Drug combination leads to renal failure & hyperkalaemia

An 82 year old man was admitted to hospital recently with acute renal failure and hyperkalaemia following treatment for urinary symptoms and presumed UTI.

The man had several risk factors prior to treatment:
- Chronic kidney disease
- Prostatic hypertrophy
- Age
- ACE inhibitor therapy

He was prescribed a 5 day course of trimethoprim 200mg b.d. and a 2 day course of Effercitrate® by his GP.

A U&E taken by the GP 6 days later revealed the decline in renal function and serum potassium >7 mmol/L (normal range 3.5 - 5.2) and the patient was referred to hospital.

The combination of pre-existing risk factors together with the drugs prescribed for the UTI were the cause of the hyperkalaemia and renal failure.

Some examples of potassium containing medicines are shown in the table.

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Potassium Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effercitrate®</td>
<td>13.9 mmol per tablet = 84 mmol per day</td>
</tr>
<tr>
<td>Fybogel Mebeverine®</td>
<td>7 mmol per sachet</td>
</tr>
<tr>
<td>Movicol®</td>
<td>5.4 mmol per sachet</td>
</tr>
<tr>
<td>Slow K®</td>
<td>8 mmol per tablet</td>
</tr>
<tr>
<td>Sando K®</td>
<td>12 mmol per tablet</td>
</tr>
<tr>
<td>Salt substitutes e.g. LoSalt® and Ruthmol® also contain potassium.</td>
<td></td>
</tr>
</tbody>
</table>

In addition, examples of drugs that can interfere with renal perfusion and contribute to hyperkalaemia are also listed.

<table>
<thead>
<tr>
<th>Drugs that interfere with renal perfusion</th>
<th>Drugs that contribute to hyperkalaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitors, AIIRAs</td>
<td>Trimethoprim (reduces renal K+ excretion)</td>
</tr>
<tr>
<td>Nitrates</td>
<td>Beta blockers</td>
</tr>
<tr>
<td>Nicorandil</td>
<td>Digoxin</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>K+ sparing diuretics e.g. spironolactone, amiloride</td>
</tr>
<tr>
<td>Thiazide diuretics</td>
<td>Antihypertensives</td>
</tr>
<tr>
<td>NSAIDs</td>
<td></td>
</tr>
</tbody>
</table>

Advice for prescribers and pharmacists:
- Be aware of products containing potassium and avoid in chronic kidney disease
- Be aware of the increased risk of renal impairment and hyperkalaemia when certain drug combinations are used
- Check & monitor U&E when drugs known to affect serum potassium & renal function are prescribed for patients with chronic kidney disease.

N.I. Guidelines for Acute Kidney Injury
N.I. Guidelines for the management of chronic kidney disease
N.I. Guidelines for the treatment of hyperkalaemia in adults
Updated MHRA guidance issued in May 2012 advises that oral tacrolimus products should be prescribed and dispensed by brand name only. Inadvertent switching between products has been associated with reports of toxicity and graft rejection. Recently there have been a number of cases in NI where patients have been prescribed tacrolimus suspension by generic name and products from different manufacturers dispensed. The recommendations do not imply that a patient’s treatment cannot be changed to a different formulation or brand if the prescriber considers this appropriate. However, any changes between brands should be accompanied by careful therapeutic monitoring under the supervision of a specialist.

Useful links for further information:
http://www.ipnsm.hscni.net/library/TacrolimusPostTransplantSCG.pdf
See further info on items unsuitable for generic prescribing on p.3

