Common pitfalls in kidney transplant patients
(for the non-nephrologist)

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Menu

✓ Basic transplant nephrology in 5 slides

✓ 10 cases

✓ No guidelines (promised)

✓ Contact details if you need our help
How to get a kidney transplant

- Deceased renal transplantation is from donor with trauma and brain stem death
- Live donation is from a related or unrelated healthy person
- Younger type 1 diabetics with renal failure may qualify for combined kidney pancreas transplantation
- There is altruistic and paired/pooled live donation as well
- Some patients buy a kidney in Pakistan, China
Renal transplantation is not a life-saving procedure; the focus is on gain in quality of life. We therefore spend a lot of time on selecting those patients who we think will benefit.

- **6922 patients were listed for a kidney transplant in the UK as of March 09**
- **FY 2008/2009: 1363 cadaveric kidney transplants**
- **FY 2008/2009: 864 Live kidney donations (20 from RPH)**
- **Locally 5-year graft survival is 81%, patient survival 98%**
The plumbing

- A. iliaca
- V. iliaca
- Donor ureter
- Urinary bladder
Transplant nephrology is like investment banking: You can't have everything

- High immunosuppression
  - No rejection
  - High infection

- Low immunosuppression
  - High rejection
  - No infection
Immunosuppression

- Cyclosporine/Tacrolimus
- Sirolimus
- Azathioprine
- Cellcept
- Prednisolone
Some common and/or dangerous problems
Case 1: Infection in the renal transplant patient

A 32 year-old patient had his first kidney transplant six months ago. He now presents on a bright Lakeland Sunday with fever 38.5. dipstick is positive for leukocytes. The immunosuppression is Tacrolimus 2 mg BD, Prednisolone 5 mg OD, MMF 500 mg TDS. CRP is 180.

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

Admit

Culture, culture, culture

Augmentin, Tazocin, Cephtriaxone/Piperacillin

Ultrasound to exclude obstruction
Case 2: Pneumonia in the transplant patient

✓ A 35 year-old patient with type 1 diabetes and renal failure had a cadaveric kidney pancreas transplant five years ago. He now presents with lobar pneumonia. The immunosuppression is Tacrolimus 3 mg BD, Prednisolone 5 mg OD, MMF 500 mg TDS. CRP 250

✓ 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 taken
✓ Do not underestimate infection.
✓ eg. Tazocin iv
✓ have a low threshold for bronchoscopy (beware of Pneumocystis)
✓ An extra slug of 200 mg Hydrocortisone does no harm if intake of immunosuppression in doubt
Case 3: Abdominal pain in the transplant patient

- 72 year old renal transplant patient (transplant in 2001), serum creatinine 180 umol/l
- Immunosuppression is with Cyclosporine, Cellcept, Prednisolone
- Admitted with left-sided abdominal pain and nausea. CRP 70
- CT Abdomen: Diverticulitis
- What will be the likely outcome

A) treatment with Ciprofloxa zone and Metronidazole, discharge after 1 week
B) Surgery and discharge after 2 weeks in hospital
C) Laparotomy, three revisions, colostomy, discharge after 6 months in hospital
D) Death from sepsis
Case 3: Abdominal pain in the transplant patient

- Diverticulitis is a life-threatening emergency in transplant patients
- High likelihood of failure of medical treatment (e.g. 100% in Perkins et al., Am J Surg 1984 Dec;148(6):745-8)
- High mortality e.g. 100% in contemporary series (Transplant Proc. 2007 39(4):1054-6.)
- Serious consideration should be given to surgery even after the first attack
- Beware of pancreatitis, cholecystitis
Case 4: 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 and LP
- Infection of the CNS? Other infection?
- If not: this is still a dangerous situation
- Does the patient take his immunosuppression?
- 200 mg iv Hydrocortisone cannot do harm
Case 5: Renal transplant and angiography

✓ A 65 year-old renal transplant patient (tx 1994, serum creatinine 300 umol/l) is admitted with angina and scheduled for next-day coronary angiography. He is on Tacrolimus, Prednisolone, Frusemide, Aspirin, Simvastatin, Metoprolol, Irbesartan, Doxazosin and a thiazide diuretic.

