Pharmacotherapy of Heart failure with multiorgan dysfunction

Islam Hassan aldafrawy
Pharm.D.
Senior clinical pharmacist

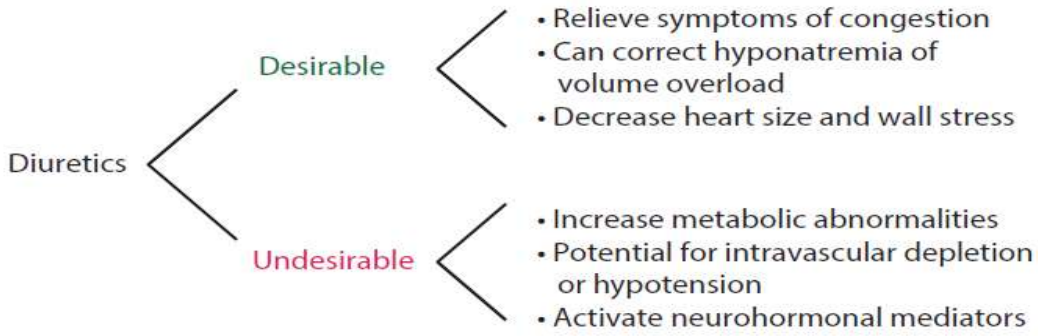
Agenda:-

- 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:-

TYPE 1 ACUTE CARDIORENAL SYNDROME	Rapid worsening of cardiac function leading to acute kidney injury.
TYPE 2 CHRONIC CARDIORENAL SYNDROME	Chronic abnormalities in cardiac function causing progressive chronic kidney disease.
TYPE 3 ACUTE RENOCARDIAC SYNDROME	Abrupt and primary worsening of kidney function leading to acute cardiac dysfunction.
TYPE 4 CHRONIC RENOCARDIAC SYNDROME	Primary chronic kidney disease contributing to decreased cardiac function, ventricular hypertrophy, diastolic dysfunction, and/or increased risk of adverse cardiovascular events.
TYPE 5 SECONDARY CARDIORENAL SYNDROME	Presence of combined cardiac and renal dysfunction due to acute or chronic systemic disorders.[4]

Volume Management of acute Heart Failure



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.*

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

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

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.

Factors that Affect Target Rates of Fluid Removal in Heart Failure

Baseline factors that may warrant slower target rates of fluid removal

- Low systolic blood pressure
- Low glomerular filtration rate
- Low central venous pressure
- Low initial volume overload
- Diabetes mellitus
- Proteinuria
- Small body size

Once therapy is initiated, other factors that may suggest a need for slower target rates of fluid removal

- Creatinine rise
- Decreases in systolic blood pressure / hypotension
- Urine output < 125 cm^3/6 hr
- Hemoconcentration

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

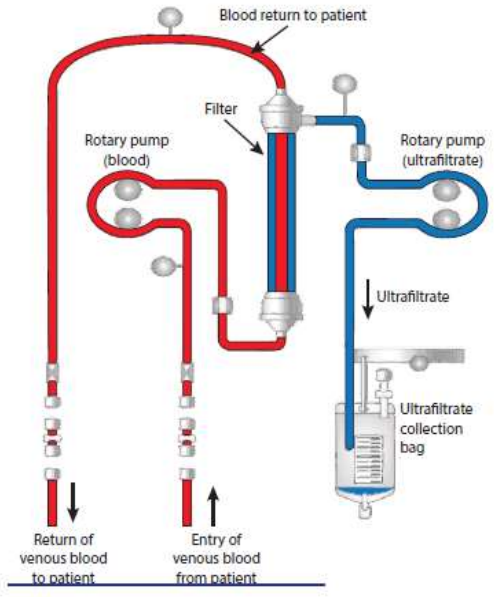
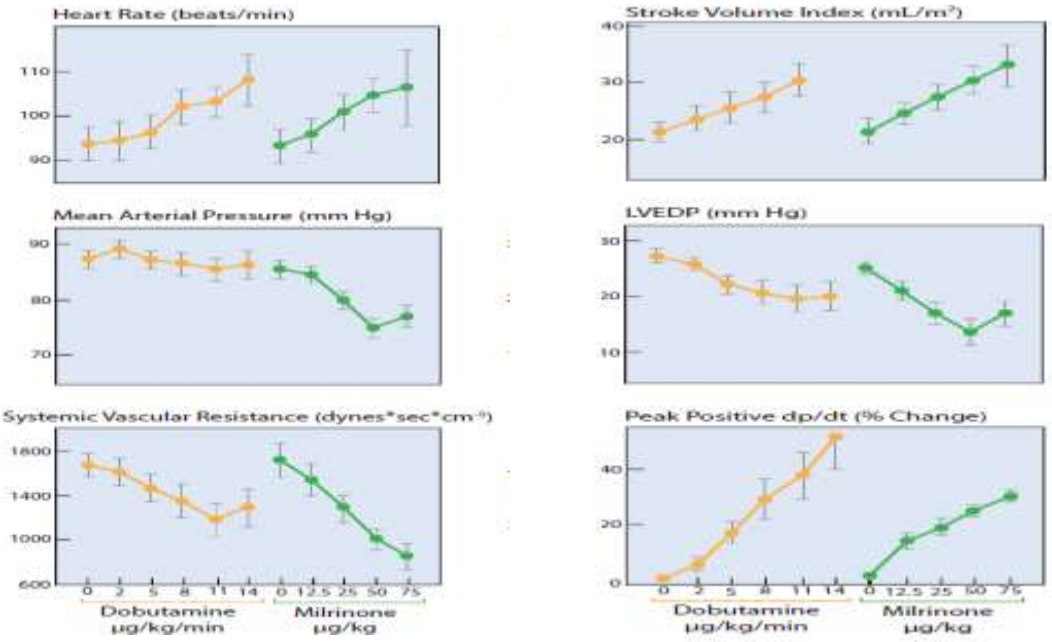