<table>
<thead>
<tr>
<th>Form</th>
<th>Dose Frequency</th>
<th>Brand Names</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate Release capsules</td>
<td>Twice daily</td>
<td>Adoport®, Aletris®, Capexion®, Evenil®, Miloprosan®, Prograf®, Tacni®, Takon®, Talixium®, Tamitec®, Vivadex®</td>
<td>Prograf® and Advagraf® are the brands listed in the N.I. shared care guideline for tacrolimus (adults).</td>
</tr>
<tr>
<td>Prolonged release capsules</td>
<td>Once daily</td>
<td>Advagraf®</td>
<td>Belfast Trust use tacrolimus 5mg/5ml suspension made by Specials Laboratories Ltd or Prograf® capsules for renal transplant patients.</td>
</tr>
<tr>
<td>Granules for oral suspension</td>
<td>Twice daily</td>
<td>Modigraf®</td>
<td>Modigraf® may be used by other UK paediatric transplant centres.</td>
</tr>
<tr>
<td>Oral suspension</td>
<td>Twice daily</td>
<td>Unlicensed product. No brand name but Rx must specify strength &amp; manufacturer.</td>
<td></td>
</tr>
</tbody>
</table>

ACE–Inhibitors & AIIRAs – Avoid in pregnancy

Following a recent report from secondary care, prescribers are reminded that all ACE-inhibitors and angiotensin receptor antagonists should not be used at any stage in pregnancy unless absolutely essential. Exposure to these drugs in pregnancy has been associated with decreased renal function, oligohydramnios and retardation of skull ossification. The risk is considered greatest with 2nd and 3rd trimester exposure, however, there is some data to suggest an increase in congenital anomalies with exposure during the 1st trimester. http://www.mhra.gov.uk/home/groups/pl-p/documents/publication/con2033217.pdf

Advice for prescribers and pharmacists:
Prescribers should review the use of AIIRAs and ACE inhibitors in women of child-bearing age. These women should be advised of the risk and counselled on the use of appropriate contraception to avoid inadvertent foetal exposure. Patients should be advised to speak to their doctor if they become pregnant or are planning to become pregnant whilst on these drugs and then switched to an alternative antihypertensive if possible.
# Have you checked the date?

A number of incidents have been reported involving out-of-date medication and foods e.g.

- Out-of-date CDs held in doctors’ bags
- Supply of out-of-date baby milk
- Supply of out of date vaccines
- Supply of out-of-date medication to a nursing home patient.

Reasons for medication going out-of-date include:

- Inefficient stock re-ordering systems
- Poor stock rotation
- Inadequate date-checking procedures or existing procedures not followed.

An Excel spreadsheet tool is available to assist OOHs & GP practice staff with date-checking of medication stored in doctors’ bags or the practice. This can be downloaded from the primary care intranet:

[http://primarycare.hscni.net/PharmMM_Resources_Non%20Clinical%20Resources.htm](http://primarycare.hscni.net/PharmMM_Resources_Non%20Clinical%20Resources.htm)

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# Name that drug

Which of the following drug combination products is Omacor® and which is Maxepa®?

- Eicosapentaenoic acid 460mg & docosahexaenoic acid 380mg
- Eicosapentaenoic acid 170mg & docosahexaenoic acid 115mg

A community pharmacist reported a mix-up where a prescription for the generic combination in Maxepa® capsules was inadvertently dispensed as the Omacor® product.

Some multi-ingredient products are unsuitable for generic prescribing due to the practical issue of naming all the ingredients and the confusion in identifying the correct product.

Omacor® and Maxepa® are examples of products that should be prescribed by brand.

See HSCB guide to ‘Items Unsuitable For Generic Prescribing’ for other examples.

[http://www.hscboard.hscni.net/medicinesmanagement/Prescribing%20Guidance/index.html#P-1_0](http://www.hscboard.hscni.net/medicinesmanagement/Prescribing%20Guidance/index.html#P-1_0)

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# Methotrexate—getting it right

For almost ten years, primary and secondary care prescribers in NI have followed NPSA and DHSSPS recommendations that only methotrexate 2.5mg tablets are prescribed and dispensed.

There have been a number of reports from Trust outpatient clinics about patients who have been taking their methotrexate incorrectly e.g.

