LOTHIAN PRESCRIBING BULLETIN

Supporting prescribing excellence - informing colleagues in primary and secondary care

NHS Lothian

In this issue …

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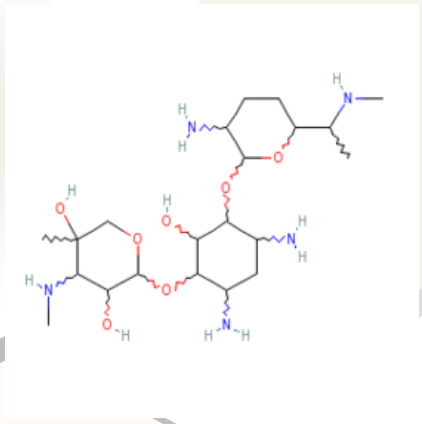
Improving the quality and safety of gentamicin prescribing

In NHS Lothian gentamicin is recommended for treatment of infection associated with pyelonephritis and sepsis (intra-abdominal, biliary, severe sepsis of unknown origin and neutropenic). It is less likely to cause *Clostridium difficile* infection and the development of antibiotic resistance due to its narrow spectrum. Side-effects can be serious and include renal failure, deafness and loss of balance. The gentamicin dosage regimen for every patient is determined by a treatment dose calculator. Gentamicin is noted on the prescription chart and the dose calculator worksheet is printed out. Gentamicin is then prescribed, doses and times administered are recorded and monitoring parameters such as daily creatinine and gentamicin level are documented.



A quality improvement project recently carried out by trainee pharmacists tested interventions by medical and nursing staff. The aim was to improve prescribing and monitoring of gentamicin in three wards across Lothian hospitals (admissions unit, medicine and surgery). Initial interviews with the multidisciplinary team identified lack of knowledge of the process, issues with communication and lack of defined roles and responsibilities for monitoring and follow up. The Antimicrobial Management Team, senior medical/nursing staff, and pharmacists participated in discussions and agreed a range of interventions.

Thanks to Laura Colman, Amy Comyns and Lucie Robb, Pre-registration Trainee Pharmacists, Alison Mackie, Lead Pharmacist for Medical Education and Caroline Souter, Principal Pharmacist, Education, Research and Development, for contributing this article.

Baseline data were collected for four to eight weeks (total 98 doses) and then data collected for patients prescribed gentamicin from November 2016 to February 2017 (total 121 doses). Run charts were generated for the following process measures: sample taken at correct time (12 hours post dose rather than 6 to 14 hours); daily creatinine documented; next dose prescribed at correct interval; gentamicin prescribed correctly.

Ward	Results (comparison to median at baseline)
Admissions Unit	sample taken at correct time improved from 38% to 67% daily creatinine documented improved from 17% to 40%
Medicine	daily creatinine documented improved from 0% to 33%
Surgery	sample taken at correct time improved from 63% to 95% daily creatinine documented improved from 33% to 50%

The project demonstrated an improvement in gentamicin levels being sampled at the correct time. However, there was no improvement in the writing of gentamicin prescriptions on the administration charts or the prescribing of the next dose at the correct interval. Prescribing and monitoring of gentamicin is complex and processes vary across wards and these factors were considered to have contributed to non-adherence. A foundation year doctor was involved in the latter stages of the project but input would be valuable from the start in future work. Further work is required to improve prescribing and monitoring of gentamicin and to reduce variation in processes across wards.

Key messages:

- **Monitoring of gentamicin levels requires a team based approach.**
- **A range of interventions led to improvement in correct sampling time of gentamicin and documentation of creatinine.**

Clinical pharmacologists add value to the NHS

Clinical pharmacologists represent a diverse clinical specialty focused on the safe and effective use of drugs. All prescribers use the discipline of clinical pharmacology to inform their decisions in rational prescribing. A few of its guiding principles are discussed below.

Pharmacokinetics *'what the body does to the drug'*

Pharmacokinetics has direct relevance to clinical practice, determining the recommended dose, route and frequency of administration in a variety of clinical scenarios. This principle allows a prescriber to adjust their prescribing accordingly.

Pharmacodynamics *'what the drug does to the body'*

Pharmacodynamics is relevant to prescribers because it explains the relationship between drug concentration and its effect; ultimately balancing clinical benefit and poisoning.

Clinical toxicology

Poisoning is one of the most common causes of admission to hospital. Clinical pharmacologists, with specialty training in toxicology, oversee acute admissions and provide advice on acute poisoning cases. They are also responsible for managing Toxbase®, an evidence-based toxicology database, and drive forward research in this field.

