Pharmacotherapy of Heart failure with multiorgan dysfunction

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Agenda:-

• Cardiorenal syndrome
• Continuous infusions loop diuretics VS bolus
• Pharmacological VS Ultrafiltration in management of Cardiorenal syndrome with volume over load
• Comparison between different inotropic agents used in the management of acute decompensated heart failure
• Hints and notes about inotropic agents
Cardiorenal syndrome:

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type 1</strong></td>
<td><strong>Acute Cardiorenal Syndrome</strong></td>
</tr>
<tr>
<td><strong>Type 2</strong></td>
<td><strong>Chronic Cardiorenal Syndrome</strong></td>
</tr>
<tr>
<td><strong>Type 3</strong></td>
<td><strong>Acute Renocardiac Syndrome</strong></td>
</tr>
<tr>
<td><strong>Type 4</strong></td>
<td><strong>Chronic Renocardiac Syndrome</strong></td>
</tr>
<tr>
<td><strong>Type 5</strong></td>
<td><strong>Secondary Cardiorenal Syndrome</strong></td>
</tr>
</tbody>
</table>

### Volume Management of acute Heart Failure

- **Desirable**
  - Relieve symptoms of congestion
  - Can correct hyponatremia of volume overload
  - Decrease heart size and wall stress

- **Undesirable**
  - Increase metabolic abnormalities
  - Potential for intravascular depletion or hypotension
  - Activate neurohormonal mediators
Intravenous loop diuretics

Recommended for patients with ADHF and evidence of significant volume overload as

- Furosemide
- bumetanide
- Torsemide

After an intravenous bolus, *loop diuretics reduce preload within 5–15 minutes through functional venodilation*

Later (after more than 20 minutes) by sodium and water excretion

In patients receiving chronic loop diuretic therapy before admission intravenous loop diuretics should be administered *at a dose that equals or exceeds the chronic oral daily dose*

Cont. infusion VS bolus of loop diuretics

*Table 2: Secondary End Points for Each Treatment Comparison.*

<table>
<thead>
<tr>
<th>End Point</th>
<th>Bolus Every 12 Hr (N = 156)</th>
<th>Continuous Infusion (N = 152)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC for dyspnea at 72 hr</td>
<td>4456 ± 1468</td>
<td>4699 ± 1573</td>
<td>0.36</td>
</tr>
<tr>
<td>Freedom from congestion at 72 hr — no./total no. (%)</td>
<td>22/153 (14)</td>
<td>22/144 (15)</td>
<td>0.78</td>
</tr>
<tr>
<td>Change in weight at 72 hr — lb</td>
<td>-6.8 ± 7.8</td>
<td>-8.1 ± 10.3</td>
<td>0.20</td>
</tr>
<tr>
<td>Net fluid loss at 72 hr — ml</td>
<td>4237 ± 3208</td>
<td>4249 ± 3104</td>
<td>0.89</td>
</tr>
<tr>
<td>Change in NT-proBNP at 72 hr — pg/ml</td>
<td>-1316 ± 4364</td>
<td>-1773 ± 3828</td>
<td>0.44</td>
</tr>
<tr>
<td>Worsening or persistent heart failure — no./total no. (%)</td>
<td>38/154 (25)</td>
<td>34/145 (23)</td>
<td>0.78</td>
</tr>
<tr>
<td>Treatment failure — no./total no. (%)</td>
<td>59/155 (38)</td>
<td>57/147 (39)</td>
<td>0.88</td>
</tr>
<tr>
<td>Increase in creatinine of &gt;0.3 mg/dl within 72 hr — no./total no. (%)</td>
<td>27/155 (17)</td>
<td>28/146 (19)</td>
<td>0.64</td>
</tr>
<tr>
<td>Length of stay in hospital — days</td>
<td>5</td>
<td>5</td>
<td>0.97</td>
</tr>
<tr>
<td>Median</td>
<td>3–9</td>
<td>3–8</td>
<td></td>
</tr>
<tr>
<td>Interquartile range</td>
<td></td>
<td></td>
<td>0.36</td>
</tr>
<tr>
<td>Alive and out of hospital — days</td>
<td>51</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>42–55</td>
<td>38–55</td>
<td></td>
</tr>
<tr>
<td>Interquartile range</td>
<td></td>
<td></td>
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Adapted from *DOSE* study The NEW ENGLAND JOURNAL of MEDICINE
According to the results of the Diuretic Optimization Strategies Evaluation (DOSE) trial

