Symptom management for patients with end stage renal disease and palliative care patients with renal impairment

Dr Jo Chambers
North Bristol Trust (Southmead Hospital)
Palliative Care Team & Richard Bright Renal Unit
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THE RICHARD BRIGHT RENAL UNIT

DR. RICHARD BRIGHT (1789-1858) IS REGARDED AS THE FOUNDER OF MODERN RENAL MEDICINE. HE WAS BORN IN BRISTOL AND LIVED AT HAM GREEN; HIS FAMILY HOME LATER BECAME HAM GREEN HOSPITAL WHERE THE FIRST RENAL UNIT IN BRISTOL WAS ESTABLISHED.
Contents

- Patients with end stage kidney disease (ESKD)
- Symptom prevalence in ESKD
- Pain and pain management
- Management other symptoms
  - General principles
  - A specific symptom
  - Drugs to modify or avoid
- End of life symptoms and prescribing in ESKD
- Summary
- References
The ESKD population UK 2007

- UK (2007) approx 45,500 RRT pts
- Prevalent renal replacement therapy (RRT)
  - 47% transplant - mean age 49
  - 43% haemodialysis (65)
  - 10% Peritoneal dialysis PD (69)
- However at any one time of ESKD stage 5 pts
  - 15% conservative pathway (cons kidney care)
Fig 6.3b  Kaplan-Meier 9-year survival of incident patients 1997-2005 combined cohort (from day0) with transplant censored

UK Renal Registry 10th Annual Report 2007
Prevalence of symptoms in dialysis and conservatively managed patients

- Fatigue
- Dry mouth
- Itch
- Pain
- Poor appetite
- Breathlessness
- Anxiety
- Sleep disturbance
- Depression
- Restless legs
- Nausea
Causes of symptoms in ESRD

- Uraemia
- Co-morbid conditions
  - Diabetes
  - Vascular disease
  - musculoskeletal
- Related to dialysis
  - Hypotension, cramps, nausea, post dx washed out
- Related to primary renal condition
Pain in ESKD

- **Incidence**
  - 50% dialysis pts
  - >50% conservative pathway

- **Severity**
  - Mod – severe in ¾ dialysis

- **Impact**
  - Q of L
  - Positive correlation with depression
Causes of pain in ESKD

- Concurrent co-morbidity
  - diabetic neuropathy, peripheral vascular disease, arthritis, malignancy
- Primary renal disease
  - adult polycystic kidney disease
- Disease consequent on renal failure
  - renal osteodystrophy, calciphylaxis
- Dialysis related pain
  - PD pts recurrent abdominal pain
  - A-V fistulae leading to ‘steal syndrome’
  - Cramps and headaches
Pain Management

- Assessment
- Explanation
  - Realistic goals
- Short acting preparations while titrating
- Increase dosing interval
- Warn patient of side effects and what to do
Pain Management

- Use modified WHO ladder
- Steps 1 and 2
  - Paracetamol full dose
  - NSAIDS (only if not wanting to preserve renal function)
  - Tramadol (reduced dose)
    - Dialysis 50 mg qid;
    - Conservative kidney care 50 mg bd
- Step 3
## Overview of opioids in renal impairment and ESKD

