Electrolytes and Heart Failure

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Conflicts of interest: Education consultant for Medtronic
Electrolyte abnormalities in HF

Common
Potentially serious
Associated with poor prognosis
Often iatrogenic
Vigilence is vital
First presentation - DCM

52 year old lady

NYHA III on admission, peripherally overloaded, raised JVP, third heart sound, congestion on CXR

Started on IV furosemide bolus then infusion

Echo shows LV dilated, EF 10-15%, BNP ~2000

In sinus tachycardia, BP stable
Causes of Electrolyte Abnormalities

- Decrease in cardiac output leads to decrease in renal blood flow:
  - Reduced glomerular filtration
  - Impairs excretion of water and electrolytes
- Activates the neurohormonal response
  - Renin-angiotensin-aldosterone system
  - Sympathetic nervous system
  - Arginine vasopressin (AVP)
- Diuretics, ACE inhibitors/ARB/MRAs

Ronco C et al. J Am Coll Cardiol 2008; 52:1527
Arginine vasopressin (AVP)

- Low dose: Stimulates V2 receptors
  - Increases aquaporin 2 channels
  - Increased water permeability
  - Increased water reabsorption
  - Concentrated urine (More water retention) (Antidiuresis)

- Higher dose: Stimulates V1a receptors
  - Decreased flow through vasa recta
  - Increased hepatic urea production
  - Increased urea reabsorption

Verbrugge FH et al. J Am Coll Cardiol 2015; 65:480
Inappropriate AVP in HF patients

- Plasma AVP levels progressively increase as HF worsens according to cardiac index and NYHA class.

- Aquaporin 2 water channels progressively increase as HF worsens according to cardiac index and NYHA class.

Abnormal U&Es

- Diuretic naïve
- 2 litres negative fluid balance overnight
- 2 kg weight loss
- BP holding
- No PND for the first time
- JVP still elevated ++

- Na 134
- K+ 3.3
- Urea 11.6
- Creatinine 114
- eGFR 72

- 3rd HS persists
A rise in urea may serve as an indicator of neurohormonal activation

Angiotensin and adrenergic stimulation

- Renal vasoconstriction
- Reduced GFR
- Reduced renal blood flow

Increased proximal tubular sodium and water reabsorption

Decreased distal fluid delivery slows tubular flow in the collecting duct

Reabsorption of urea in the collecting duct is mediated by AVP

Enhances flow-dependent urea reabsorption

Urea story summary

- A rise in urea may serve as an indicator of neurohormonal activation
- Significant rise in JVP with higher urea levels
- Patients with higher urea levels may need the cardioprotective effect of ACE inhibitors the most
- This cardioprotective effect of ACE inhibitors has been shown to be effective across a spectrum of urea values

Klein L et al. OPTIME CHF Circ HF 2008;1:25
RW Schrier Circ Heart Fail. 2008;1:2
Creatinine increase with decongestion

- ROSE AHF data analysed – 283 patients
- Small to moderate increases in creatinine commonly complicate decongestion
- Aggressive dosing of loop diuretics was not associated with elevation in markers of tubular injury
- Perhaps continue decongestion and uptitration of neurohormonal blockade?
  - Note patients selected for clinical stability
  - Close clinical assessment required

Renal summary

- Sodium and water retention is caused by poor cardiac output activating RAAS, SNS, AVP
- HF patients often have inappropriately elevated plasma AVP levels
- A rise in urea may serve as an indicator of neurohormonal activation
- Bumps in creatinine of uncertain significance – careful clinical assessment
SODIUM
Abnormal sodium levels in HF

1000 HF patients – any cause or severity (inpatient or clinic)

5 year follow-up

Deubner N et al. Eur J Heart Failure 2012;14:1147
Sodium and mortality risk

Both hypernatraemia and hyponatraemia indicate a 2-fold increase in the 5-year mortality risk in patients with HF

Both HF REF and HF PEF

Even within the normal range, hyponatraemia is associated with adverse long-term prognosis

Deubner N et al. Eur J Heart Failure 2012;14:1147
Optimum sodium level

Optimum sodium levels 140-145 mmol/L
Possibly indicates a lower degree of neurohormonal activation, therefore inhibits non-osmotic AVP secretion
Perhaps indicates a favourable water balance achieved by fluid restriction and diuretics
Differential prognosis within the normal sodium range

