Common renal pitfalls
(for the non-nephrologist)

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Menu

✓ Common pitfalls in the CKD patient (6 cases)

✓ Common pitfalls in the dialysis patient (2 cases)

✓ Common pitfalls in the transplant patient (6 cases)
Common problems in the patient with chronic renal failure
Case 1: Chronic renal failure „out of the woodwork“

- 72 year old man admitted with hypertension
- Blood pressure 180/100. Creatinine 200 umol/l (GFR 28)
- Dipstick trace positive for protein. Ultrasound L kidney 9.8 cm, R kidney 9.5 cm
- Referral to nephrology

A proper referral should contain

- A list of previous creatinine results
- Comorbidity
- And ALL medication
All medication?

Avoid NSAIDs in all renal patients.
## COX-2 inhibitors and renal failure

<table>
<thead>
<tr>
<th>Age/Sex</th>
<th>Drug</th>
<th>Daily Dose (mg)</th>
<th>Duration (days)</th>
<th>Salt-depletion</th>
<th>Degree of Nephrotoxicity</th>
<th>Renal Biopsy</th>
<th>Outcome (renal function)</th>
</tr>
</thead>
<tbody>
<tr>
<td>63/M</td>
<td>Celecoxib</td>
<td>400</td>
<td>16</td>
<td>No</td>
<td>Rise in serum creatinine; edema</td>
<td>No</td>
<td>Full recovery</td>
</tr>
<tr>
<td>Perazella, et al(^{12}) Case 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>68/M</td>
<td>Celecoxib</td>
<td>400</td>
<td>13</td>
<td>No</td>
<td>Rise in serum creatinine; edema; Mild hyperkalemia</td>
<td>No</td>
<td>Full recovery</td>
</tr>
<tr>
<td>Perazella, et al(^{12}) Case 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>73/F</td>
<td>Rofecoxib</td>
<td>25</td>
<td>14</td>
<td>No</td>
<td>Acute renal failure with 1 session of hemodialysis; marked hyperkalemia</td>
<td>No</td>
<td>Full recovery</td>
</tr>
<tr>
<td>Perazella, et al(^{12}) Case 3 (Added in proof)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>49/M</td>
<td>Rofecoxib</td>
<td>25</td>
<td>2</td>
<td>No</td>
<td>Rise in serum creatinine</td>
<td>No (solitary kidney)</td>
<td>Full recovery</td>
</tr>
<tr>
<td>This report, Case 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yes</td>
<td>Full recovery</td>
</tr>
<tr>
<td>43/M</td>
<td>Rofecoxib</td>
<td>25</td>
<td>5</td>
<td>No</td>
<td>Acute renal failure with 3 sessions of hemodialysis; edema</td>
<td>Yes</td>
<td>Full recovery</td>
</tr>
<tr>
<td>This report, Case 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Woywodt et al., J Rheumatol 2001
Home blood pressure monitoring
If GFR above 30 compliant + renovascular Unlikely and K ok Beware of spironolactone

If edema and thiazides not enough Low potential for trouble

Thiazides

If other Indication or “stress”

Low potential for trouble

If pregnant

If compliant with diuretics and Beta-Bl. Admission?

Only add-on dizziness Excellent add-on e.g. evening Low potential for trouble

ACE-I ARB CCB

Beta-Blocker

Doxazosin Moxonidin

Thiazides

Loop diuretics

Alpha-MD

Minoxidil

If mild edema Avoid if low clearance
Protection of forearm veins

Hands off, please!
Case 2: Chronic renal failure and angiography

A 65 year-old patient with CRF (serum creatinine 300 umol/l) is admitted with angina and scheduled for next-day coronary angiography. He is on Frusemide, Aspirin, Simvastatin, Metoprolol, Irbesartan, Doxazosin and a thiazide diuretic.

Contrast-mediated renal failure is common and often preventable

The risk relates to GFR, renal disease, amount and type of contrast and hydration

Is the indication compelling?

Admit. Stop ARB and all diuretics the evening before. Hydrate.