Drug regulation

Clinical pharmacologists play a vital role in the Medicines and Healthcare Regulatory Agency (MHRA), which is responsible for assuring that medicines licensed in the UK are acceptably safe and operates post-licensing surveillance for adverse events. The Yellow Card Scheme, the MHRA subsidiary responsible for collecting information on adverse events, is also led by clinical pharmacologists.

Pharmacogenomics

Pharmacogenomics refers to how the genome may affect drug metabolism, a significant contributor to drug response variation between patients. Studying this effect can help target drugs towards those most likely to benefit (and away from those that may suffer harm). For example, restricting the use of abacavir based on a patient's HLA subtype reduces the risk of severe allergic reactions.

Adverse drug reactions

It is estimated that adverse drug reactions account for 6.5% of hospital admissions in adults and affect around 15% of adult inpatients. Clinical pharmacologists lead research into the causes and prevention of adverse drug reactions (and interactions). They also contribute to pharmacovigilance activities, encouraging use of adverse reaction reports to inform future prescribing advice and regulatory action.

Research Ethics Committees

Clinical pharmacologists play an integral role in these committees by ensuring that research proposals pass muster in terms of scientific plausibility and design. Trial design and interpretation is critical to minimising risk to participants in clinical research and ensuring clinical trial results accurately reflect if a treatment is effective for patients.

Pharmacoeconomics / Health technology assessment

The UK's health technology appraisal organisations, SMC (Scotland), NICE (England) and AWMSG (Wales) were established to ensure the best use of NHS resources. All three were established by clinical pharmacologists who have expertise in assessing the cost-effectiveness of new medicines alongside the medical knowledge to make complex clinical judgements. Clinical pharmacologists are also key members of guideline and formulary committees both nationally and locally.

Key messages:

- **Clinical pharmacologists add value to the NHS.**
- **The principles of clinical pharmacology underpin rational prescribing.**
- **Clinical pharmacologists play a key role in prevention of adverse drug reactions, good clinical practice in drug trials and play a central role in medicines policy and management.**
- **We will celebrate the contributions that clinical pharmacologists have made (past, present and future) in October during Clinical Pharmacology Month. For further information, visit www.bps.ac.uk/october**

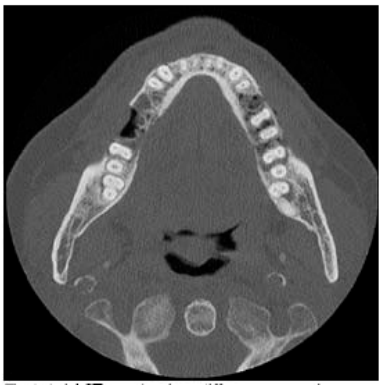
Clinical research/clinical trials

Clinical pharmacologists provide expertise in conducting early phase clinical trials interrogating the safety of novel compounds. They carry these skills through the drug development process to later phase trials, demonstrating the efficacy and safety of new medicines in the population. Clinical pharmacologists work alongside other healthcare professionals, notably pharmacists, while caring for all patients. Clinical pharmacology is a small specialty but makes a disproportionately strong contribution to quality use of medicines. Over recent years, healthcare interventions have become more complex and consequently, the balance of benefit, risk and uncertainty for an individual has become more nuanced. During this dawn of personalised medicines, clinical pharmacologists are vital to ensure effective prescribing for an individual, while maintaining equitable use of our finite resources at a societal level.

Useful links:
A prescription for the NHS: www.bps.ac.uk/about/our-campaigns/clinical-pharmacology-in-the-nhs

Thanks to Professor Simon Maxwell, Senior Lecturer in Clinical Pharmacology, Dr Thomas Caparrotta, ST3 Clinical Pharmacology and General Medicine and Dr Emma Morrison, Clinical Pharmacology Trainee for contributing this article.

Guidance for medication-related osteonecrosis of the jaw



The Scottish Dental Clinical Effectiveness Programme (SDCEP) updated their guidance on Oral Health Management of Patients at Risk of Medication-related Osteonecrosis of the Jaw (MRONJ) in March 2017. Patients taking bisphosphonates, denosumab or some antiangiogenic drugs (bevacizumab, sunitinib, aflibercept) have a small risk of developing this condition.

Recommendations:

- Dental practitioners should assess a patient's risk of MRONJ; this requires the dental practitioner to be aware that the patient is taking one or more of the implicated medicines and to have up-to-date details of the patient's medical condition, medication history and duration of treatment.
- Before commencement of treatment with these medicines, or as soon as possible thereafter, the patient should undergo a thorough dental assessment.

