Understanding Kt/V and Volume Control

Its practical use to determine dialysis and improve outcomes

Caroline Williams RD
May 23, 2017
Volume Control in Dialysis Patients

BAD

"FLUID RESTRICTION?!?!"

"BUT WHY?!!"

@rn_mfkr8
Pathogenesis

* In the 1960s and early 1970s, the success rate of BP control without antihypertensive drugs was about 90% by UF during 8-10 hours of HD, dietary salt restriction, and low dialysate Na\textsuperscript{1, 2}

* In the late 1970-1980s, weekly HD duration was shortened, dietary salt intake largely disregarded and dialysate sodium levels increased (to reduce intradialytic symptoms). In addition antihypertensive drugs were more frequently needed\textsuperscript{3}

* Unfortunately, both BP drugs and lack of volume control methods used have been unsuccessful.

Currently, despite that 2/3 of HD patients use antihypertensive drugs, at least 2/3 of these still have high BP\(^1,2\)

These results suggest that

* the primary cause of hypertension in HD patients is volume overload (90%)

* increased sympathetic activity and/or renin activity are the primary responsible factors in the minority of hypertensive HD patients (10%)

Hypertension
Mechanisms

- Increased cardiac output due to hypervolemia
- Increased peripheral resistance

- \[ BP = \text{cardiac output} \times \text{peripheral resistance} \]
Volume Overload, Cardiovascular Disease, and Mortality

* Volume overload at the beginning of dialysis is present in almost all HD patients
* It remains even after the treatment in many (those with post-HD hypertension, intradialytic hypertension, large IDWG and systolic or diastolic LV dysfunction) i.e. ‘dry’ weight not attained PLUS cardiac dysfunction
* Pre-HD ECV overload assessed by several methods and large IDWG\(^1\) quite frequent and predicts mortality independent of BP

- Chest x-ray\(^2\)
- Plasma monitoring\(^4\)
- Echocardiography\(^3\)
- Bioimpedance methods\(^5\)
- Crit Line

3. Am Heart J 2010; 159: 1089
4. Hypertension 2010; 56: 512
5. Nephrol Dial Transplant 2009; 24: 157
Hypertension, Cardiovascular Disease and Mortality

Many studies have reported an association between hypertension, CV events:

- LV hypertrophy
- LV systolic dysfunction
- LV diastolic dysfunction
- Cardiac failure
- Ischemic heart disease
- Myocardial infarction
- Stroke
- CV mortality
- Overall mortality
- Sudden cardiac death

Agarwal R, Hypertension 2010; 55: 762
Tozawa M et al. Kidney In. 2002; 61: 717
Degoulet P et al. Nephron 1982; 31: 103
Greatly increased CV mortality in hemodialysis patients

- Comparison of CV and non-CV mortality in patients starting dialysis (ERA-EDTA registry) and in general population (Eurostat)

- CV mortality 8.8 times higher in dialysis patients than in general population

*de Jager DJ et al. JAMA 2009; 302: 1782*
Consequences of Sodium Loading/Restriction

- Thirst
- Blood pressure
- Intradialytic Morbid Events (Hypotension)
- Inflammation
- Left Ventricular Hypertrophy
- Hospitalizations
- Mortality
Salt intake and hypertension

- **No salt, no hypertension**: In Yanomamo Indians, urinary Na excretion 1 mmol/day; no hypertension, no BP increase with age

  *Oliver WJ, Circulation 1975*

- **Relationship between salt intake and BP**

  *Intersalt Study, BMJ 1988*

- **Progressive decrease in BP during weeks following dietary salt restriction**

  *Obarzanek E, Hypertension 2003*
Short HD, high dietary Na intake, high dialysate sodium, gradient with serum sodium

* All necessitate high ultrafiltration rates
* High UF rates lead to intradialytic hypotension
* Intradialytic hypotension causes
  * Ischemic damages in the body including myocardium (myocardial stunning, wall motion abnormalities), brain and gut damage-endotoxin released: inflammation
  * Difficulty to reach dry weight; overhydration, cardiac enlargement and hypertrophy, systolic and diastolic dysfunction
Determinants of interdialytic weight gain

* Main driving factor is dietary salt intake; others are:
  * Dialysate Na level (especially gradient to plasma Na level)
  * Hyperglycemia,
  * Fluid intake for social reasons/habit/addiction

* Fluid intake without salt has limited effect on IDWG because hyponatremia develops and limits further fluid intake

* Focus on cause of thirst
In contrast to adopting the short HD fashion, the Tassin (FRANCE) group continued to practice long HD sessions (24 h/week) and ECV reduction to treat hypertension instead of using drugs. Later this was reduced to 5 to 8 hrs/week

- **Controlled UF to achieve normal post-HD and pre-HD BP**
- **Low salt diet** (mean IDWG 1.6±0.4 kg)
- **Cessation of antihypertensive medications**

