Dietary trials in Heart Failure: SODIUM-HF

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March 2019
Disclosures / COI / RWI / RWA

- Available online: thecvc.ca
- PI of SODIUM-HF trial
- Not a dietician
*There are no RCT involving pepper or Salt’n’Pepa for patients with HF
What’s the real issue with salt?

• Which population?
  • HTN, CAD, prevention, elderly, kids.....
  • PURE etc is all non-HF

• What dietary context?
  • Eating what, when, with whom, and how?

• Sodium measurement issues?
  • Spot urinary sodium vs diet intake

• What outcome?
  • BP vs. mortality
But where did this salt business all start?

Skipping 1800s till 1970s
DASH Trial

<table>
<thead>
<tr>
<th>Sodium Intake</th>
<th>3200mg</th>
<th>2400mg</th>
<th>1600mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 wks</td>
<td>g</td>
<td>g</td>
<td>g</td>
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</tbody>
</table>

Systolic Blood Pressure (mmHg)

Diastolic Blood Pressure (mmHg)

24 h Urinary Sodium (mmol)

~400 patients w/HTN
Metabolic kitchen making all meals
12 weeks total
Surrogate outcomes

Figure adapted from: He J and MacGregor GA. Prog in Cardiovasc Dis. 2010; 52:363-82
Heart Failure and Sodium

• Heart failure (HF) is associated with neurohormonal activation and abnormalities in autonomic control that lead to sodium and water retention

• Clinicians have focused on dietary sodium and water restriction to minimize the risk of volume overload

• Little evidence supports this practice

• We spend +++time ($) doing this – VALUE?
LOW SODIUM INTAKE

- Diuretics
- Mean PCWP
- Myocardial Wall Stress & Functional MR
- Congestion
- Decompensated Heart Failure

-Gupta et al. Circulation 2012
Observational data
Clinical question

Does advising a patient to lower the amount of sodium in their diet change the clinical outcome?
Observational studies: HF

n= 123 patients with HF

HF Hospitalization

Mortality

RCTs
Parenterally administered saline solutions
250–1000 mg of furosemide daily
Fluid restriction 1 litre/day

Forest plot of relative risks for mortality
Low quality RCTs: helpful?

- Small RCT in AHF with HFpEF
- N=53 patients, 2 groups, 7 days
- 0.8 g/sodium + 800 mls fluid vs usual care (~4g sodium, unlimited fluid)
- No change in BNP, weight, congestion etc
- Increase in thirst in restricted group

Dalmedia, nutrition 2018
Small RCT

n= 195 patients with HF, Outpatient, Mexico city

- **Intervention group:** Dietary recommendations for sodium restriction to <2400 mg/day provided by a dietitian.

- **Control Group:** Usual dietary recommendations for dietary sodium reduction.

<table>
<thead>
<tr>
<th>Guideline and year</th>
<th>Sodium restriction recommendation / day</th>
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<tbody>
<tr>
<td>Canadian Cardiovascular Society 2017</td>
<td>&lt;2300 mg</td>
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<tr>
<td>AHA/ ACC/ HFSA 2017</td>
<td>None</td>
</tr>
<tr>
<td>European Society of Cardiology 2016</td>
<td>None</td>
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</tbody>
</table>

IOM = <1500 mg/day for all people
HFC Dietician waiting to pounce....
Measurement
Measuring Sodium/Adherence?
Measuring Sodium/Adherence?

**Plasma**
Easy

Tightly regulated, physiologically

Well-validated lab technique

Reflects acute change
<table>
<thead>
<tr>
<th></th>
<th>Plasma</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Easy</strong></td>
<td>Easy</td>
<td>Easy (spot), hard (24H)</td>
</tr>
<tr>
<td>Variability/debate on methods</td>
<td>Depends on excretion /reabsorption</td>
<td>Well-validated lab technique</td>
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<tr>
<td>Tightly regulated, physiologically</td>
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<td>90-95% ingested is excreted (assumed)</td>
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## Measuring Sodium/Adherence?

