

North West Surrey Clinical Commissioning Group

Monitoring Drug Therapy

Introduction

It is estimated that 6-7% of hospital admissions are due to adverse drug reactions (ADRs) with about half of these being thought to be preventable. The risk of adverse drug reactions increases with age and with the number of drugs a patient is taking.

ADRs leading to hospital admissions audit

An audit was conducted by ASPH NHS Foundation Trust to attempt to identify the magnitude of the problem and to try and identify the common medications that lead to hospitalisation. The audit was conducted looking at patients who had been admitted to MAU. 272 notes were reviewed over the defined data collection period of 23 days. 22 of these admissions (8%) were linked to potential adverse drug reactions, which is roughly in line with the anticipated national figures. The majority of the ADR cases identified were linked to a small number of drugs with polypharmacy being repeatedly highlighted as an issue.

Monitoring Requirements for drugs that commonly cause ADRs leading to hospital admissions

The aim of this document is to provide information on the monitoring requirements for the drugs that have been identified as having common adverse drug reactions leading to hospitalisation. The following drugs are covered:

- o ACE inhibitors and angiotensin II receptor antagonists
- o Digoxin
- NSAIDs (including COX IIs)
- o Diuretics

ACE inhibitors and angiotensin II receptor antagonists

Tests prior to starting treatment

- U&Es (incl urea and creatinine)^{1,3} and eGFR¹
- BP ^{1,3,6}

See BNF for more detail regarding initiation in patients with hyponatraemia, hypovolaemia, severe or unstable heart failure, known renovascular disease, hypotensive or taking multiple or high-dose diuretics or high-dose vasodilators.⁴

Seek further advice if patient with hypertension eGFR < 30ml/min, or confirmed renovascular disease before initiating treatment.⁵

In patients with CKD, ACEI / ARB therapy should not normally be started if the pre-treatment serum potassium is significantly above normal reference range (typically >5.0mmol/L)^{1,2}

Monitoring until patient is stabilised

Heart Failure:

- Measure serum urea, creatinine and electrolytes 1-2 weeks after initiation and after each dose increment.¹ In Best Practice series it is advised that these tests are conducted after 5-7 days in higher-risk patients (e.g. those receiving spironolactone, those with existing renal dysfunction, and those receiving combination therapy)⁵
- Monitor BP.¹

Hypertension:

NICE do not provide specific advice on monitoring ACEI / ARB therapy in hypertension except when using further diuretic therapy for resistant hypertension at step 4, where they suggest monitor blood sodium and potassium and renal function within 1 month.³

In Best Practice series it is advised that renal function should be checked one week after starting treatment or changing dose in patients with hypertension. If patient is judged to be at higher risk of developing hyperkalaemia or deteriorating renal function (e.g. peripheral vascular disease, diabetes, pre-existing renal impairment or an older patient) renal function should be checked within 4-10 days.⁵

CKD

Measure serum urea, creatinine and electrolytes 1-2 weeks after initiation and after each dose increment. $^{\rm 2}$

Post-MI

Measure renal function (serum creatinine), electrolytes and BP 1-2 weeks after initiation and after each dose increment.³

Ongoing Monitoring

Heart Failure:

- Measure serum urea, creatinine and electrolytes every 3 months and more frequently in patients taking combined loop and thiazide diuretic therapy and in those taking aldosterone antagonists.¹
- Monitor BP routinely¹

Hypertension:

NICE do not provide advice on monitoring ACEI / ARB therapy in hypertension except in when using further diuretic therapy for resistant hypertension at step 4, where they suggest monitor blood sodium and potassium and renal function within 1 month and repeat as required thereafter.³

CKS advise checking electrolytes and renal function at least annually in stable hypertensive patients that do not have diabetes.⁶

Produced by Linda Honey, Chief Pharmacist NW Surrey CCG in conjunction with Dr Richard Barnett, Clinical Lead for MM NW Surrey CCG, Dr Keefai Yeong, Consultant Orthogeriatrician Ashford & St Peter's NHS Foundation Trust and Holly Mitchell OPAL Pharmacist Ashford & St Peter's NHS Foundation Trust and Holly Mitchell OPAL Pharmacist Ashford & St Peter's NHS Foundation Trust

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CKD:

NICE do not provide specific advice on monitoring ACEI / ARB therapy in stable patients. CKS advise that in patients with CKD that is not due to diabetes BP should be measured every 3–6 months, and urea and electrolytes, and eGFR, every 12 months (unless required more frequently because of impaired renal function).⁷

Post-MI:

Measure renal function (serum creatinine), electrolytes and BP at least annually. More frequent monitoring may be needed in patients who are at increased risk of deterioration in renal function. Patients with chronic heart failure should be monitored in line with 'Chronic heart failure' described above.³

Dual blockade of the renin-angiotensin-aldosterone system (RAAS)

There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren increases the risk of hypotension, hyperkalaemia and decreased renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is therefore not routinely recommended.

