

# Common Adverse Drug Reactions

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## 1. DIGOXIN

**Study:** 30 patients mean age 81.3 yrs receiving digoxin were compared to age- matched control group in regard to extensive color vision tests .Pts. with glaucoma, retinal/optic nerve disease, cataract, DM and congenital color deficiency excluded. In 20-30% of pts. taking dig, slight to moderate red-green impairment was observed, with 20% exhibiting severe titran deficiency. There was no correlation between vision impairment and dig levels.

**Toxicity:** arrhythmias, VTach, HA, dizziness, fatigue, nausea/vomiting , blurred / yellow-tinged vision, “halo” vision

- Low therapeutic index; Therapeutic Range 0.8-2 ng/ml T ½ 1.5-1.8 days , 70% renally cleared

### Risk factors for toxicity:

- Serum level > 2ng/ml(may see toxicity w/in normal range if underlying disease)
- Hypokalemia, hypomagnesemia, ischemic heart disease, hypothyroidism(decreased volume of distribution), impaired renal function, advanced age

CrCl                      % of normal rec maintenance dose

>50 ml/min              100%

10-50ml/min            75%

<10ml/min              10-25%

- Monitor dig level q 3-5days initially; regular monitoring of SrCr,K levels

## 2. VANCOMYCIN

**Case Report:** 46 y/o male receiving vancomycin slow infusion while under anesthesia for continuing orthopedic procedures experienced hypotension, bradycardia , and erythematous skin rash after 10 minutes of infusion. Pt. received supportive care, vancomycin infusion d/c'd and pt. was discharged next day.

- 80-90% IV dose renally cleared-not highly nephrotoxic in itself but requires dose adjustment for renal impairment to avoid accumulation to toxic levels

Sampling Time

Therapeutic Range

Trough < 1 hr prior to next dose

5-15 mg/L (HMC 5-10)

Peak 2 hrs post infusion(not always necessary)

20-40 mg/L

### Toxicity:

Concentration related:

- Monitor renal function QD to QOD in patients with unstable renal function or patients receiving concomitant nephrotoxic drugs such as aminoglycosides.
- Used as a single agent, vanco is rarely nephrotoxic
- If patient has normal renal function, one trough level should be sufficient

Non concentration related:

- Rapid administration may result in hypotension and rarely cardiac arrest
- “Redman’s Syndrome”-histamine-like reaction which may include flushing, tachycardia, rash involving upper torso, face and neck, and pruritis
- Administer dose over 1 hour to avoid above
- Occasional reversible neutropenia appearing 1 week or later after start of therapy

## 3. ACE INHIBITORS

**Case Report:** 73 y/o female presented to ER with 5hr h/o tongue swelling. Pt. stabilized on enalapril 20mg BID for 3 years. NKDA, neg for EtOH. No h/o injury, change in habits or meds. Blood workup WNL; no cervical lymphadenopathy. Pt. began Solu-Medrol, PCN and diphenhydramine; improved markedly

overnight. Patient again presented to ER 3 weeks later with same problem. ACE I was d/c'd, and pt. received similar supportive care. Pt showed no recurrence @ 1,3 and 12 months.

### **Acute renal failure**

- Adverse effects primarily related to decrease in angiotensin II formation
- seen in patients with CHF, bilateral renal artery stenosis, CRF, and polycystic kidney disease
- Increase in SrCr usually seen in 3-5 days
- Recommend strict monitoring of serum K

### **Hyperkalemia**

- MOA - reduction of ACE reduces aldosterone secretion which is responsible for excretion of urinary potassium
- Overall incidence of hyperkalemia (defined as plasma K concentration > 5.1 meq/L) is 10%
- Risk increased in CRI, DM, concomitant use of K sparing drugs(diuretics, spironlactone), elderly
- Serum K @ 1-2 weeks after initiation; monitor q 3 months thereafter

### **Cough**

- Incidence is 3-20%, appears in 1 week to 6 months of initiation of therapy
- Thought to be attributed to increase in concentration of prostaglandins, kinins and substance P, thromboxane, genetic factors may play a role
- Not seen in ARB's-may convert patient or lower dose of ACE I.

### **Angioedema**

- Rare, BUT potentially fatal (0.1-0.7%)
- May occur within a few hours to 1 year after initiation of therapy
- Pharyngeal, face, tongue edema; may lead to laryngeal obstruction
- Discontinue drug immediately; supportive care

## **4.SEROTONIN SYNDROME**

**Case Report:** 47 yo male with h/o major depression stabilized on venlafaxine XR 300mg/day and mirtazapine 30mg/day for 4 months. Pt. was started on tramadol secondary to chronic pain issues. Tramadol was titrated to 300mg/day over 4 weeks without consequence; dose further increased to 400mg/day to optimize pain relief.

After approx. 6 weeks pt. developed shivering, diaphoresis, agitation, confusion, hyperreflexia and mydriasis. U tox was negative All labs WNL. Pill count revealed compliance with meds. All meds d/c'd; pt. became tachycardic and febrile over the next 4 hours. Given IV hydration; symptoms resolved over 36 hrs. Venlafaxine and mirtazapine were restarted and titrated up; patient remained symptom free.

- SS occurs as a result of over stimulation of 5-HT receptors by serotonergic agents which include SSRI's, MAOI's(monoamine oxidase inhibitors), TCA's
- Amphetamines increase release of stored serotonin (HMC patients)
- Onset of symptoms can occur as early as 24hrs post dose increase of serotonergic agent or addition of second agent.
- Presents as confusion, fever, hyperhidrosis, myoclonus, hyperreflexia, tremors, chills, nervousness, insomnia, tachycardia, diarrhea, hypo/hypertension, mydriasis
- Supportive care: IV fluids for hydration, benzodiazepines for anxiety/agitation, discontinue serotonergic agent(s) immediately.
- Some cases may require anticonvulsants, ventilation and antihypertensives

## **5. STATINS**

**Case Report:** 42 y/o male developed myalgia, arthralgia and proximal muscle weakness 3 months after starting simvastatin 20mg QD. CK was elevated to 503 IU/L. Simvastatin d/c'd; NSAIDs used for 5 days without benefit; remission occurred 1 week after therapy with methylprednisolone 50mg QD

## Rhabdomyolysis/Myopathy

- Of 871 FDA reports of statin-related rhabdo , in 72% of cases a statin was the primary suspected cause, in 28% of cases a statin was a concomitantly administered drug or secondary suspect
- Increased risk of rhabdo when statins co-administered with gemfibrozil, macrolides, antifungals, protease inhibitors, warfarin and cyclosporine-**ARF a concern**
- Myopathy- seen from 1-2 weeks to 4 months after initiation of therapy; elevated CPK 3X ULN seen in 3-5% of patients treated with simvastatin
- Increase in serum CK, myalgias and weakness resolve within days to 4 weeks after discontinuation
- Pravastatin, fluvastatin preferred agents to be used in combo with gemfibrozil
- Routine monitoring of serum CK levels not generally recommended; however patients should be informed to report any new onset of myalgias or muscle weakness

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