Initial loop diuretic therapy may be administered as either intermittent boluses or continuous infusion because no differences occurred in

• Co-primary end points of patient global assessment of symptoms

• Mean change in serum creatinine when either intermittent bolus versus continuous infusion administration

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**Fluid balance**

• After a single intravenous bolus of loop diuretic, *250–500 mL of fluid loss should occur within 4 hours*

• Common 24-hour goals for fluid loss are *1–2 L net negative*, although some patients may experience and tolerate greater net fluid loss.

• Selected patients (e.g., those with poor renal function, low (albumin)) may only tolerate being *net negative less than 1 L/day.*
Ultrafiltration

When to consider ultrafiltration

- Marked volume overload, including patients with anasarca
- Patients with decompensated heart failure and reduced renal function With creatinine < 3.0 mg/dL,
- Patients with fluid retention symptoms refractory to intravenous diuretics
Comparing ultrafiltration and Pharmacological therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>Results</th>
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<tbody>
<tr>
<td>(UNLOAD) study Intravenous Loop diuretics vs ultrafiltration in patients with ADHF.</td>
<td>Trial suggested that ultrafiltration improved weight loss and net fluid loss compared with intravenous diuretics, as well as reduced readmissions and urgent office or emergency department visits.</td>
</tr>
<tr>
<td>Cardiorenal Rescue Study in Acute De-compensated Heart Failure (CARRESS-HF) trial, a more recent study of patients with ADHF, persistent congestion, and renal impairment.</td>
<td>The study used algorithmic of stepped pharmacologic therapy (i.e., loop diuretics, thiazide-type diuretics, vasodilators, and inotropes) was superior to ultrafiltration at preserving renal function with a similar amount of weight loss.</td>
</tr>
</tbody>
</table>

Comparison between inotropic agents in hemodynamics effect
Effect on myocardial oxygen consumption

Source: Adapted from Colucci et al

FIGURE 9.15 The effects of nitroprusside, milrinone, and dobutamine on myocardial oxygen consumption. Nitrates decrease myocardial oxygen consumption by decreasing preload and afterload due to vasodilation. Milrinone has a balanced effect on myocardial oxygen consumption acting as a vasodilator (similar to nitrates) offset by increases in contractility. Dobutamine will increase contractility and lead to a moderate increase in myocardial oxygen consumption. Source: Adapted with permission from Monrad et al., Circulation, 1986;73(3 Pt 2): III168-III174.
Hints about notes about the Inotropic agents

- At lower doses dobutamine have vasodilation effect

- Dobutamine **not eliminated renally** so its preferred in patients with Renal impairment over milrinone

- Milrinone is often recommended in patients receiving chronic β-blockers because it bypasses β receptors although there is no strong evidence support this
Dobutamine can be titrated every 5–15 minutes depending on response. A notable exception is patients receiving dobutamine (greater than 24 hours) because down-regulation of β-adrenergic receptors.

Milrinone is primarily eliminated by renal clearance, and its half-life can be especially prolonged in patients with significant renal impairment.

Milrinone should be titrated more slowly because of its slower onset of action and longer half-life (e.g., every 6–12 hours, or up to every 12 hours in patients with renal impairment).

The systemic vasodilating effects of milrinone may be problematic in patients with low blood pressure. Therefore, dobutamine is usually preferred in patients with marginal blood pressure, although it, too, can lower blood pressure at low doses.
Ref:-


• Pharmacotherapy principle and practice 2016


• Four stages of Heart failure 2016


Thank you for Your Attention