MAGGIC Meta-analysis data

14,766 patients from 22 studies

A linear increase in 3 year mortality was identified at levels < 140 mmol/L

Rusinaru D et al. Eur J Heart Fail 2012;14,1139
Hyponatraemia

- Most hyponatraemia is mild, asymptomatic and easily correctable
- Otherwise, differentiate dilutional hyponatraemia from depletional hyponatraemia
- Most HF hyponatraemia is dilutional rather than depletional
Dilutional hyponatraemia

- Treat congestion with diuretics
- Stop MRA/thiazides/amiloride
- Improve distal nephron flow
  - ACEi/ARB
  - Vasodilators
- Consider acetazolamide if combination diuretics required for resistant congestion

Verbrugge FH et al. J Am Coll Cardiol 2015; 65:480
Imiela T el at. Clin Drug Investig 2017;37:1175
Depletional hyponatraemia

- Hypovolaemia – assess fluid status
- GI or other fluid losses?
- High dose or combination diuretics?
- Check plasma and urine osmolality
- Check for potassium and magnesium depletion
- Treat with saline

Verbrugge FH et al. J Am Coll Cardiol 2015; 65:480
Tolvaptan

- AVP V$_2$ antagonist
- Promotes free water excretion by preventing aquaporin 2 channels so water not reabsorbed
- EVEREST Studies - Addition of tolvaptan to standard HF treatment:
  - Reduced weight and oedema
  - No worsening renal function
  - No improvement in mortality or HF-related morbidity at 1 year

Konstam MA et al. JAMA. 2007;297:1319
SECRET of CHF Trial

- Challenging decongestion:
  - hyponatraemia
  - renal dysfunction
  - suboptimal diuretic response to initial treatment

- SECRET of CHF Trial – Diuretics plus Tolvaptan 30mg/day versus placebo

- More weight loss but no improvement in dyspnoea

Konstam MA et al. J Am Coll Cardiol 2017;69:1409
Hyponatraemia in EVEREST

- 92 patients sodium < 130 – fewer clinical events when treated with tolvaptan
- Tolvaptan could be considered for patients with volume overload and symptomatic hyponatraemia (<130 mmol/L)
- Watch for hypokalaemia
- Maximum treatment 30 days

Hauptman PJ et al. J Cardiac Fail 2013;19:390
Hypernatraemia

Sodium > 145 mmol/L
Associated with loop diuretics – often hypovolaemic
Patients at risk have:
  - Impaired thirst sensation
  - Poor mobility/mental problems impairing access to water
  - Parenteral nutrition
  - Older
  - Less often treated with beta blockers

Treat with 5% dextrose – careful review and assessment of fluid status

Deubner N et al. Eur J Heart Failure 2012;14:1147
Sodium summary

- Hyponatraemia and hypernatraemia both associated with poorer prognosis
- Optimum sodium 140-145 mmol/L
- Most hyponatraemia is dilutional
- No firm data that treating hyponatraemia improves outcomes
- Unclear whether hyponatraemia is a marker or mediator
POTASSIUM
Dyskalaemia

- Hypokalaemia and hyperkalaemia both potentially dangerous
- Prevention crucial
  - regular monitoring
- Loop diuretics decrease potassium
- MRA/RAASi increase potassium
Optimum potassium 4.0-5.0

All cause mortality significantly elevated for every 0.1 mEq/L below 4.0 or above 5.0

Acute HF post MI

Substantially increased risk of death with K+ levels outside 3.9-4.5 mmol/L

Hypokalaemia

- Risk of Torsades de Points
- Give oral or IV potassium
- 1 tablet of sando K is 12 mmol K+
- Up to three tablets tds
Why does MRA cause hyperkalaemia?

- Usually, reabsorption of sodium creates an electrical gradient
- So potassium is secreted into the urine
- If the aldosterone-sensitive sodium channels are blocked, then potassium is not secreted
- Either less hypokalaemia, or hyperkalaemia
RAAS inhibitor use after hyperkalemia

Epstein Am J Manag Care 2015;21:S212
Benefit of spironolactone

Rates of death after visit 2 (4 weeks) by treatment, based on serum potassium levels at visit 2.

