MANAGING HEART FAILURE:

...ALL DIURETICS ARE NOT CREATED EQUAL

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Impact of Heart Failure

- In 2010, 6.6 million US adults ≥18 years of age (2.8%) had HF
- It is estimated that by 2030, an additional 3 million people will have HF, a 25.0% increase in prevalence from 2010
- In 2010, estimated heart failure costs the United States...
  34.4 BILLION dollars

YOU will treat patients with heart failure....

- As our population ages, this epidemic of heart failure will only continue to grow. The cost of providing heart failure ranks among the leading U.S. healthcare expenditures.
- Additionally, the toll of heart failure on life, both in quality and longevity, is sobering.
  * 50% of patients diagnosed with HF will die within 5 years
  * 30 day readmission rate - 25%
  * 6 month readmission rate- 50%
**Progressive Mortality**

All-Cause Mortality After Each Subsequent Hospitalization for HF

- 1st admission: p = 0.0194
- 2nd admission: p = 0.0058
- 3rd admission: p = 0.0128
- 4th admission: p = 0.0126

**Cause of Readmission**

Causes of Hospital Readmission for Heart Failure

- Diuretic Noncompliance: 24%
- Rx Noncompliance: 14%
- Inappropriate Rx: 16%
- Failure to Seek Care: 11%
- Other: 19%

**Historical Perspective**

- Dropsy: from the Greek word "hydrōp" or water described volume overload
- Caused by water retention in the soft tissues or cavities.
- Related to circulatory issues such as increase in hydrostatic pressure, decreased oncotic pressure or both.

**Treatment development**

- Bloodletting / leeches
- Salt restriction
- IV/M renal agents
- Sulfonamides (1937): weak diuretic effect
- Thiazides (1957)
- Loop diuretics (1960s): potent diuretics
Types of Heart Failure

HF with Reduced EF (HFrEF) ≤ 40%
- Systolic

HF with Preserved EF (HFpEF) > 40%
- Diastolic

Approach to Treatment of HFrEF

Assessment of EF
- NYHA Class II-IV, EF < 35%
- NYHA Class III-IV, EF < 35%, QRS > 120 ms

Apply evidence-based medications
- ICD
- CRT-P/CRT-D
- Cardiac Resynchronization Therapy

In selected patients:
- Aldosterone antagonists
- Digoxin

Apply evidence-based medications
- Diuretic
- ACEI/ARB & Beta-blocker Therapy
- Calcium channel blockers
- NSAIDS

Stop aggravating meds
- Select anti-arrhythmics
- Transplant
- LVAD
- Palliative Care

Approach to Treatment of HFpEF

Assessment of EF
- NYHA Class II-IV, EF > 40%

Control DBP and SBP
- Use BB, CCB, ACE, ARB

Control HR
- Tachy-arrhythmias such as atrial fibrillation or atrial tachycardia (decrease diastolic filling)

Optimize treatment of comorbidities
- Diabetes
- CAD
- Sleep apnea
- COPD
- Obesity
- Smoking cessation

Use cautiously
- NSAIDS
- Steroids (cause fluid retention)
Goals of Treatment & Self Care

Green Zone: All-clear: This zone is the goal; symptoms are under control
- Weight has not changed by more than 2 lbs
- No swelling in feet, legs, and abdomen
- No shortness of breath

Yellow Zone: Caution: This zone is a warning
- Weight gain of 2-3 lbs overnight or 4-5 lbs in a week
- Symptoms of HF
- USE ACTION PLAN: Diuretic titration? Who to call if not feeling better in 24 hours

Red Zone: DANGER: ACT NOW TIS IS AN EMERGENCY CALL 911
- Short of breath while sitting
- Chest pain
- Confusion: cannot think clearly

How do Hypervolemic Patients Present?
- Acute dyspnea/orthopnea/PND
- Extreme fatigue
- Decreased exercise tolerance
- Massive volume overload (2.2 lbs = 1 liter)
- Chest pain
- Pre-syncope / syncope
- Organ dysfunction (renal and liver)
- Abdominal edema and decreased appetite
- Lower extremity edema