<table>
<thead>
<tr>
<th>Drug</th>
<th>Metabolite</th>
<th>+/-</th>
<th>Exc&lt;sup&gt;n&lt;/sup&gt;</th>
<th>Metabs Accum&lt;sup&gt;n&lt;/sup&gt;</th>
<th>Removed by dialysis</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>M3G M6G</td>
<td>+/-</td>
<td>K</td>
<td>yes</td>
<td>yes no</td>
<td>Avoid chronic dosing</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>H3G ++ +others</td>
<td>+/-</td>
<td>K</td>
<td>yes</td>
<td>H no H3G yes</td>
<td>Use with caution in dialysis pt</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Oxymorph noroxycod</td>
<td>+?</td>
<td>K</td>
<td>yes</td>
<td>reduced</td>
<td>Little evidence; no long term studies</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Norfent</td>
<td>-</td>
<td>K</td>
<td>&lt;10% 1%</td>
<td>no</td>
<td>Useful parenteral drugs &amp; TD F for stable pain</td>
</tr>
<tr>
<td>Methadone</td>
<td>a pyrrolidine</td>
<td>-</td>
<td>K Gut</td>
<td>no</td>
<td>No</td>
<td>Use with care if familiar with its use.</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>B3G + norbup</td>
<td>-</td>
<td>B Gut Metabs -K</td>
<td>↑ x 15 ↑ x 4</td>
<td>Prob not</td>
<td>Theoretical reason why may be safe, no long term studies</td>
</tr>
</tbody>
</table>
WHO Step 3: **dialysis patients**
with chronic pain able to swallow oral medication
+ paracetamol +/- NSAID +/- adjuvant

- Hydromorphone (H) 1.3mg 4-6 hourly regularly
  - + 1.3 mg prn for breakthrough pain
- If pain **not** controlled and ≥ 6 X 1.3mg H used
- **Substitute** TD fentanyl 12mcg/hr for regular H
  - continue prn H
- Continue to titrate upwards if pain not controlled increasing
dose of fentanyl patch according to prn dose H used
  - prn dose H adjusted according to 24 hour H dose
- **Monitor for toxicity or change in pain at all times –**
educate patient
Management of ESRD non pain symptoms: principles

- Severity of symptom
  - Interference with function and Q of L
  - Side effects from any new medication

- Context
  - Stage of disease; life expectancy
  - Other symptoms
    - Might we make them worse
    - Will one drug manage more than one symptom
  - Other medication
  - Drug interactions
Pruritus and dry skin

- Early in dialysis good life expectancy
  - Emollients
  - UVB light
  - Gabapentin
- Increasing co-morbidity but not at end of life
  - Emollients
  - Topical treatments (capsaicin if itch localised)
  - Gabapentin
- End of life
  - Emollients
  - Anti histamines
Drugs to modify in impaired renal function

- Gabapentin
- Pregabalin
- Metoclopramide – GFR<20 use 50%
- Haloperidol - GFR<10, accumulates with repeated doses
- Levomepromazine – start v low
- Cyclizine if cardiac history
- Clonazepam –↑ risk sedation start low max 2mg/24hrs
- Diazepam active metabolites accumulate normal renal function
- Midazolam active metabolites accumulate renal impairment
- Fluoxetine, Mirtazapine, Zopiclone
Drugs to avoid in impaired renal function

- Pethidine
- Morphine chronic dosing
- Dextropropoxyphene
- Dihydrocodeine
- Treatment doses **LMW heparin**
Incidence of symptoms at end of life from retrospective chart reviews

Between 1/3 to 2/3 pts cognitively impaired at time of stopping dialysis
Anticipatory prescribing at end of life

- Pain
  - Fentanyl 12.5 -25mcg s.c prn hourly

- Dyspnoea
  - Opioid as above

- Agitation
  - Midazolam 2.5 – 5mg s.c  prn hourly
  - Haloperidol 1.5mg s.c  prn 8hrly

- Retained secretions
  - Hyoscine butylbromide 20mg prn 2 hourly – may need 240mg

- fluid overload
  - Ultrafiltration - rarely

- Nausea
  - LCP: haloperidol
  - Levomepromazine 5mg s.c prn 8 – 12 hourly.
Summary

- Renal impairment common in palliative care patients; retention of drug or its metabolites the main cause of toxicity
- ESKD patients highly symptomatic group many of whom have a poor prognosis
- Management needs to take account of the whole situation for the patient
- Many drugs need their dose modifying in the presence of renal failure to prevent toxicity
References

- Supportive Care for the Renal Patient Ed Chambers EJ, Germain M, Brown E OUP 2004
- End of Life Care in nephrology Brown E, Chambers EJ, Eggeling C. OUP 2007