Acetylcysteine: conflicting data

Limit amount of dye. Skip LV angiogram if possible

Post-procedural dialysis: no convincing data
Hospital-acquired renal failure: The usual suspects

- NSAIDs and COX-2 inhibitors
- Contrast media
- Aminoglycosides
- Dehydration
- Sepsis
- Cirrhosis and ascites
- Classical: ACE-Inhibitor + Spironolactone + NSAID („renal survival test“)
- Cholesterol embolism post angiogram
Case 3: Renal failure and aminoglycosides

✓ A 45 year-old man with CRF has biliary sepsis with Pseudomonas. The microbiologist recommends Tazocin and gentamycin. The serum creatinine is 200 umol/l

✓ All aminoglycosides are nephrotoxic
✓ There are alternatives, e.g. Tazocin and Cipro
✓ Judicious dosing AND monitoring are essential – seek expert advice
✓ Renal failure usually due to lack of hydration plus wrong dosing plus lack of monitoring
✓ Do not withhold or downsize antibiotic regime if life-threatening situation
✓ Keep patient well hydrated

It needs water…

To produce pee!
Case 4: Chronic renal failure and congestive heart failure

- A 75 year-old patient with CRF (baseline serum creatinine 250 umol/l) is admitted with shortness of breath; he has ++ edema and pleural effusions. He is on Frusemide 40 mg OD, Aspirin 75 mg OD, Simvastatin 40 mg OD. His creatinine on admission is 300 umol/l. Diuretic regime? ACE Inhibitor?

- Always give Frusemide BD
- Alternative: Torasemide OD
- Avoid ACE Inhibitor. Avoid Spironolactone
- Seek advice from nephrologist. Do eGFR
- Chart in/output. Restrict salt
- High throughput not beneficial
Case 5: Chronic renal failure and diabetes

A 72 year-old patient is admitted with type II diabetes. Diet has failed. The HbA1c is 8.4%.

Serum creatinine is 180 umol/l. BP is 160/95.

Dipstick is ++ for protein.

- Do eGFR
- Be careful about metformin
- Gliquidone is oral antidiabetic of choice
- BP control is key
- Glitazones: no definitive data
Case 6: ACE inhibitors and ARBs

A 72 year-old patient is admitted with type II diabetes. The HbA1c is 8.4%. Serum creatinine is 180 umol/l (GFR 35). BP is 160/95. Dipstick is ++ for protein. ACE inhibitor?

Check for abdo bruit and renal size and be careful in vasculopaths

ARBs safer than ACE inhibitors

Start Enalapril 5mg BD

Avoid concomitant use of Spironolactone and NSAIDs

Do not use if potassium 5.5 or higher

CHECK POTASSIUM AND CREATININE !!
Common problems in the dialysis patient
Case 7: Dialysis and thrombosis

A 65 year-old patient on peritoneal dialysis is admitted on a weekend with femoral vein thrombosis and mild pulmonary embolism. What about anticoagulation?

This is not as easy as it seems

LMW heparins all accumulate in renal failure

Option 1: 50% LMW / enoxaparin with measurement of anti-Xa activities

Dalteparin: no data

Option 2: conventional heparin

Beware of renal impairment with LMW heparins – common and pot. deadly pitfall

HIT II: Beware of lepirudin and renal impairment – rare but pot. deadly pitfall
Renal failure and drugs

- Many drugs accumulate in renal failure
- Some need to be avoided
- Others are ok with dose reduction
- Every new drug in a renal patient should be scrutinized
- Ask pharmacologist if available or nephrologist or look it up (e.g. UpToDate)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Protein binding</th>
<th>VD</th>
<th>Renal elimination</th>
<th>GFR 20-30</th>
<th>GFR &lt;15</th>
<th>HD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepin</td>
<td>Tegretal</td>
<td>75</td>
<td>(+)</td>
<td>+++</td>
<td>75 (A, P)</td>
<td>n</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Rivotril</td>
<td>85</td>
<td>+</td>
<td>+++</td>
<td>10 (P)</td>
<td>n</td>
</tr>
<tr>
<td>Ethosuximid</td>
<td>Suxinutin</td>
<td>7</td>
<td>(+)</td>
<td>++</td>
<td>20 (S, A, P)</td>
<td>n</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Neurontin</td>
<td>3</td>
<td>(+)</td>
<td>—</td>
<td>90 (S)</td>
<td>25 %</td>
</tr>
<tr>
<td>Lamotrigin</td>
<td>Lamictal</td>
<td>55</td>
<td>(+)</td>
<td>++</td>
<td>75 (S, P)</td>
<td>c</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>Keppra</td>
<td>10</td>
<td>(+)</td>
<td>(+)</td>
<td>95 (S, P)</td>
<td>50 %</td>
</tr>
<tr>
<td>Oxcarbazepin</td>
<td>Triptal</td>
<td>38</td>
<td>(+)</td>
<td>++</td>
<td>95 (P)</td>
<td>50 %</td>
</tr>
<tr>
<td>Phenoobarbital</td>
<td>Luminal</td>
<td>50</td>
<td>(+)</td>
<td>+++</td>
<td>95 (S, A, P)</td>
<td>50 %</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Phenyldan</td>
<td>90</td>
<td>(+)</td>
<td>+++</td>
<td>80 (A, P)</td>
<td>n</td>
</tr>
<tr>
<td>Primidon</td>
<td>Mylepsinum</td>
<td>20</td>
<td>(+)</td>
<td>++</td>
<td>100 (A, P)</td>
<td>50 %</td>
</tr>
<tr>
<td>Sulthiam</td>
<td>Osilodot</td>
<td>30</td>
<td>KA</td>
<td>+</td>
<td>80 (S, P)</td>
<td>50 %</td>
</tr>
<tr>
<td>Tiagabin</td>
<td>Gabitril</td>
<td>96</td>
<td>(+)</td>
<td>++</td>
<td>15 (P)</td>
<td>n</td>
</tr>
<tr>
<td>Topiramat</td>
<td>Topamax</td>
<td>15</td>
<td>(+)</td>
<td>—</td>
<td>70 (S)</td>
<td>50 %</td>
</tr>
<tr>
<td>Valproinsäure</td>
<td>Ergenyl</td>
<td>90</td>
<td>—</td>
<td>+++</td>
<td>90 (A, P)</td>
<td>75 %</td>
</tr>
<tr>
<td>Vigabatrin</td>
<td>Sabril</td>
<td>0</td>
<td>(+)</td>
<td>—</td>
<td>70 (S)</td>
<td>25 %</td>
</tr>
</tbody>
</table>
Case 8: Dialysis and bleeding

