

Question 32

A 75 year old man with non small cell lung cancer and mild chronic renal failure <his serum creatinine is usually 0.15 mmol/L (0.06-0.12)> is recovering from hip replacement surgery. He has been receiving intravenous pethidine via a patient-controlled analgesia for the past three days. Over the last 24 hours, he has developed myoclonic twitching of all limbs and then has a grand mal seizure.

The most likely cause of his neurological signs is:

- A. Brain mets
- B. Uraemia
- C. Hypercalcaemia
- D. Pethidine metabolites
- E. Stroke

Answer:

Commonest cause of seizures in those age >65 is stroke but this man has other risk factors for seizures

In the setting of renal impairment and a drug with seizure potential, the answer is D.

- Pethidine: synthetic opiod
- **Pethidine 75mg-100mg IV equivalent to morphine 10mg IV** in terms of analgesic/ euphoric/ sedative/ respiratory depressive properties, but suppressive effects on cough reflex less
- Other off-label use: 12.5mg IV stat for **rigors**
- *Faster onset of action* (more lipid soluble and more addictive) but *shorter duration of effect* compared to morphine
- 70% protein bound
- Mainly metabolised by **liver**
- Pethidine hydrolysed (liver) to pethidinic acid, and demethylated to norpethidine
- **Norpethidine** is neurotoxic -> dose related PAN (pethidine associated neurotoxicity)
- Causes:
 - o Tremor/ twitches
 - o Hallucinations
 - o Mood changes
 - o Seizures and myoclonus
- Long half-life (8-12 hours)
- Norpethidine mainly **cleared by kidneys so accumulates in renal failure**
- Half the analgesic properties of pethidine
- **Toxic effects not counteracted by opiod antagonist eg naloxone**
- Seizures should be managed supportively +/- benzodiazepines, and use of other analgesia is recommended
- Has **anti-cholinergic effects**
- Many drug interactions:
 - o Avoid respiratory depressants/ CNS depressants
 - o MAO inhibitors -> excitation, sweating, hypo/hypertension +/- fatal
 - o Phenytoin/ phenobarbitone -> ↑ metabolism thus more norpethidine

Uraemia can also cause seizures but unlikely to have such high urea levels with a Cr of 150. Typically it is hypocalcaemia rather than hypercalcaemia that causes seizures.

Other clinical features of hypocalcaemia

- Tetany, myopathy and weakness, cramps, QT prolongation, papilloedema, mental changes