If dual blockade therapy is considered necessary, this should only occur under specialist supervision and subject to frequent close monitoring of renal function, electrolytes and blood pressure.⁸

Action required if abnormal results

If serum potassium rises above 5.5mmol/L re-test and at levels of >6.0mmol/L stop ACEI/ARB therapy if other drugs known to promote hyperkalaemia have been modified or discontinued.^{1,2}

If eGFR falls by 25% or more or plasma creatinine increases by 30% or more from baseline, stop the ACEI/ARB or reduce to a previously tolerated dose once potential alternative causes of renal impairment have been ruled out. If the changes indicating a decrease in renal function are less than described do not modify the dose but repeat the test in 1-2 weeks. ^{1,2}

If Na <132mmol/L specialist advice should be obtained.⁵

Significant drug interactions

- Ciclosporin
- Potassium-sparing diuretics and aldosterone antagonists
- Gold (sodium aurothiomalate) (applies to ACEIs only)
- Lithium
- Potassium salts

References

- 1. NICE Clinical Guideline 108 Chronic heart failure Appendix D (2010)
- 2. Chronic Kidney Disease: early identification and management of chronic kidney disease in adults in primary and secondary care. NICE Clinical Guideline 73 (2008)
- 3. NICE Clinical Guideline 172 Secondary prevention for patients in primary and secondary care following a myocardial infarction (2014)
- 4. BNF Issue 66
- 5. Best Practice in primary care pathology: review J Clin Pathol 2007;60:225-234
- 6. CKS Guideline on hypertension (not diabetic) (2012)
- 7. CKS Guideline on chronic kidney disease (not diabetic) (2009)
- 8. Lisinopril SPC: available on line at <u>http://www.medicines.org.uk/emc/medicine/23998</u> (last accessed 31st December 2014)

With thanks to UKMI: Suggestions for drug monitoring in adults in primary care Feb 2014

 $\underline{http://www.medicinesresources.nhs.uk/upload/documents/Evidence/Drug\%20monitoring\%20document\%20Feb\%202014.pdf$

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Digoxin

Tests prior to starting treatment

- Renal function¹
- U&Es² (paying particular attention to potassium level)^{1,3}

Monitoring until patient is stabilised

Routine digoxin measurement is not recommended in clinically and biochemically stable patients, but may be warranted if there are changes in clinical state, concomitant use of drugs that may impact on toxicity, recognition of situations predisposing to toxicity, notably renal insufficiency.¹

Samples for digoxin measurement should be taken at least 8-12 hours after the last dose.¹

Ongoing monitoring

Routine monitoring of serum digoxin concentrations is not recommended.^{1,4}

The presence of toxic symptoms such as nausea, vomiting, visual disturbance (yellow-green discoloration), or severe dysrhythmias may prompt an urgent measurement.¹

A digoxin level may be useful to confirm a clinical impression of toxicity or nonadherence.⁴

Appropriate electrolyte monitoring should be carried out in patients predisposed to hypokalaemia (e.g. on loop diuretics), and in patients with renal dysfunction.³

Action required if abnormal results

If toxicity occurs, digoxin should be withdrawn; serious manifestations require urgent specialist management. Digoxin-specific antibody fragments are available for reversal of life-threatening overdosage.⁵

Hypokalaemia predisposes the patient to digoxin toxicity.⁵

If toxicity is suspected potassium level should also always be measured – if it is low, digoxin toxicity should be assumed without waiting for digoxin level.⁶

Low potassium levels require correction.⁵

Significant drug interactions

- Acetazolamide
- Amiodarone
- Amphotericin
- Chloroquine
- Ciclosporin
- Colchicine
- Diltiazem
- Dronedarone
- Hydroxychloroquine
- Itraconazole
- Lercanidipine

- Loop diuretics
- Nicardipine
- Nifedipine
- Propafenone
- Quinine
- Spironolactone
- St John's Wort
- Thiazides and related diuretics,
- Ticagrelor
- Verapamil

References

- 1. Smellie,WSA, Coleman JJ. Pitfalls of testing and summary of guidance on safety monitoring with amiodarone and digoxin. BMJ 2007;334:312-5
- 2. Aspen. Lanoxin 125 Tablets. SPC (date of revision 10 March 2012)
- 3. Smellie WSA, Forth J, Sundar S. Best practice in primary care pathology: review 4. J Clin Pathol. 2006 September; 59 (9): 893–902
- 4. NICE. Chronic heart failure: Clinical guideline 108 (25 August 2010)
- 5. BNF 66 (September 2013)
- 6. Aronson JK, Hardman M. ABC of monitoring drug therapy. Digoxin. BMJ 1992, 305: 1149-52

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With thanks to UKMI: Suggestions for drug monitoring in adults in primary care Feb 2014 <u>http://www.medicinesresources.nhs.uk/upload/documents/Evidence/Drug%20monitoring%20document%20Feb%202014.pdf</u>

NSAIDs (including COX IIs)