- Taking the full weekly dose every day
- Splitting their weekly dose and taking it over a number of days

Prescribers should continue to use only the 2.5mg tablets and if a 10mg dose is recommended on a clinic letter, this is not an endorsement to prescribe the 10mg tablet and the prescription should be written as “four x 2.5mg”.

Systems currently in place to reduce the risk of high strength or daily administration of oral methotrexate being prescribed in primary care include:

- Information for GP practices about their methotrexate prescribing, available in the practice COMPASS report.
- GP clinical systems will issue a warning when the 10mg tablet strength is chosen from the drug dictionary and will also default to weekly dosing instructions.
- Community pharmacists have been advised to query any new prescriptions for methotrexate 10mg directly with the prescriber.
- Implementing the recommendations in the HSCB Guidance for improving the safe use of oral methotrexate in primary care (updated August 2012).

Links to HSCB Methotrexate Guidance:

Intranet for GPs: [http://primarycare.hscni.net/PharmMM_Resources_Clinical%20Resources.htm](http://primarycare.hscni.net/PharmMM_Resources_Clinical%20Resources.htm)

Internet for pharmacists: [http://www.hscboard.hscni.net/medicinesmanagement/Prescribing%20Guidance/index.html#P-1_0](http://www.hscboard.hscni.net/medicinesmanagement/Prescribing%20Guidance/index.html#P-1_0)
Clinical governance resources for GP practices

The medicines governance audits and workbooks available on the primary care intranet are resources that can be considered as part of the practice’s clinical governance plan e.g.

Clinical Audit (clinical resources section):
- Warfarin audit (cardiovascular section)
- Methotrexate audit (specialist medicines section)
- Antibiotic audit

Practice systems (non clinical resources section)
- Acute prescribing Audit
- Repeat prescribing audit
- Controlled drug SOP workbook
- Checking expiry dates tool
- Prescription security (see below)

Missing and stolen prescriptions—updated guidance

Recent adverse incident reports reported to the HSCB include:
- Theft of doctors bags containing drugs and prescription forms
- Theft of prescriptions from GP reception areas

These incidents highlight the need for all prescribers and practices to have procedures in place to ensure the security of prescription forms both within the practice and when attending patients outside of the practice.

Summary of recent safety advice from MHRA

www.mhra.gov.uk/drugsafetyupdate

May 2012
- Fingolimod
- Domperidone
- Strontium ranelate

New monitoring
Cardiac risks
Risks with current VTE

June 2012
- Oral tacrolimus
- Topical tacrolimus
- Caffeine citrate
- Febuxostat
- Leflunomide

Prescribe & dispense by brand
Risk of malignancies
Two products available—care with dosing
Serious skin reactions
Blood and liver toxicities, birth defects & infections

July 2012
- Dabigatran

Updated advice on contraindications & warnings including; drug interactions, bleeding risks, monitoring renal function, switching treatment to & from dabigatran

Guidance for Prescription Security in Primary Care - Information for GP Practices’ updated August 2012 is available on the primary care intranet.

http://primarycare.hscni.net/PharmMM_Resources_Non%20Clinical%20Resources.htm

Who to inform:
If prescriptions are missing or stolen, the practice should notify:
- Local HSCB Medicines Management Office
- CFPS Fraud Hotline (phone number 08000963396)
- Local district police station.

Nurse prescribers employed by the Trusts must also inform their nurse manager.

Missing or stolen prescriptions for Controlled Drugs must always be reported to the HSCB Accountable Officer by contacting your local medicines management office.

Incidents involving lost or stolen prescriptions should be reviewed promptly by relevant members of the practice team and appropriate actions taken. An adverse incident form (AIF1) should be completed and submitted to the HSCB to allow learning from the incident to be shared.

‘Guidance for Prescription Security in Primary Care - Information for GP Practices’ updated August 2012 is available on the primary care intranet.

http://primarycare.hscni.net/PharmMM_Resources_Non%20Clinical%20Resources.htm