Prescribers and dispensers of antiresorptive or antiangiogenic drugs can play a key role by:

- Ensuring patients are aware of the type of medication they are taking and the need to inform their dentist about their medical condition and their medicines.
- Advising patients at the start of treatment that there is a small risk of MRONJ and that they should make an appointment for a dental examination as soon as possible.
- Cancer patients should preferably undergo a thorough dental assessment, with dental treatment where required, prior to commencement of the drug therapy.

Full guidance, patient information leaflets and an information sheet detailing the recommendations are available from the SDCEP website www.sdcep.org.uk

Thanks to Dr Samantha Rutherford, Research and Development Manager, SDCEP, for contributing this article.

Drug interaction website for HIV medicines

Systemic corticosteroid effects have been reported in patients receiving the antiretroviral ritonavir and inhaled or intranasally administered fluticasone; this could also occur with other corticosteroids metabolised via the P450 3A pathway, e.g. budesonide.

The University of Liverpool has developed a website www.hiv-druginteractions.org for checking interactions with medicines used in the management of HIV. It is a comprehensive, up-to-date, evidence-based drug-drug interaction resource, freely available to healthcare workers, patients and researchers.

The website includes

- An 'interaction checker'.
- 'Treatment selectors' that identify interactions between key antiretrovirals (ARVs) and medicines used to treat a range of common co-morbidities. They are designed to show which ARVs and co-medications are 'more risky'.
- A range of charts, including for recreational drugs, food requirements for ARVs, ARV-dosing modifications in renal impairment, and ARV formulations that can be used for patients with swallowing difficulties.
- Fact sheets with information on the pharmacokinetics, metabolism and disposition of each drug.

LJF update

Smoking cessation

The LJF section on cigarette smoking has been updated. Varenicline is now joint first choice with nicotine replacement therapy (long- and short-acting). These should be prescribed with cessation support by specialist stop-smoking services and community pharmacies. The decision to add varenicline as joint first choice was made after extensive discussion and research into the evidence of benefit and risk of side effects. A study published in the Lancet in 2016 (EAGLES) did not show a significant increase in neuropsychiatric adverse events attributable to varenicline relative to nicotine patch or placebo.

The prescribing notes highlight the potential for suicidal thoughts and behaviour associated with varenicline. Prescribers must be aware of the cautions and side-effect profile of varenicline both during treatment and on treatment cessation. Care should be taken with patients with a history of psychiatric illness and patients advised accordingly.

H. pylori-associated dyspepsia

The LJF recommendations for the treatment of H. pylori-associated dyspepsia have been updated. First choice eradication and second choice (for eradication failure) both include a proton pump inhibitor and amoxicillin and are for seven days treatment only. Metronidazole is part of the first choice regimen and clarithromycin is part of the second choice regimen. Levofloxacin has been removed from the formulary choices and may only be prescribed under the recommendation of a specialist.

Patients with penicillin sensitivity being treated with the first line regimen may receive tetracycline 500mg twice daily instead of amoxicillin 1g twice daily. Patients with penicillin sensitivity being treated with the second line regimen may receive metronidazole 400mg three times daily instead of amoxicillin 1g twice daily. Please refer to the prescribing notes in the LJF and eLJF-CLINICAL for further information.

A sweet solution to hypoglycaemia

Key messages:

- **Consider an alternative carbohydrate source, for example: glucose tablets, glucose oral gel, pure fruit juice, granulated sugar, sugar lumps or sweets such as jelly babies.**
- **If using a soft drink check the product label for the glucose content and adjust the volume accordingly.**

Several soft drinks manufacturers are reducing the sugar content in their products in response to the Sugary Drinks Industry Levy. Patients who use soft drinks to treat hypoglycaemia should be advised that old and new recipe non-diet soft drinks may be available. The recipe of soft drinks may change without publicity, therefore to avoid confusion patients are advised to consider alternative carbohydrate sources. Patients who wish to use soft drinks should check the product label and adjust the volume accordingly to provide the correct amount of glucose.

Seek advice from the diabetes team if required. Further information can be found on the Diabetes UK website.

See also LJF recommendations for hypoglycaemia in adults and in known diabetes in children.

Supplements:

Recent SMC and Lothian Formulary Committee Recommendations

The supplements can be accessed via the LJF website www.ljf.scot.nhs.uk in 'Prescribing Bulletins'.

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View the Lothian Joint Formulary at www.ljf.scot.nhs.uk