GREY’S HOSPITAL

PROTOCOL FOR MANAGEMENT OF DIURETIC RESISTANCE:
COMBINATION DIURETIC THERAPY AND CONTINUOUS INTRAVENOUS DIURETIC THERAPY
February 13, 2008

1. Diuretic resistance is multifactorial, including: hypoalbuminemia; increased sodium avidity in the post diuretic interval; decreased GFR; individual variations in bioavailability; protein binding in the tubule. Combination diuretic therapy, once maximum doses of Lasix have been reached is a viable option and ought to be considered. Continuous intravenous Lasix is effective and allows for larger doses with fewer side effects. Doses of greater than 1g have been tolerated well when given as an infusion over 24 hours.

2. Ceiling doses for Lasix (Bolus Dosing) are as follows:
   i. Renal Insufficiency: GFR 20-50ml/min, 80mg IV, 80-160 po
   ii. Renal Insufficiency: GFR<20mL/min, 200mg IV, 240mg po
   iii. Severe ARF: 500mg IV, NA po
   iv. Nephrotic normal GFR: 120mg IV, 240mg po
   v. Cirrhosis normal GFR: 40-80mg IV, 80-160mg po
   vi. CCF normal GFR: 40-80mg IV, 160-240mg po

3. Continuous Infusion of Lasix dosing schedule:
   i. Starting Bolus Dose 40mg IV
   ii. GFR< 25 mL/min: 20 then 40mg hourly
   iii. GFR 25-75 mL/min: 10 then 20mg hourly
   iv. GFR >75 mL/min: 10mg hourly

4. Combination Diuretic Therapy (to add to a ceiling dose of loop diuretic)
   a. Distal Convulated Tubule Diuretics (DCT)
      o Metolazone, 2.5-10mg po daily
      o Hydrochlorothiazide, 25-100mg po daily
      o Chlorothiazide, 500-1000mg IV
   b. Proximal Tubule Diuretics (PT)
      o Acetazolamide, 230-375 mg po daily, or up to 500mg po
   c. Collecting Duct Diuretics (CD)
      o Spironolactone, 100-200mg po daily
      o Amiloride, 5-10mg po daily

5. Combination Diuretic Therapy produces true synergism, the combination of agents is more effective than the sum of the responses to each agent alone. DCT diuretics are the class of drug most commonly combined with loop diuretics.
6. The DCT diuretic is administered 1 hour before the morning dose of the loop diuretic to ensure that NaCl transport in the distal nephron is blocked when it is flooded with solute.

7. Metolazone is the DCT diuretic most commonly combined with loop diuretics, because its half-life is relatively long and it has been reported to be effective when renal failure is present. Other thiazide and thiazide-like diuretics appear to equally effective, even in severe renal failure.

8. Complications of Diuretics:
   - Contraction of the vascular volume/circulatory collapse
   - Orthostatic hypotension
   - Hypokalemia
   - Hyperkalemia (spironolactone, triamterene and amiloride)
   - Hyperuricemia
   - Hypercalcemia
   - Hypercholesterolemia (beta adrenergic blocker or thiazide)
   - Hyponatremia
   - Metabolic alkalosis
   - Skin rash
   - Gastrointestinal upset
   - Hyperglycemia
   - Pancreatitis (thiazides)
   - Acute interstitial nephritis (thiazides, furosemide, triamterene)
   - Ototoxicity (furosemide)

9. When therapy with diuretics fails, ultrafiltration using hemodialysis equipment has been used.

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