<table>
<thead>
<tr>
<th>Method</th>
<th>Difficulty</th>
<th>Notes</th>
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<td><strong>Plasma</strong></td>
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<td></td>
<td></td>
<td>90-95% ingested is excreted (assumed)</td>
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<tr>
<td><strong>Diet</strong></td>
<td>Easy-Hard</td>
<td>Variability in reporting</td>
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<tr>
<td></td>
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<td>Need to know food (exact)</td>
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<tr>
<td></td>
<td></td>
<td>Well-validated technique</td>
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<td>Reflects consumption</td>
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Food vs. Urine: Diuretics

Patients with HF not on loop diuretics (n=47)

Est. Sodium Intake (mg/day) vs. Urinary Sodium Excretion (mg/day)

$r=0.678$
$p<0.001$
Food vs. Urine: Diuretics

Patients with HF not on loop diuretics (n=47)

Urinary Sodium Excretion (mg/day)
Est. Sodium Intake (mg/day)

r=0.678
p<0.001

Non-HF cardiac patients (n=96)

Urinary Sodium Excretion (mg/day)
Est. Sodium Intake (mg/day)

r=0.624
p<0.001
Food vs. Urine: Diuretics

Patients with HF not on loop diuretics (n=47)

Non-HF cardiac patients (n=96)

Patients with HF on loop diuretics (n=62)

Est. Sodium Intake (mg/day) vs. Urinary Sodium Excretion (mg/day)

- Patients with HF not on loop diuretics: r=0.678, p<0.001
- Non-HF cardiac patients: r=0.624, p<0.001
- Patients with HF on loop diuretics: r=0.131, p=0.312

Arcand, AJCN 2011
**Food vs. Urine: Diuretics**

**Patients with HF not on loop diuretics (n=47)**

- Urinary Sodium Excretion (mg/day)
- Est. Sodium Intake (mg/day)
  - Correlation: \( r = 0.678 \)
  - Significance: \( p < 0.001 \)

**Non-HF cardiac patients (n=96)**

- Urinary Sodium Excretion (mg/day)
- Est. Sodium Intake (mg/day)
  - Correlation: \( r = 0.624 \)
  - Significance: \( p < 0.001 \)

**Patients with HF on loop diuretics (n=62)**

- Urinary Sodium Excretion (mg/day)
- Est. Sodium Intake (mg/day)
  - Correlation: \( r = 0.131 \)
  - Significance: \( p = 0.312 \)

**HF patients not on a loop diuretic (n=47)**

- Avg Sodium Intake (UC+FR)/2 (mg/day)
- Difference in Sodium (UC-FR)
  - Mean Diff = 393 mg
  - \( +1.96 \text{ SD} = 2396 \text{ mg} \)
  - \( -1.96 \text{ SD} = -1610 \text{ mg} \)
Food vs. Urine: Diuretics

Patients with HF not on loop diuretics (n=47)

Avg Sodium Intake (UC+FR)/2 (mg/day)

Difference in Sodium (UC- FR)

+1.96 SD = 2396 mg

-1.96 SD = -1610 mg

Mean Diff = 393 mg

Patients with HF on loop diuretics (n=62)

Avg Sodium Intake (UC+FR)/2 (mg/day)

Difference in Sodium (UC- FR)

+1.96 SD = 3773 mg

-1.96 SD = -2245 mg

Mean Diff = 764 mg

Non-HF cardiac patients (n=96)

Urinary Sodium Excretion (mg/day)

Est. Sodium Intake (mg/day)

r=0.624

p<0.001

Patients with HF not on loop diuretics (n=47)

Urinary Sodium Excretion (mg/day)

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Patients with HF on loop diuretics (n=62)

Urinary Sodium Excretion (mg/day)

