam treatment at admittance was associated with a decreased risk of mortality and was not associated with AKI. This antibiotic regime may be an alternative to

broad-spectrum antibiotic treatment of community-acquired sepsis.

Sia, C. S., et al. (2018). "**Renal safety of short-term empiric gentamicin therapy in aged patients.**" *Australasian journal on ageing 37*(3): 227-231. Full text.
To determine the incidence of acute kidney injury (AKI) in aged patients receiving empiric gentamicin therapy. Most patients (95%) received a single dose of gentamicin. The incidence of AKI was 15% (36/242 patients. Empiric gentamicin use in patients with advancing age is associated with low rates of predominantly transient renal impairment.

Cobussen, M., et al. (2016). **"No increased risk of acute kidney injury after a single dose of gentamicin in patients with sepsis."** *Infectious diseases 48*(4): 274-280. Request article.
Data is lacking on the renal safety of a single dose of aminoglycosides in septic patients visiting the emergency department (ED). This study showed no increased risk of AKI after a single dose of gentamicin to patients with sepsis in the ED, suggesting that a single dose of gentamicin can, with regard to renal function, be safely administered to septic patients.

INTENSIVE CARE UNIT

Pitta, R. D., et al. (2020). **"Antimicrobial therapy with aminoglycoside or meropenem in the intensive care unit for hospital associated infections and risk factors for acute kidney injury."** *European journal of clinical microbiology & infectious diseases 39*(4): 723-728. Full text.

The present study aimed to compare the AKI incidence and mortality rate between critically ill patients treated with aminoglycoside or meropenem in the intensive care unit setting using a propensity score matching approach. Patients on the aminoglycoside regimen neither presented a higher AKI incidence nor mortality rate when compared with those on the meropenem regimen. Aminoglycosides may be a safe option for the treatment of critically ill patients on carbapenem sparing antimicrobial stewardship programs.

Ong, L.-Z., et al. (2016). **"Aminoglycoside-associated acute kidney injury in elderly patients with and without shock."** *The Journal of antimicrobial chemotherapy 71*(11): 3250-3257. Full text.
We aimed to evaluate AG-associated acute kidney injury (AG-AKI) in elderly inpatients, with and without shock. Hospital mortality was 30% versus 7% with AG-AKI versus none (P < 0.001). Twenty-three of 211 (11%) patients with extended analysis had ERD, with 47% experiencing renal recovery following AG-AKI. Mechanical ventilation and contrast administration during index hospitalization predicted ERD (P < 0.05)., CONCLUSIONS: AG-AKI is common in the elderly, with a significant risk of ERD, but the cause and severity are greatly influenced by critical illness and shock, more so than AG therapy alone.

Picard, W., et al. (2014). **"Propensity-based study of aminoglycoside nephrotoxicity in patients with severe sepsis or septic shock."** *Antimicrobial agents and chemotherapy 58*(12): 7468-7474. Full text.

To assess the risk of acute kidney injury (AKI) attributable to aminoglycosides (AGs) in patients with severe sepsis or septic shock, we performed a retrospective cohort study in one medical intensive care unit (ICU) in France. After adjustment to the clinical course and exposure to other nephrotoxic agents between day 1 and day 3, a propensity-adjusted Cox proportional hazards regression analysis showed no increased risk of AKI in patients receiving AGs (adjusted relative risk = 0.75 [0.32 to 1.76]). In conclusion, in critically septic patients presenting without early renal failure, aminoglycoside therapy for less than 3 days was not associated with an increased risk of AKI.

SURGICAL DEPARTMENT

Bankhead-Kendall, B., et al. (2019). **"Antibiotics and open fractures of the lower extremity: less is more."** *European journal of trauma and emergency surgery 45*(1): 125-129. Full text.
Infectious complications in open lower extremity fractures contribute to significant morbidity. Few studies have evaluated the utility of adding an aminoglycoside in this patient population. At our trauma center, we have a unique trauma service where half of our surgeons treat Grade III open fractures with a cephalosporin alone and half use a cephalosporin + aminoglycoside. We hypothesized that our outcomes were the same between the two groups. The addition of an AG to antibiotic prophylaxis in open lower extremity fractures was associated with a significant increase in AKI with no change in the incidence of wound infection or hardware removal. Cephalosporins alone may be sufficient for prophylaxis in Grade III open fractures of the lower extremity. A large-scale prospective randomized trial is needed to confirm these findings and inform clinical practice.