✓ Contrast-mediated renal failure is common and often preventable

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

✓ 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
A 35 year-old renal transplant patient is hypertensive. He is on Tacrolimus 3 mg BD and MMF 500 mg BD. Should he have an ACE-Inhibitor?

Transplant renal artery stenosis is not rare

> ARBs safer than ACE inhibitors

> Do not use if potassium 5.5 or higher

CHECK POTASSIUM AND CREATININE !!

Ask specialist advice before starting ACEI or ARB in renal transplant recipients
More problems related to drugs and the immunosuppression
Renal failure, transplantation and drugs

- Many drugs accumulate in renal failure
- Some need to be avoided
- Others are ok with dose reduction
- 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>Carbamazepine</td>
<td>(+)</td>
<td>+++</td>
<td>75 (A, P)</td>
<td>n</td>
<td>75 %</td>
<td>—</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>(+)</td>
<td>+++</td>
<td>10 (P)</td>
<td>n</td>
<td>n</td>
<td>—</td>
</tr>
<tr>
<td>Ethosuximide</td>
<td>(+)</td>
<td>++</td>
<td>20 (S, A, P)</td>
<td>n</td>
<td>50 %</td>
<td>++</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>(+)</td>
<td></td>
<td>90 (S)</td>
<td>25 %</td>
<td>15 %</td>
<td>+</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>(+)</td>
<td>++</td>
<td>75 (S, P)</td>
<td>c</td>
<td>KI</td>
<td>—</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>(+)</td>
<td>(+)</td>
<td>95 (S, P)</td>
<td>50 %</td>
<td>c</td>
<td>+</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>(+)</td>
<td>++</td>
<td>95 (P)</td>
<td>50 %</td>
<td>c</td>
<td>(+)</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>(+)</td>
<td>+++</td>
<td>95 (S, A, P)</td>
<td>50 %</td>
<td>25 %</td>
<td>+</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>(+)</td>
<td>+++</td>
<td>80 (A, P)</td>
<td>n</td>
<td>n</td>
<td>(+)</td>
</tr>
<tr>
<td>Primidone</td>
<td>(+)</td>
<td>++</td>
<td>100 (A, P)</td>
<td>50 %</td>
<td>KI</td>
<td>+</td>
</tr>
<tr>
<td>Sultiam</td>
<td>KA</td>
<td>+</td>
<td>80 (S, P)</td>
<td>50 %</td>
<td>v</td>
<td>KA</td>
</tr>
<tr>
<td>Tiagabin</td>
<td>(+)</td>
<td>++</td>
<td>15 (P)</td>
<td>n</td>
<td>n</td>
<td>—</td>
</tr>
<tr>
<td>Topiramate</td>
<td>(+)</td>
<td></td>
<td>70 (S)</td>
<td>50 %</td>
<td>25 %</td>
<td>+</td>
</tr>
<tr>
<td>Valproinsäure</td>
<td>(+)</td>
<td>+++</td>
<td>90 (A, P)</td>
<td>75 %</td>
<td>v</td>
<td>—</td>
</tr>
<tr>
<td>Vigabatrin</td>
<td>(+)</td>
<td></td>
<td>70 (S)</td>
<td>25 %</td>
<td>KI</td>
<td>+</td>
</tr>
</tbody>
</table>
Case 7: Statins in the renal transplant patient

A 65 year-old patient had her first cadaveric kidney transplant two years ago. The immunosuppression is Sandimmun Neoral 150 mg BD, Prednisolone 7.5 mg OD. LDL sky high. 40 mg Simvastatin is begun.

The patient dies a week later of rhabdomyolysis.