Tests prior to starting treatment

For daily NSAID use in patients with risk factors for **GI bleeding:** baseline haemoglobin or haematocrit ³ (factors that increase risk of gastrointestinal bleeding are defined as any of the following: age \geq 75, peptic ulcer disease, history of gastrointestinal bleeding, or glucocorticoid use).³

For daily NSAID use in patients with risk factors for developing **renal insufficiency**: baseline creatinine ³ (risk factors for renal insufficiency are defined as any of the following: age \geq 75, diabetes mellitus, hypertension, angiotensin converting enzyme (ACE) inhibitor use or diuretic use). ³

Monitoring until patient is stabilised

For patients with severe heart failure:

All NSAIDs are contra-indicated in patients with severe heart failure and diclofenac, celecoxib and etoricoxib are contraindicated in patients with any degree of heart failure.⁴

For patients with mild-to-moderate heart failure:

Monitor weight, jugular venous distension, crepitations, hepatomegaly, ascites, and peripheral oedema 1–2 weeks after starting or increasing NSAID dose. Consider monitoring U&Es 1–2 weeks after starting or increasing NSAID dose, particularly in people taking an ACE inhibitor, an angiotensin-II receptor antagonist, a diuretic, or in those with impaired renal function.²

For patients with hypertension:

Monitor BP 2–4 weeks after starting or increasing dose. Etoricoxib — check BP within 2 weeks of starting and periodically thereafter.²

For patients with renal impairment:

Monitor U&Es 1–2 weeks after starting or increasing NSAID dose then regularly thereafter.²

For patients with risk factors for developing renal insufficiency (see above): Monitor creatinine within the first 3 months. ³

For hepatic impairment:

Enquire about adverse effects.²

Ongoing monitoring

For daily NSAID use with risk factors for **GI bleeding** (see above): haemoglobin or haematocrit after one year of treatment.³

For daily NSAIDs and risk factors for developing **renal insufficiency** (see above): creatinine should be assessed at least annually.³

Action required if abnormal results

Review risks vs benefits in light of any changes in patient's baseline parameters.

Additional notes

NSAIDs should always be used at the lowest effective dose and for the shortest period of time to control symptoms and the need for long-term treatment should be reviewed periodically.¹

Asthma: any degree of worsening of asthma may be related to the ingestion of NSAIDs, either prescribed or purchased over the counter.¹

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Significant drug interactions

(Interactions generally do not apply to topical NSAIDs, see BNF appendix 1 for more details)

- Analgesics (concomitant NSAIDs or aspirin, keterolac)
- Antibacterials (quinolones)
- Anticoagulants (coumarins,dabigitran, phenindione, heparins).
- Antidepressants (SSRI, venlafaxine)
- Antidiabetics (sulphonylureas).
- Antivirals (ritonavir).
- References
 - 1. BNF 66 (September 2013- March 2014)
 - 2. CKS: NSAIDs. Last revised in January 2013
 - 3. American College of Rheumatology. Drug safety alert: http://www.rheumatology.org/Practice/Clinical/Quality/Drug-Safety/
 - 4. MHRA: Diclofenac: new contraindications and warnings after a Europe-wide review of cardiovascular safety (June 2013). Accessed via http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON286975

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- Ciclosporin.
- Cytotoxics (methotrexate, erlotinib)
- Dimethyl sulfoxide
- Diuretics (triamterene)
- Lithium
- Pentoxifylline
- Probenecid
- Tacrolimus.

Diuretics

Tests prior to starting treatment

- U&Es² (paying particular attention to potassium level)^{1,2}
- Glucose (urine analysis)- for thiazides ¹

Monitoring until patient is stabilised

U&Es should be monitored 1 month after starting treatment and also 1-2 weeks after a change of dose or clinical circumstances (after 5-7 days in high risk patients eg those receiving spironolactone, those with existing renal dysfunction, those receiving combination therapy).

Ongoing monitoring

U&Es should be performed annually

Thiazides: blood glucose should be performed annually

Action required if abnormal results

If potassium falls below 3 mmol/L it may be necessary to review diuretic therapy.¹

Renal function should be remeasured within 2 weeks if serum creatinine rises by > 20% or eGFR falls by 15%. 2

Significant drug interactions

- ACE inhibitors and angiotensin II antagonists
- Alpha-blockers
- Analgesics (indomethacin)
- Anti-arrhythmics (disopyramide, flecainide, lidocaine, mexiletine)
- Antibacterials (aminoglycosides, polymixins, vancomycin with loop diuretics)
- Antiepileptics (carbamazepine with acetazolamide)
- Antipsychotics (pimozide, amisulpiride, sertindole)
- Atomoxetine
- Beta-blockers (sotolol)
- Cardiac glycosides
- Ciclosporin
- Lithium
- Potassium salts
- Tacrolimus

References

- 1. Monitoring requirements for cardiovascular drugs: Prescriber 2000, 11(2): 43-56
- 2. Best practice in primary care pathology: review 6. J. Clin Pathol. 2007; 60: 225-234