- A 70 year-old patient on haemodialysis is admitted on a Sunday with a first upper GI bleed. Endoscopy shows an ulcer and no ongoing bleeding. He is hemodynamically stable – Hb is 7.8. He will have dialysis in Kendal on Monday.

- This patient should be admitted to a renal unit

- Transfusion should be done as 1 unit - potassium check - 1 unit - potassium check (unless bleeding profusely)

- Transfusion should be done during the day

- Close liaison with dialysis – heparin dose

- AV fistula needs protection during endoscopy / surgery
Common problems in the transplant patient
Case 9: Pneumonia in the transplant patient

- A 45 year-old patient had his first cadaveric kidney transplant five years ago. He now presents with pneumonia. The immunosuppression is Sandimmun Neoral 150 mg BD, Prednisolone 5 mg OD, MMF 500 mg TDS.

- **Ask specialist advice early on - immunosuppression?**
  - **Do NOT** change the immunosuppression
  - **Do NOT** give immunosuppression iv without specialist advice
  - Make sure immunosuppression is available AND ingested
  - Do not underestimate infection.
  - eg. Tazocin iv plus Moxi-/Levofloxazin iv
  - admit
  - Have a low threshold for bronchoscopy
  - An extra slug of 200 mg Hydrocortisone does no harm if intake of immunosuppression in doubt
Case 10: Urinary tract infection in the transplant patient

✓ A 32 year-old patient had his first cadaveric kidney transplant six months ago. He now presents on Sunday with fever and dipstick is positive for leukocytes. The immunosuppression is Tacrolimus 2 mg BD, Prednisolone 5 mg OD, MMF 500 mg TDS.

✓ Ask specialist advice early on
✓ Nephrologist may know microbiology if „frequent flyer“
✓ Signs and symptoms may be absent / misleading
✓ Leukocyturia may be absent but microscopy will show bacteria
✓ Culture, culture, culture
✓ Ciprofloxazin po if well
✓ Ceftriaxone and Piperacillin iv if unwell
✓ Ultrasound to exclude obstruction
Case 11: Statins in the renal transplant patient

✓ A 65 year-old patient had his first cadaveric kidney transplant two years ago. He now presents with acute anterior myocardial infarction.

The immunosuppression is Sandimmun Neoral 150 mg BD, Prednisolone 7.5 mg OD. LDL sky high.

Pravastatin and Fluvastatin are safe, Simvastatin and Atorvastatin interact. Ezetimib is safe. Fibrates: not recommended

<table>
<thead>
<tr>
<th>Statin</th>
<th>Daily dosage (mg/day)</th>
<th>CYP metabolism</th>
<th>P-glycoprotein substrate</th>
<th>OATP2 substrate</th>
<th>Lipophilic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>10-80</td>
<td>3A4</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>20-40</td>
<td>2C9</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>20-80</td>
<td>3A4</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>10-80</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>10-40</td>
<td>2C9 (minor)</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>20-80</td>
<td>3A4</td>
<td>Yes</td>
<td>Possibly</td>
<td>Yes</td>
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</tbody>
</table>
## Drugs and the transplant patient