FIGURE 9.6 Diagram of a peripheral venous access ultrafiltration device. In the filtration column the rotary pump creates a pressure gradient for extraction of fluid by the process of convection.[11] *Source:* Adapted from CHF Solutions Inc., Brooklyn Park, MN, with permission.

Comparing ultrafiltration and Pharmacological therapy

Study	Results
(UNLOAD) study Intravenous Loop diuretics vs ultrafiltration in patients with ADHF.	Trial suggested that ultrafiltration improved weight loss and net fluid loss compared with intravenous diuretics, as well as reduced read-missions and urgent office or emergency department visits
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.	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

Comparison between inotropic agents in hemodynamics effect



Source: Adapted from Colucci et al

Effect on myocardial oxygen consumption

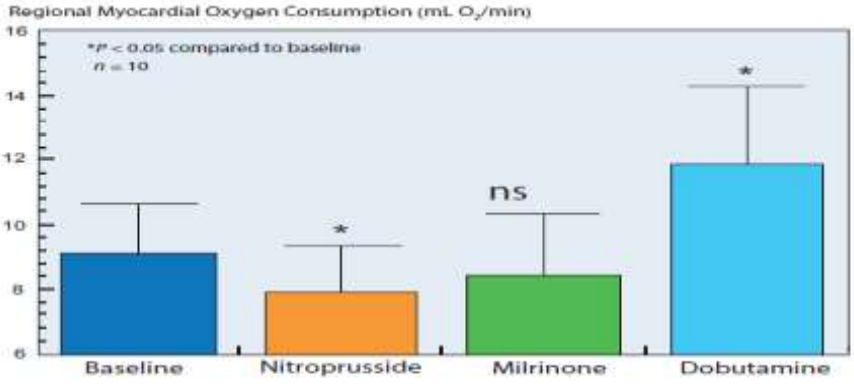
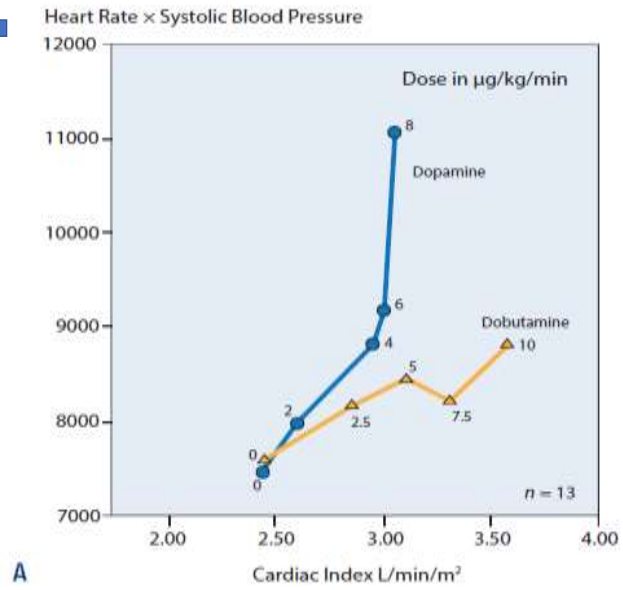


FIGURE 9.15 The effects of nitroprusside, milrinone, and dobutamine on myocardial oxygen consumption. Nitrates decrease myocardial oxygen consumption by decreasing preload and afterload due to vasodilation. Milrinone has a balanced effect on myocardial oxygen consumption acting as a vasodilator (similar to nitrates) offset by increases in contractility. Dobutamine will increase contractility and lead to a moderate increase in myocardial oxygen consumption.[28] *Source:* Adapted with permission from Monrad et al., *Circulation*. 1986;73(3 Pt 2): III168-III174.

Used as indicator of myocardium oxygen consumption



Comparison between dobutamine and dopamine and dose related effect of both in Cardiac index and Oxygen consumption
Adapted from Leier et al.,

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 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

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Thank you for Your Attention