An update on the use of **nitrofurantoin** in patients with **renal impairment**

The Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom (UK) have updated their guidance to allow nitrofurantoin to be prescribed to patients with reduced renal function. This change was influenced by increasing resistance to trimethoprim and amoxicillin in the UK; meaning that there is an increased need to prescribe nitrofurantoin to patients with acute cystitis.[1] The Medicines Adverse Reactions Committee (MARC) recently discussed whether a similar change in guidance was appropriate for New Zealand.

It was concluded by MARC that **the contraindication of creatinine clearance of < 60 mL/min for the use of nitrofurantoin**, as listed on the New Zealand medicine datasheet, **should remain**.[2, 3] The recent Best Tests article on treating urinary tract infections (UTIs) in older people (July, 2015) reported guidance on the use of nitrofurantoin in patients with reduced renal function consistent with the UK position, i.e. avoid in patients with estimated glomerular filtration rate [eGFR] < 45 mL/min/1.73m^2; this advice has now been updated in the online version of this article to account for the recent decision by MARC.

For further information, see: "A pragmatic guide to asymptomatic bacteriuria and testing for urinary tract infections (UTIs) in people aged over 65 years", Best Tests (Jul, 2015).

The role of nitrofurantoin in the treatment of acute cystitis

Nitrofurantoin or trimethoprim are suitable first-line treatment options for non-pregnant females and males with acute cystitis.[4–7]

Use of nitrofurantoin can be problematic for patients with renal dysfunction. Reduced renal function may lead to toxicity due to an increase in nitrofurantoin serum levels.[1] Impaired renal function also decreases the efficacy of nitrofurantoin as an antibacterial medicine in the urinary tract.[1]

Serious pulmonary reactions, both acute and chronic, and which can be fatal, have been reported secondary to treatment with nitrofurantoin.[8] The incidence of acute pulmonary reactions in patients taking nitrofurantoin is estimated to be less than 1% and it most often affects females aged 40 – 50 years.[8] Acute pulmonary reactions are reported to occur more frequently after repeated courses of nitrofurantoin treatment.[8]

Trimethoprim is generally considered to be better tolerated than nitrofurantoin and the dosing regimen is simpler as it is taken once daily, at night. However, antibiotic resistance levels for *Escherichia coli*, the most frequent cause of cystitis, are reported to be higher for trimethoprim compared with nitrofurantoin. In 2013, the percentage of urinary *E. coli* reported as resistant to nitrofurantoin from hospital and community laboratories was 1.3% (from almost 100 000 isolates tested).[9] During the same period the percentage of urinary *E. coli* reported as resistant to trimethoprim was 26.2% (from approximately 98 000 isolates tested).[9]

Deciding whether to prescribe trimethoprim or nitrofurantoin

The patient's renal function, tolerance, the complexity of the dosing regimens and local bacterial susceptibility are relevant considerations when prescribing antibiotics for acute cystitis.

Comment from Associate Professor Mark Thomas, Infectious Diseases Specialist, University of Auckland:

> *I would recommend nitrofurantoin, 50 mg, four times daily, for five days in females and seven days in males, as the first-line treatment for uncomplicated acute cystitis in patients with creatinine clearance > 60 mL/min (avoid*

in women who are 36+ weeks pregnant). In patients with renal impairment or known intolerance or allergy to nitrofurantoin, use trimethoprim 300 mg, once daily for three days in females (avoid during the first trimester of pregnancy) and seven days in males. If there is a known high rate of resistance (> 15%) to trimethoprim in E. coli *in the local area, consider taking a urine sample and adjust treatment based on the susceptibility results of the organism isolated.*

While norfloxacin is an alternative antibiotic for the treatment of cystitis, it should be strictly reserved for isolates resistant to trimethoprim or nitrofurantoin.[7] Norfloxacin should be avoided in pregnant women or in patients who have severe renal impairment (refer to the New Zealand Formulary for details).[6]

For further information about the use of norfloxacin see: "Quinolone antibiotics – limit use", BPJ 35 (Apr, 2011).

References

1. Medicines and Healthcare product Regulatory Agency (MHRA). Nitrofurantoin now contraindicated in most patients with an estimated glomerular filtration rate (eGFR) of less than 45 ml/min/1.73m^2. MHRA, 2014. Available from: www.gov.uk/drug-safety-update (Accessed Oct, 2015).
2. New Zealand Medicines and Medical Devices Safety Authority (Medsafe). Minutes of the 163rd medicines adverse reactions committee meeting – 10 September 2015. Medsafe, 2015. Available from: www.medsafe.govt.nz (Accessed Oct, 2015).
3. W. M. Bamford & Company Limited. Nifuran. Medicine Datasheet, 2004. Available from: www.medsafe.govt.nz (Accessed Oct, 2015).
4. Scottish Intercollegiate Guidelines Network (SIGN). Management of suspected bacterial urinary infection in adults. Edinburgh: SIGN, 2012. Available from: www.sign.ac.uk (Accessed Oct, 2015).
5. Auckland District Health Board (ADHB). Adult empirical antimicrobial treatment guidelines. ADHB, 2014. Available from: www.adhb.govt.nz (Accessed Oct, 2015).
6. New Zealand Formulary (NZF). NZF v40. 2015. Available from: www.nzf.org.nz (Accessed Oct, 2015).
7. bpacnz. Antibiotics: choices for common infections. Available from: www.bpac.org.nz (Accessed Oct, 2015).
8. Kanji Z, Su VCH, Mainra R. Nitrofurantoin-induced pulmonary reaction involving respiratory symptoms: case report. Can J Hosp Pharm 2011;64:362–5.
9. The Institute of Environemental Science and Research Ltd (ESR). Antimicrobial resistance data from hospital and community laboratories. ESR, 2013. Available from: https://surv.esr.cri.nz/PDF_surveillance/Antimicrobial/AR/National_AR_2013.pdf (Accessed Oct, 2015).

CORRESPONDENCE

Should antibiotics be continued for a sore throat if GAS negative?

Dear Editor,
There are occasional exceptions to every rule, including Mark Thomas' generally good advice to stop antibiotics if a throat culture fails to confirm GAS. Throat cultures, if properly taken, are 90-95% sensitive for GAS, not 100%, and that is only if they are properly taken from the tonsils and the posterior pharynx. If a child has a classic appearance with fever, tachycardia, dusky red moist tonsils, tonsillar pillars and pharynx, quite large neck nodes, a bit of a scarlatiniform rash, and the complete absence of nasal or chest symptoms, I would want that child to complete ten days of antibiotics regardless of the swab result.

Dr Ronald Baker [Online comment]

Dear Editor,
Mark Thomas might spare a thought for the mountains of unused antibiotics that might appear in vulnerable households from those who stop a ten day course early. Surely this is a greater risk than one unnecessary but properly completed course. While awaiting swab results a more practical option might be to prescribe a five day course with one repeat available at no extra charge if the swab returns positive.

Is near-patient testing for GAS likely to become a practical option in New Zealand? And how did the UK manage to eliminate rheumatic fever from its morbidity profile?

Dr David Smith, *General Practitioner*
Pahiatua
(Personal view only)