Orly Vardeny et al. Circ Heart Fail. 2014;7:573
Definitions of hyperkalaemia

- Mild hyperkalaemia 5.5-6.0 mmol/L
- Moderate hyperkalaemia 6.0-6.5 mmol/L
- Severe hyperkalaemia > 6.5 mmol/L
  - Most studies have intervention required at 5.5
  - (eg reduce drug and repeat)

- Is this true hyperkalaemia?
  - Delayed separation and processing cause pseudohyperkalaemia

Clinical Practice Guidelines, UK Renal Association 2014
ECG Changes

Figure 2: Progressive changes in ECG with increasing severity of hyperkalaemia.
Arrhythmias
Treatment of hyperkalaemia

- Calcium
- Insulin/dextrose
- Beta 2 agonists
- Loop diuretics
- Dialysis

Figure 4: There are five key steps in the treatment of hyperkalaemia (*never walk away without completing all of these steps*).
Protect the heart

- 30mls of calcium gluconate required
- Duration of action only 30-60 minutes

10 ml 10% Calcium Chloride = 6.8 mmol Ca$^{2+}$

10 ml 10% Calcium Gluconate = 2.26 mmol Ca$^{2+}$
Serum K+ 9.3 mmol/L

Following 20ml 10% calcium gluconate IV
Potassium summary

- Hypokalaemia and hyperkalaemia both potentially dangerous
- Optimum potassium 4.0-5.0 mmol/L
- Replace K+ if hypokalaemia
- Protect with calcium if severe hyperkalaemia
- Then shift potassium into cells and out of the body
- ECG and rhythm monitoring
MAGNESIUM
Magnesium

- Earlier studies suggested arrhythmias with low magnesium
- ? Before routine beta blocker use
  

- EVEREST data – higher magnesium levels poorer outcome
  
  Vaduganathan M et al. Am J Cardiol 2013;112:176

- Lower magnesium levels may reflect aggressive use of diuretics and hence better prognosis
  
  Angkananard T et al. Medicine 2016;95:5016
Magnesium replacement

- Magnesium toxicity rarely occurs
- The risk of adverse events with magnesium administration is small
- Magnesium administration can specifically help to suppress Torsades de Points arrhythmias

2015 ESC Guidelines Ventricular arrhythmias and prevention of SCD

- Subclinical magnesium deficiency common

DiNicolantonio JJ et al. Open Heart 2018;5

- No role for routine measurement or magnesium supplements in HF

Adamopoulos et al. Int J Cardio 2009;36:270
Electrolyte abnormalities in HF:
- Common
- Potentially serious
- Associated with poor prognosis
- Often iatrogenic
- Vigilence is vital
Common electrolyte abnormalities

- Hyponatraemia
- Hypernatraemia
- Hypokalaemia
- Hyperkalaemia
- Hypomagnesaemia

Table 7: Treatment on discharge for LVSD in 2015/16

<table>
<thead>
<tr>
<th>Medication</th>
<th>Total prescribed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor</td>
<td>72</td>
</tr>
<tr>
<td>ARB</td>
<td>21</td>
</tr>
<tr>
<td>ACE or ARB</td>
<td>83</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>87</td>
</tr>
<tr>
<td>MRA</td>
<td>53</td>
</tr>
<tr>
<td>ACE and ARB</td>
<td>0.5</td>
</tr>
<tr>
<td>*ACEI or ARB, beta blocker and MRA</td>
<td>44</td>
</tr>
<tr>
<td>Loop diuretic</td>
<td>92</td>
</tr>
<tr>
<td>Thiazide diuretic</td>
<td>6</td>
</tr>
<tr>
<td>Digoxin</td>
<td>23</td>
</tr>
</tbody>
</table>
**Action of diuretics**

- **Acetazolamide** acts in the proximal tubule.
- **Thiazide-type diuretics** act in the distal tubule.
- **Loop diuretics** act in the thick ascending limb of the loop of Henle.
- **Potassium-sparing diuretics** act in the collecting tubules.