HYPERTENSION

1. Pathophysiology of Hypertension Secondary to Chronic Renal Failure

- Renal clearance of sodium and water is reduced causing accumulation of intravascular fluid contributing to hypertension.

- In some patients there is diminished renal perfusion causing inappropriate activation of the renin-angiotensin system.
    - Angiotensin II produces vasoconstriction and increased vascular resistance causing increased blood pressure.
    - Further reduced renal perfusion results in further increased sodium and fluid retention.

2. Therapy for Hypertension in Chronic Renal Failure

a) Goals of Therapy

- Prevent or slow further decline in renal function
- Prevent atherosclerosis, stroke, and cardiovascular disease
- Usual goal blood pressures:

    Systolic blood pressure < 130 mm Hg
    Diastolic blood pressure < 85 mm Hg

b) Lifestyle modifications

- Salt restriction
- Weight reduction
- Avoid tobacco
- Limit alcohol consumption
- If appropriate, start a regular exercise program

c) Pharmacotherapy

Empiric Drug Selection for Chronic Renal Insufficiency

- Elderly: Diuretics
- Diabetics: ACE inhibitors
- End Stage Renal Disease: Calcium Channel Blocker or ACE inhibitors
- Bilateral Renal Artery Stenosis: Calcium Channel Blockers
- Renovascular Hypertension: Calcium Channel Blocker or ACE inhibitors
- Others: Calcium Channel Blocker or ACE inhibitors

3. Clinical Pearls

- Goal blood pressure should be achieved gradually to allow adaptation to reduced perfusion pressures and to prevent ischemic episodes.
- Often multiple drugs at doses much greater than normally used are required to control hypertension in chronic renal failure patients.

4. Clinical Drug Reviews

Diuretics

- Diuretics have the added advantage of helping to control sodium and water retention in addition to blood pressure.

- The more proximal the site of action the greater the potency of the diuretic
  - Loop diuretics > Thiazides > Potassium Sparing Diuretics

- Diuretics with different sites of action work together synergistically. Profound diuresis can be a concern.

- **Thiazides** (hydrochlorothiazide, metolazone, chlorthalidone etc.)
  - Inhibits Na reabsorption at the distal portion of the ascending Loop of Henle
  - Natriuresis results in reduced peripheral vascular resistance
  - Alone they are not effective at creatinine clearances below 30 mL /min, but metolazone may still be useful for synergy with Loop Diuretics, since metalazone may also block proximal tubule sodium resorption

- **Loop Diuretics** (furosemide)
  - Inhibits Na reabsorption in the proximal portion of the Loop of Henle
  - Some vasodilating properties resulting in reduced renal vascular resistance
  - High doses are effective even at relatively low creatinine clearances. Are frequently discontinued when dialysis is initiated.

- **Potassium Sparing Diuretics** (amiloride, triamterene)
  - Inhibits reabsorption at the distal site of the renal tubule
  - Least potent class of diuretic – used with other diuretics to counteract their hypokalemic effect
  - Usually avoided in renal failure due to hyperkalemia and poor efficacy

Beta-Blockers

- Inhibit stimulation of beta-adrenergic receptors by catecholamines
- Can reduce renal blood flow secondary to negative cardiac inotropic effects

Angiotensin Converting Enzyme Inhibitors (and AIIRA)

- Prevent production of Angiotensin II (potent vasoconstrictor) causing vasodilation and dilation of efferent arteriole. In some patients can increase renal blood flow
- Reduce proteinuria and rate of progression of renal failure, especially in diabetics (Class A evidence)
- Hyperkalemia can be a problem during initial stages of renal dysfunction. The complete loss of renal function however, also produces the loss of the mechanism causing hyperkalemia.
- Most are cleared renally and have prolonged half – lives in renal failure

Calcium Channel Blockers (usually diltiazem, felodipine, amlodipine etc.)

- Reduce renal vascular resistance and increase renal blood flow

Alpha-Blockers

- Block activation of alpha receptors preventing catecholamine induced vasoconstriction

Central Acting Agents (clonidine)

- Stimulates postsymptomatic alpha 2 adrenergic receptors in the CNS, activating inhibitory neurons to produce a decrease in sympathetic outflow. Also has antagonist actions at presynaptic alpha receptors.

- Also can be used to treat restless leg syndrome (see BC Provincial Renal Agency website)

Vasodilators (hydralazine, minoxidil)

- Hydralazine reduces total peripheral resistance by direct action on vascular smooth muscle, with an effect greater on arterioles than on veins.

- Minoxidil causes direct relaxation of arteriolar smooth muscle, resulting in a reduction in total peripheral resistance.

Hypertension: Useful References

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