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>CsA Level</th>
<th>Renal Effects</th>
<th>Additional Effects†</th>
<th>Citations</th>
</tr>
</thead>
<tbody>
<tr>
<td>pravastatin</td>
<td></td>
<td></td>
<td>Increased risk of myopathy and rhabdomyolysis; CsA may inhibit the metabolism of pravastatin. Increased pravastatin levels by 10-fold in pediatrics. However, compared to Lovastatin, the interaction between pravastatin and CsA is clinically insignificant. No changes in CsA pharmacokinetics.</td>
<td>335, 336, 440-442, 490, 531, 660</td>
</tr>
<tr>
<td>prazosin</td>
<td></td>
<td>Protective renal effect; increases RBF; small reduction in GFR</td>
<td></td>
<td>14, 337</td>
</tr>
<tr>
<td>prednisolone</td>
<td>![Increase]</td>
<td></td>
<td>Increased AUC and t½ of CsA; decreased clearance of CsA may decrease metabolism and clearance of prednisolone. Synergistic immunosuppressive effect when given with CsA</td>
<td>14, 338, 339, 469-472, 491, 518</td>
</tr>
<tr>
<td>prednisone</td>
<td>![Increase]</td>
<td></td>
<td></td>
<td>14, 57, 340</td>
</tr>
<tr>
<td>prenylamine</td>
<td>![Increase]</td>
<td></td>
<td></td>
<td>39</td>
</tr>
<tr>
<td>primidone</td>
<td>![Decrease]</td>
<td></td>
<td></td>
<td>39, 57</td>
</tr>
<tr>
<td>pristinamycin</td>
<td>![Increase]</td>
<td>nephrotoxic (isolated reports)</td>
<td></td>
<td>16, 39, 53</td>
</tr>
<tr>
<td>probucol</td>
<td>![Decrease]</td>
<td></td>
<td></td>
<td>341-343, 443</td>
</tr>
<tr>
<td>progesterone</td>
<td>![Decrease]</td>
<td></td>
<td></td>
<td>122</td>
</tr>
<tr>
<td>propafenone</td>
<td>![Increase]</td>
<td>Decreased renal function</td>
<td></td>
<td>39, 344</td>
</tr>
<tr>
<td>propionyl carnitine</td>
<td>![Decrease]</td>
<td></td>
<td></td>
<td>519</td>
</tr>
<tr>
<td>propranolol</td>
<td></td>
<td>Protective against CsA nephrotoxicity</td>
<td></td>
<td>35, 542</td>
</tr>
<tr>
<td>prostaglandins</td>
<td></td>
<td></td>
<td>Antagonizes the immunosuppressive effects of CsA. CsA increases the elimination of propranolol and also reduces first pass effects and increases propranolol GI absorption</td>
<td>345</td>
</tr>
<tr>
<td>purified Helleborus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>species extract</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

[†] Additional effects may not be specific to transplant patients and may occur in other patient populations.

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Over-the counter drugs and the transplant patient

- St. Johns wort
- And, again, NSAIDs

*Hands off, please!*

*No new drugs or OTC drugs without specialist advice*
Case 12: Gout in the transplant patient

A 72 year-old patient had his second cadaveric kidney transplant ten years ago. He is on Cyclosporine 100 mg BD and Azathioprine 100 mg OD. He now presents with a second episode of gout.

Avoid NSAID
Colchicine not contraindicated but not well tolerated
Seek expert advice – steroid pulse?
BEWARE Allopurinol – Azathioprine
Elevated urate is not an indication for allopurinol
Case 13: Psychiatric problems in the transplant patient

A 38 year-old patient had his first kidney transplant (live donation) one year ago. He is on Tacrolimus, MMF and steroids. He now presents with a short history of restlessness and delusion. On the ward, he is seen to hide in the toilet.

- Ask specialist advice early on
- Exclude meningitis and do a CT
- Infection of the CNS? Other infection?
- If not: this is still a dangerous situation
- Does the patient take his immunosuppression?
- 200 mg iv Hydrocortisone do not do any harm
Case 14: Abdominal pain in the transplant patient

✓ A 72 year-old patient had her first kidney transplant seven years ago. She is on Cyclosporin and steroids. She now presents with left lower abdominal pain. She had a similar episode three years ago.

✓ Ask specialist advice early on
✓ Diverticulitis potentially fatal
✓ Admit
✓ Intravenous antibiotics
✓ CT
✓ Should be in a renal unit
Some rules for non-nephrologists and the renal transplant patient

- These patients are at above average risk for many things
- Seek expert advice early on
- Beware of Interactions and over-the-counter drugs
- Beware of the transplant patient with infection
- Beware of the transplant patient with abdominal pain
- Beware of the immunosuppression
- Make sure the immunosuppressive drugs are available and ingested
“Learning is a like a sea without a shore”

Konfuzius