Pravastatin and Fluvastatin are safe, Simvastatin and Atorvastatin interact. Ezetimib is safe. Fibrates: not recommended.
# Drugs and the transplant patient: Interactions

<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 (HMG-CoA reductase inhibitors)</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>Protective renal effect; increases RBF; small reduction in GFR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>prednisolone (see glucocorticoids)</td>
<td></td>
<td></td>
<td>Decreases arterial blood pressure</td>
<td>14, 337</td>
</tr>
<tr>
<td>prednisone (see glucocorticoids)</td>
<td></td>
<td></td>
<td>Increased AUC and t&lt;sub&gt;1/2&lt;/sub&gt; 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>prenylamine</td>
<td></td>
<td></td>
<td>Increased liver enzymes; hirsutism; hyperlipidemia</td>
<td>14, 57, 340</td>
</tr>
<tr>
<td>primidone (see anticonvulsants &amp; barbiturates)</td>
<td></td>
<td></td>
<td>Induces metabolism of CsA</td>
<td>39, 57</td>
</tr>
<tr>
<td>pristinamycin (see macrolides)</td>
<td>nephrotoxic (detailed reports)</td>
<td></td>
<td>Inhibits Cytochrome P-450 3A4 metabolism of CsA</td>
<td>16, 39, 53</td>
</tr>
<tr>
<td>probucol</td>
<td></td>
<td></td>
<td>Increases clearance of CsA</td>
<td>341-343, 443</td>
</tr>
<tr>
<td>progesterone</td>
<td></td>
<td></td>
<td>Inhibits CsA metabolism</td>
<td>122</td>
</tr>
<tr>
<td>propafenone</td>
<td></td>
<td>Decreased renal function</td>
<td></td>
<td>39, 344</td>
</tr>
<tr>
<td>propionyl carnitine</td>
<td>Protective against CsA nephrotoxicity</td>
<td></td>
<td></td>
<td>519</td>
</tr>
<tr>
<td>propranolol (see beta-blockers)</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>35, 542</td>
</tr>
<tr>
<td>prostaglandins</td>
<td>Protective renal effect</td>
<td></td>
<td></td>
<td>345</td>
</tr>
<tr>
<td>purified Helleborus species extract</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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 8: 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

Joseph Goupy: The charming Brute. c.1754
Case 9: A renal transplant patient in pain

- A 71 year-old female patient had her first cadaveric kidney transplant 12 years ago. She now presents with fractured hip after a fall. Immunosuppression is Sandimmun Neoral 100 mg BD, Pred 7.5 mg OD.

- Serum creatinine 150 umol/l

- She is in pain

- The orthopaedic SHO suggests Ibuprofen

- The anaesthetist suggests Etoricoxib iv
# COX-2 inhibitors and renal failure

Woywodt et al., J Rheumatol 2001

### Table 1. Cases of nephrotoxicity reported in association with selective COX-2 inhibitors.

<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(^2) 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(^2) 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(^2) 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></td>
<td></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>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

No NSAID and no COX-2 inhibitors in renal transplant patients, please!
Case 10: Another renal transplant patient in pain

A 71 year-old female patient had her first cadaveric kidney transplant 4 years ago. She now presents with fractured hip after a fall. The immunosuppression is Sandimmun Neoral 100 mg BD, Prednisolone 7.5 mg OD. Serum creatinine 150 umol/l

She is in pain after surgery

The clever medical registrar, knowing that NSAID and Etoricoxib are evil, opts for a Fentanyl patch

The patient reciprocates with profuse vomiting for an entire day

Where is the problem?

Vomiting and loss of immuno-suppressive cover. Needs 200 mg Hydrocortisone
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 taken
How to get help

- Weekdays 9 a.m. to 5 p.m.
- RPH renal transplant team 01772523475 (Answerphone)
- Weekdays 5 p.m. to 7 p.m. renal SpR RPH
- Weekends 9 a.m. to 10 p.m. renal SpR RPH
- All other times: on-call renal consultant RPH

Leaflet collection at

http://www.lancsteachinghospitals.nhs.uk/cont/renal_medicine_
“Learning is a like a sea without a shore”

Konfuzius