Salim, S. A., et al. (2018). **"Aminoglycoside impregnated cement spacer precipitating acute kidney injury requiring hemodialysis."** *Seminars in dialysis 31*(1): 88-93. Full text.
The current standard of care for prosthetic joint infection includes two-stage arthroplasty, with antibiotic-impregnated cement spacers (ACS) utilized between the stages. This paper reviews the published literature regarding the accumulation, toxicity and removal dynamics of aminoglycoside (AG) antibiotics and vancomycin in renal patients. Obtaining serum AG level should be strongly considered in patients experiencing AKI after ACS. Renal replacement therapy may assist in reducing toxic AG levels.

Giri, V. P., et al. (2016). **"Risk of acute kidney injury with amikacin versus gentamycin both in combination with metronidazole for surgical prophylaxis."** *Journal of Clinical and Diagnostic Research 10*(1): FC09-FC12. Full text.
Aminoglycosides are indicated as surgical prophylaxis for prevention of surgical site infection in patients with B-lactam allergy A total of 16% patients of amikacin group and 24% patients of gentamycin group developed acute kidney injury within one week of drug administration. The rise in serum creatinine was temporary as all patients had normal serum creatinine level at one month follow up. Aminoglycoside intravenous single high dose is not safe as surgical prophylaxis.

Bell, S., et al. (2014). **"Risk of AKI with gentamicin as surgical prophylaxis."** *Journal of the*

American Society of Nephrology 25(11): 2625-2632. Full text.
In 2009, Scottish hospitals changed from cephalosporins to gentamicin for surgical antibiotic prophylaxis. This study examined rates of postoperative AKI before and after this policy change. Most patients who developed AKI after prophylactic gentamicin had stage 1 AKI, but some patients developed persistent stage 2 or stage 3 AKI. The antibiotic policy change was not associated with a significant increase in AKI in the other groups. These results suggest that gentamicin should be avoided in orthopedic patients in the perioperative period. Our findings also raise concerns about the increasing prevalence of postoperative AKI and failures to consistently measure postoperative renal function.

Nielsen, D. V., et al. (2014). **"Is single-dose prophylactic gentamicin associated with acute kidney injury in patients undergoing cardiac surgery? A matched-pair analysis."** *The Journal of thoracic and cardiovascular surgery 148*(4): 1634-1639. Full text.
Although aminoglycoside treatment has been associated with nephrotoxic effects, single-dose gentamicin has been considered safe in surgery. A single-dose prophylactic aminoglycoside in adult cardiac surgery patients was associated with an increased risk of acute kidney injury but not with a greater frequency of postoperative dialysis or mortality. No differences in the incidence of sternal infections between groups were observed.

APPENDIX

SEARCH METHODOLOGY

A systematic search was conducted for literature. The results were screened by librarians using Covidence.

SEARCH LIMITS

- English-language
- Published within the last 10 years

DATABASES SEARCHED

- Medline – index of peer reviewed articles across health sciences and medicine.
- Embase – index of biomed and pharmacological peer reviewed journal articles.
- Emcare – index of nursing, allied health, critical-care medicine and more.
- Cochrane Library – collection of databases containing high-quality independent evidence.
- UpToDate – synthesised evidence for patient care.
- Grey literature – Google, Google Scholar, Trip database, Biomed Central Proceedings.

SEARCH TERMS

Concept	MeSH headings	Keywords
Aminoglycosides	Aminoglycosides	Aminoglycoside, aminoglycosides, gentamicin, tobramycin, amikacin, plazomicin, streptomycin, neomycin, paromomycin
Acute Kidney Injury	Acute Kidney Injury	Acute kidney injury, acute renal failure
Geriatric Patients	Aged, 80 and over, Aged, Geriatrics	Old age, geriatric, geriatrics, elder, elderly, older adult, older adults

MEDLINE SEARCH STRATEGY

Ovid MEDLINE(R) ALL <1946 to April 12, 2024>

1 *Aminoglycosides/ 5038
2 ((single? dose or single-dose) and (amino?glycoside* or Gentamicin or Tobramycin or Amikacin or Plazomicin or Streptomycin or Neomycin or paromomycin)).tw,kw. 617
3 1 or 2 5644
4 Acute Kidney Injury/ 56531
5 (acute kidney injur* or acute renal failure*).tw,kw. 65435
6 4 or 5 84929
7 "Aged, 80 and over"/ or Aged/ 3490685
8 Geriatrics/ 31616
9 (old age or geriatric* or elder* or older adult).tw,kw. 413623
10 7 or 8 or 9 3624640
11 3 and 6 and 10 37
12 limit 11 to last 10 years 18

PRISMA CHART