

Managing Adverse Effects of ACE-I/ARB Therapy

Hypotension, early decrease in GFR, and hyperkalemia are all dose-related adverse effects related to the reduced Angiotensin II levels, through the inhibition of ACE or blockade of the Angiotensin II (AT1) receptor. These adverse effects may be avoided by gradual dose titration and carefully managed by decreasing or discontinuing the dose. The National Kidney Foundation guidelines suggest checking serum creatinine and potassium levels at baseline and at least every two weeks while titrating to the appropriate dose.¹

GFR

- There are a number of mechanisms for which this transient decline of GFR in CKD occurs. ACE-I/ARBs produce this effect through angiotensin II causing contraction of the mesangial cells, which thereby decrease the GFR by lowering the surface area available for filtration.⁴ Some additional causes of acute decline in GFR in CKD patients include decreased kidney perfusion, obstruction of urinary tract, and drug induced toxicity.¹
- Decline in GFR usually occurs within the first few days of starting therapy.¹
- If decrease in estimated GFR is 30-50%, reduce dose of ACE-I/ARB and monitor GFR every 5-7 days until GFR is within 30% baseline value.¹
- If decrease in estimated GFR is > 50%, discontinue ACE-I/ARB and monitor every 5-7 days until GFR is within 15% of baseline value.¹

Hyperkalemia

- The definition of hyperkalemia from the National Kidney Foundation guidelines is a serum potassium concentration >5.0 mEq/L.¹
- "The initial dose of the ACE-I/ARB should be 15% to 25% of the maximal recommended dose. If the initial dose is well tolerated, then cautiously titrate up. Give the dose once daily in the morning to permit nocturnal excretion of potassium, which may lower the risk of hyperkalemia."³
- Check for other clinical factors that may cause hyperkalemia in CKD (i.e. diet, acidosis, hyperglycemia (in diabetes), hyporeninemic hypoaldosteronism, oliguria, medications, laboratory error).¹
- Review patient's medication profile and discontinue medications that can impair renal potassium excretion (i.e. NSAIDS, beta blockers, heparin, cox-2 inhibitors, insulin antagonists, hypertonic solutions, digoxin, potassium supplements, herbal supplements, packed RBC infusions, potassium sparing diuretics, cyclosporine, tacrolimus, pentamidine, trimethoprim, lithium).¹
- Start patient on a low potassium diet (<=2-3 g/d) and avoid foods with a high potassium content (i.e. citrus fruits, bananas, cantaloupes, kiwis, mangos, strawberries, fruit juice, dried fruits, asparagus, avocado, beets, broccoli, carrots, corn, cauliflower, peas, tomato, potato, mushrooms, ground beef, steak, pork, lamb, veal, nuts, bran cereals, certain high energy sports foods, chocolate, coffee, tea, mussels, salt substitutes).¹
- If hyperkalemia develops, decrease the ACE-I/ARB dose by 50% and recheck the serum potassium in 5-7 days until it has returned to baseline. If serum potassium does not return to baseline in ~2-4 weeks, discontinue ACE-I and select another agent.¹

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- Add on loop diuretic (i.e. furosemide, bumetanide, torsemide) in order to increase the urinary potassium excretion. Loop diuretics are preferred in patients with a GFR <30 mL/min/1.73m² because thiazide diuretics have minimal effectiveness for ECF volume reduction at low GFR levels.¹

- If potassium increases to a value > 5.6 mEq/L despite precautions noted above, the ACE-I/ARB should be discontinued and another class of antihypertensive therapy should be used.^{1,2}

Cough

- ACE-I induced cough occurs in about 10-20% of patients, which is thought to be due to the accumulation of bradykinin, not an allergic reaction. Since ARBs do not inhibit bradykinin degradation, ARBs are very unlikely to produce a cough and should be used as an alternative if an ACE-I cannot be tolerated.¹

- Severity and onset can vary widely and usually regresses within a few days of discontinuation.¹

Contraindications to ACE-I/ARB Therapy

- Pregnancy, history of angioedema, allergy to ACE-I/ARB¹

References:

1. National Kidney Foundation. Clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. http://www.kidney.org/professionals/KDOQI/guidelines_bp/guide_11.htm. (Accessed October 14, 2008).
2. Palmer, BF. Angiotensin converting enzymes and angiotensin receptor blockers: what to do if the serum creatinine and/or serum potassium concentration rises. *Nephrol Dial Transplan* 2003; 18: 1973-1975.
3. Hebert LA. Optimizing ACE-inhibitor therapy for chronic kidney disease. *N Engl J Med* 2006; 354:189-91.
4. Rose, BD and Kaplan, NM. "Renal effects of ACE inhibitors in hypertension." Up to date. Last updated January 18th, 2005, (Accessed October 21st, 2008).

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MO-09-04-CKD Feb 2009

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