

SBAR on Aminoglycoside use in Empirical Prescribing Guidelines

Situation

Recent recommendations from EUCAST (European Committee on Antimicrobial Susceptibility Testing) on aminoglycoside susceptibility reporting differ from current practice in NHS Scotland.

The Scottish Antimicrobial Prescribing Group (SAPG) and the Scottish Microbiology and Virology Network (SMVN) have discussed and agreed a position regarding these recommendations.

Background

EUCAST, as part of a review of antibiotic susceptibility reporting, now recommend that aminoglycoside breakpoints should only be reported with a Sensitive or Resistant interpretation where the patient's infection originates in the urinary tract.

In patients with systemic infection, it recommends that aminoglycosides must be used in combination with other active therapy and that the ECOFF (epidemiological cut off) can be used to distinguish between bacteria with and without a resistance mechanism. For bacteria where a resistance mechanism to aminoglycosides is not detected, EUCAST suggest adding the following comment to reports:

*"Aminoglycosides are often given in combination with other agents, either to support the activity of the aminoglycoside or to broaden the spectrum of therapy. In systemic infections, the aminoglycoside must be supported by other active therapy."*¹

EUCAST advise that breakpoints are set based on a gentamicin dose of 6-7mg/kg once per day and an amikacin dose of 25-30mg/kg once per day.

EUCAST aminoglycoside advice is based on limited trials data with little information on patient outcome or use in patients with sepsis not associated with urinary tract infection.²

Assessment

Clinical use

- In Scotland, there is a wealth of clinical experience in using short term (maximum 4 days) gentamicin as empirical therapy in patients with sepsis and no concerns have been reported regarding clinical efficacy or significant changes in resistance identified in surveillance reports.
- Gentamicin has been an integral component of the national antimicrobial stewardship programme to limit use of broader spectrum WHO Watch and Reserve agents in empirical therapy in hospital patients with more severe infection.
- National SAPG guidance, used by all NHS boards, recommends that gentamicin be used in combination with piperacillin/tazobactam in patients with neutropenic sepsis or in the immunocompromised host.
- Currently Gentamicin is used in many health boards in combination with amoxicillin and metronidazole for empirical treatment intra-abdominal sepsis. It is used either as monotherapy or in combination with amoxicillin for treatment of febrile urinary infections and gentamicin is also used in combination with amoxicillin with or without flucloxacillin for sepsis of unknown source.
- As amoxicillin resistance is high amongst Gram negative bacteria and this combination could be considered aminoglycoside monotherapy. However, EUCAST does suggest 'it is possible that the combination of an aminoglycoside with an agent to which the pathogen is resistant may still have useful clinical activity, although this has never been studied formally.'³

Dosage regimens

SAPG supports the use of two gentamicin dosing regimens (based on 5 or 7mg/kg)⁴ and boards use amikacin dosing aligned with that in the BNF, not exceeding 15mg/kg once per day.⁵ Therefore, in Scotland dosing is not fully compliant with EUCAST aminoglycoside dosing recommendations, particularly for amikacin, where a lower dose is recommended and where the safety of higher doses, above the UK licensed dose, is unclear.

Microbiology reporting

Continued reporting from laboratories of aminoglycoside susceptibility with Sensitive or Resistant interpretation regardless of infection source is important for antimicrobial resistance surveillance. At national level, ECOSS (Electronic Communication of Surveillance in Scotland) currently only receives susceptibility interpretation data from several boards and not MIC (Minimum Inhibitory Concentration) data. It has been agreed in Scotland that a comment should accompany Gram negative bacteraemia reports advising that gentamicin should not be used for definitive monotherapy.

SAPG/SMVN recommendations have been agreed supported by the following information:

- gentamicin prescribing practice is well established and monitored through the national antimicrobial stewardship programme
- empirical gentamicin is the backbone of sepsis management in NHS Scotland and significantly contributes to stewardship measures to limit use of WHO Watch and Reserve antibiotics
- there has been no observed loss of efficacy in gentamicin-based regimens in the management of patients with sepsis
- there has been no significant change observed in gentamicin susceptibility in patients with infections due to Gram negative organisms
- change of gentamicin dosing recommendations would be a resource intensive, high risk task for SAPG and NHS boards due to the complex development and governance processes and the education and training requirements.

Recommendations

SAPG and SMVN agree that:

1. **NHS boards can continue with gentamicin-based empirical therapy where Gram negative infection may be suspected e.g. intra-abdominal sepsis, urinary infection, infection unknown source, without additional Gram negative cover except in specific high-risk situations e.g. neutropenic sepsis and fever in immunocompromised host.**
2. **Gentamicin monotherapy should only be used for targeted therapy for confirmed Gram negative infection of urinary source or on infection specialist advice, but its duration should continue to be limited and IV to oral switch optimised to reduce risk of toxicity.**
3. **Within NHS Scotland the existing national gentamicin dosing guidance should remain, acknowledging that there are two agreed dosing regimens.**⁴

References

1. European Committee on Antimicrobial Susceptibility Testing https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_11.0_Breakpoint_Tables.pdf
2. Vidal L, Gafter-Gvili A, Borok S, Fraser A, Leibovici L, Paul M. Efficacy and safety of aminoglycoside monotherapy: systematic review and meta-analysis of randomized controlled trials. J Antimicrob Chemother. 2007;60(2):247-57.
3. European Committee on Antimicrobial Susceptibility Testing https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Rationale_documents/Gentamicin_rationale_1.2_0906.pdf
4. Scottish Antimicrobial Prescribing Group <https://www.sapg.scot/guidance-qi-tools/antimicrobial-specific-guidance/>
5. British National Formulary, National Institute for Health and Care Excellence <https://bnf.nice.org.uk/drug/amikacin.html#indicationsAndDoses>