Est. Sodium Intake (mg/day)

r=0.131

p=0.312

Est. Model = -798.0 + (0.54)*Sodium Intake

Arcand, AJCN 2011
Measurement: Food records

- **Food recall**: underestimates total c/w 24UNA
  - 15-25% underestimate

- **Food records**:
  - 1-14 days
  - Not much more info after 3-5 days
  - Actual record, not a recall

- Input into program (e.g. Food Processor, ESHA) which spits out every detail

Caggiula AJCN 1985
Espeland AJE 2001
Khaw AJCN 2004
Low Sodium vs Regular
Food Records

- Prospective
- Recording and measurement of all food and beverages each day, for any # of days
- Weighted or volume measurements
- Not dependant on memory

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<th>Meal</th>
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**Breakfast**: Rice milk 25g

- Banana bread (recipe incl) 90g

**Lunch**: Whole grain pasta 190g

- Whole grain vegan cheese 19g
- 2% organic milk 50g
- Raw cauliflower 41g
- Raw kiwi 38g
- Chocolate mousse 60g

**Dinner**: Home made pasta 168g

- Basic pasta sauce 100g
- Ragu pasta sauce 20g
- Olives 14g
- Organic milk 185g
- Oatmeal 100g
- Yogurt strawberry 15g

**Snack**: Home made smoothie 103g

- Mango 100g
- Oatmeal smoothie 100g
- Greek yogurt 7g
- Cilantro leaves 1g
Clinical/Research question

Does advising a patient to lower the amount of sodium in their diet change the clinical outcome?


SODIUM-HF

Study of Dietary Intervention Under 100 MMOL in Heart Failure

https://www.sodiumhftrial.com/

@sodiumhf
What are the main trial objectives?

• Evaluate the long-term effects of a low-sodium containing diet in patients with HF on a composite clinical outcome of:
  – All-cause mortality
  – CV hospitalizations
  – CV ED visits

• Secondary objectives include the evaluation of a low-sodium containing diet on:
  – Quality of life
  – Exercise capacity
  – NYHA class
  – Clinical outcomes (CV events + mortality) to 24 months
SODIUM-HF: Trial Design

• Multicentre, multinational
  – 25 sites
  – Canada, Mexico, Chile, Colombia, Australia, New Zealand
  – N=1000 subjects (n=650 enrolled)
  – Randomized, Open-label
  – Blinded adjudicated endpoint

• Study Population: patients with chronic HF (REF, PEF are eligible), NYHA 2-3, >1500 mg dietary Na
SODIUM-HF: Intervention

Patients randomized to one of two study arms:

1. Low-sodium containing diet (65 mmol or 1500 mg daily)

2. Usual care (general advice to limit dietary sodium as provided in routine clinical practice)
Intervention: Sample menus

Samples of menus at different levels of energy requirement (1400-2200 kcal) are available:

• In accordance with information provided in the meal plan and are intended to guide the patients in following their meal plan.

• Patient might interchange any of the food items included in the menus by another one included in the recommended foods lists of the same food group that the original one included in the menu.

• If energy requirements are adjusted during a follow-up visit, sample menus should be provided accordingly.
SODIUM-HF: Challenges

• Enrolment
• New strategies to continually engage site personnel doing the recruiting +RDs
• Lower site budget as a barrier to site participation
• Local logistics unique to each site when implementing dietary intervention
• Changing context of clinical trials research – e.g., online consent, e-signatures for patients, secular trends in volunteerism
SODIUM-HF: Successes

• Intriguing research question for MDs, RNs, NPs, RDs
• Simple, straightforward eCRF
• Top enrolling sites have a 1 FTE coordinator, available dietitian(s) and engaged PI
• Minimal source collected for adjudication of events
• Sites sought independent funding for sub-grants
• 100% remote monitoring
• Low administrative burden for sites
• Every site dietician on a Dietician Working Group
• Steering Committee: includes every site PI
Summary / conclusions

Test unproven dogma
Think about the patient, intervention, control
Time for observation fini; interv’n is needed
SODIUM-HF and other RCT ongoing