Fluid Retention....Why?
- Diet indiscretion
- Medication non-adherence
- Use of NSAIDS
- Prednisone
- TZDs
- Diuretic resistance
- Advancing disease
**HF Diuretic Profile**

- **Thiazide diuretics**
  - hydrochlorothiazide (Microzide)
  - metolazone (Zaroxlyn)
  - chlorothiazide (Diuril)
  - chlorthalidone (Apo-chlorthalidone)

- **Loop diuretics**
  - furosemide (Lasix)
  - bumetanide (Bumex)
  - torsemide (Demadex)

- **Aldosterone Antagonists**
  - spironolactone (Aldactone)
  - eplerenone (Inspra)
  - K-sparing diuretics
    - amiloride and triamterene

**HF Diuretic Profile (contd.)**

- **Thiazide diuretics**
  - HTN
  - Heart failure, liver & kidney disease

- **Loop diuretics**
  - Diastolic HF / Systolic HF
  - Peripheral edema

- **Aldosterone Antagonists**
  - Systolic HF
  - Liver disease
  - Hyperaldosteronism
  - Combine with thiazides and loops to decrease hypokalemia

**Common Adverse Effects**

- **Loop diuretics**
  - Pearl:
  - Creates substantial diuresis-excreting up to 20% of the renal load of salt (NaCl) and water into the urine. Natural filtration excretes about 0.4% of salt load in the urine
  - Lowers potassium (loop), sodium (HCTZ), chloride, and magnesium levels
  - Hypovolemia /orthostatic hypotension
  - Azotemia
  - Contraction alkalosis
  - Gout exacerbations-hyperuricemia
  - Kidney stones - calcium excretion
  - Photosensitivity
  - Caution with sulfa allergies
  - Ototoxicity w/ aminoglycosides

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Common Adverse Effects

- **Thiazide diuretics**
  - Pearl: Responsible for hyponatremia with long term use and confusion/falls in geriatric population
  - Lowers potassium (loop), sodium (HCTZ), chloride, and magnesium levels
  - Orthostatic hypotension (metolazone)
  - Azotemia
  - Contraction alkalosis
  - Gout exacerbations-hyperuricemia
  - Effects on glucose control-decreases the effectiveness of anti-diabetic medications
  - Photosensitivity
  - Ototoxicity w/ aminoglycosides
  - Caution with sulfa allergies

Common Adverse Effects

- **Aldosterone Antagonists**
  - Pearl: Remember to decrease or stop potassium supplements
  - Hyperkalemia (caution w/ ACE)
  - Gynecomastia
  - Azotemia
  - Menstrual irregularities
  - Impotence

Oral Diuretics Dosage

- Furosemide (Lasix): Start at 20-40 mg daily or BID; Max-400 mg daily
- Bumetanide (Bumex): Start at 0.5 to 1.0 mg daily or BID; Max-10 mg daily
- Torsemide (Demadex): Start at 10-20 mg daily; Max-200 mg daily
- Metolazone (Zaroxolyn): Start at 2.5 mg daily; Max-20 mg daily
- HCTZ (Microzide): Start at 25 mg daily or BID; Max-200 mg daily
- Spironolactone (Aldactone): 12.5-25 mg daily; Max-50 mg daily
- Eplerenone (Inspra): 25 mg daily; Max-50 mg daily

*Titrate quickly: Goal 0.5-1.0 kg/day (1-2 lb/day) weight loss
*Monitor labs until goal weight achieved
Mechanism of Action

**Thiazides**
- Inhibit active exchange of Cl-Na in the cortical diluting segment of the ascending loop of Henle

**Loop of Henle**
- Inhibit reabsorption of Na in the distal convoluted and collecting tubule
- Inhibit exchange of Cl-Na-K in the thick segment of the ascending loop of Henle

Electrolyte Parade......

Diuretic Pharmacokinetics

<table>
<thead>
<tr>
<th>DRUG</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
<th>BIOAVAILABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furosemide (Lasix)</td>
<td>30-60 min</td>
<td>1-2 hrs</td>
<td>4-6 hrs</td>
<td>47-64%</td>
</tr>
<tr>
<td>Bumetanide (Bumex)</td>
<td>30-40 min</td>
<td>1-2 hrs</td>
<td>6-12 hrs</td>
<td>59-69%</td>
</tr>
<tr>
<td>Torsemide (Demadex)</td>
<td>60 min</td>
<td>variable</td>
<td>6-12 hrs</td>
<td>80-90%</td>
</tr>
</tbody>
</table>

Conversion Equation:
Lasix 40 mg = Bumex 1 mg = torsemide 20mg
Diuretic Pharmacokinetics

<table>
<thead>
<tr>
<th>DRUG</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCTZ</td>
<td>2 hrs</td>
<td>6 hrs</td>
<td>12-18 hrs</td>
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<tr>
<td>metolazone</td>
<td>1.5 hr</td>
<td>6 hrs</td>
<td>12-24 hrs</td>
</tr>
<tr>
<td>chlorothalidone</td>
<td>1 hr</td>
<td>2.6 hrs</td>
<td>24-72 hrs</td>
</tr>
<tr>
<td>spironolactone</td>
<td>unknown</td>
<td>4 hrs</td>
<td>72 hrs</td>
</tr>
</tbody>
</table>

Conversion Equation:
metolazone 5 mg = HCTZ 50 mg

Do You Admit?

Warm & dry... (+) perfusion / (-) congestion
Warm & wet... (+) perfusion / (+) congestion
Cold and wet... (+) perfusion / (+) congestion
Cold and dry... (-) perfusion / (-) congestion

Inpatient Diuretics

CHOICE?

IV bolus diuretics vs diuretic infusion
- Normal daily dose of diuretics x 2.5 divided into 2 daily doses
EX: Lasix 80 mg daily x (2.5) = 200 mg/2 doses=100 mg IV q 12hr
- Goal-net negative 1-1.5 liters/day; higher in some patients; evaluate each shift
- Frequent monitoring of labs
- Hemodynamic and cardiac monitoring
- Convert to oral dosing for 24 hr before discharge

Inpatient Diuretics

G. Michael Felker, M.D., M.H.S., Kerry L. Lee, Ph.D., David A. Bull, M.D., Margaret M. Redfield, M.D., Lynne W. Stevenson, M.D., Steven R. Goldsmith, M.D., Martin M. LeWinter, M.D., et al, for the NHLBI Heart Failure Clinical Research Network

DOSE Study Findings

- Prospective, double-blind, randomized trial with 308 patients
- Compared:
  - **12 hr bolus vs continuous infusion**
  - **Utilized low dosing (patients normal daily dose) vs. high dosing (normal daily dose x 2.5)**
- Findings:
  - **No significant difference in patients’ primary endpoints in 72 hours (assessments of symptoms or renal function)**
  - **Bolus group at 48 hr likely to require a dose increase**
  - **Low dose group at 48 hr likely to require a dose increase and not likely able to convert to oral med as occurred in high dose group**
  - **Non-significant trend in high dose group toward greater efficacy at endpoints; greater relief of dyspnea, greater fluid loss and fewer adverse events**

Causes of Diuretic Resistance

- Intravascular volume depletion
- Rebound Na uptake after volume loss
- Neurohormonal activation
- Decreased renal perfusion
- Impaired gut absorption of an oral diuretic
- Hypertrophy of distal nephron
- Reduced tubular secretion (renal failure, NSAID)
- Non-compliance with drug or diet

Diuretic Action Plan

- Double daily oral diuretic
- Transition to different loop diuretic
- Add a thiazide in combination PRN
- Office IV diuretics

- Fluid retention in abdomen can affect choice of diuretic
- Need BMP and magnesium monitoring
- BNP level can act as marker for treatment
### Flexible Diuretics Prescription

Your doctor has prescribed a diuretic (water pill) to help remove excess salt and water from your body. Your dose of {diuretic name} is {diuretic dose}.

**IF** your weight increases by more than {number} pounds **OR** you feel more short of breath **OR** your feet or belly swell

**Then:** [Take additional diuretic] *(Optional additional potassium)*

**IF** your symptoms do not improve by the next day, call your doctor.

Use your laboratory slips to have blood work done in {number} days after additional diuretics.

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### CASE STUDY

HF Homeostasis…..

- Transitional Care
- PCP
- Readmission
- ED
- Patient Support
- Death
QUESTIONS?