- Mean systolic BP 119±19 and diastolic BP 70±13 mmHg (ambulatory monitoring), close to normal subjects\(^1\)

- Excellent survival rate of 87% at five years\(^2\)

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Volume Control Strategy in Long Hemodialysis Tassin Experience

* In a report of 876 incident HD patients,
  * 90% had high BP at the initiation of HD
  * 1st month: post-HD BW was reduced 2-3 kg
  * 2nd month: BW stable, BP decreased more
  * 3rd-12th month: BP continued to decrease, while BW increased (*lag phenomenon, delayed regression of peripheral resistance which had developed in response to ECV overload*)

* Normal BP was achieved in 98% at 6th month without antihypertensive drugs

Volume control policy – Dr. Dorhout Mees, pioneer Dutch nephrologist

- 12 - 15 hours HD per week
- Dialysate Na concentration 135-138 mmol/L
- Strict dietary salt restriction to reduce interdialytic weight gain below 2.5% of wt
- Only drink amount to satisfy thirst (not less) Fluid restriction alone is a failure.
- Discontinuation of anti-hypertensive medications
Implementation of “volume control strategy” in Ege University Dialysis Center

Before 1993

* 65% of patients used anti-hypertensive medications
* Interdialytic weight gain over 3 kg
* Heart failure frequent, cardiothoracic index above 0.5 in 75%
* Intradialytic hypotension and cramps frequent
* Many patients requested to stop earlier dialysis because of hypotension and cramps in the last hours of dialysis
## Salt intake, IDWG and need of anti-hypertensive medications

<table>
<thead>
<tr>
<th>Center</th>
<th>Author</th>
<th>Dietary Na intake (mmol/d)</th>
<th>IDWG (kg)</th>
<th>Anti-HT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tassin</td>
<td>Charra et al</td>
<td>50</td>
<td>1.8</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Izmir, Turkey</td>
<td>Ozkahya et al</td>
<td>50</td>
<td>1.8</td>
<td>4</td>
</tr>
<tr>
<td>Manchester</td>
<td>Goldsmith et al</td>
<td>50</td>
<td>-</td>
<td>9</td>
</tr>
<tr>
<td>Christchurch</td>
<td>Lynn et al</td>
<td>70</td>
<td>2.6</td>
<td>5</td>
</tr>
<tr>
<td>Stockholm</td>
<td>Katzarski et al</td>
<td>100</td>
<td>2.4</td>
<td>50</td>
</tr>
<tr>
<td>Maastricht</td>
<td>Luik et al</td>
<td>100</td>
<td>3.2</td>
<td>73</td>
</tr>
</tbody>
</table>

Charra B, Hemodial Int 2007; 11: 21-31
APPLICATION OF THE MEES/OK MODEL OF SODIUM RESTRICTION AND FLUID REMOVAL TO CONTROL BP IN HD PATIENTS

<table>
<thead>
<tr>
<th>SYSTOLIC BP GROUP (mm Hg)</th>
<th>&lt;120 (Mean 111)</th>
<th>140-159 (Mean 151)</th>
<th>&gt;160 (Mean 170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>18</td>
<td>127</td>
<td>103</td>
</tr>
<tr>
<td>Δ SYSTOLIC BLOOD PRESSURE (mm Hg)</td>
<td>+12.2, p&lt;.01</td>
<td>-3.8, p&lt;.01</td>
<td>-14.0, p&lt;.001</td>
</tr>
<tr>
<td>Δ POST WEIGHT (kg)</td>
<td>-1.0, ns</td>
<td>-2.5, p&lt;.001</td>
<td>-2.5, p&lt;.001</td>
</tr>
<tr>
<td>Δ IDWG (%)</td>
<td>NA</td>
<td>-1.23, P&lt;.001</td>
<td>-1.0, P&lt;.01</td>
</tr>
</tbody>
</table>
QAKC Patient Decrease in pre-HD SBP

Timepoint in reference to the start of the QIP
The effect of hypervolemia (independent of BP) on cardiac status

- Comparison of the two dialysis centers regarding BP and cardiac geometry and functions
- Center A practiced volume control strategy, Center B anti-hypertensive medication based strategy

<table>
<thead>
<tr>
<th></th>
<th>Center A (n: 190)</th>
<th>Center B (n: 204)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-hypertensive use (%)</td>
<td>7</td>
<td>42</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>IDWG (kg)</td>
<td>2.29 ± 0.83</td>
<td>3.31 ± 1.12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>126 ± 15</td>
<td>126 ± 21</td>
<td>ns</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>75 ± 12</td>
<td>76 ± 11</td>
<td>ns</td>
</tr>
<tr>
<td>Intradialytic hypotension episode per 100 sessions</td>
<td>11</td>
<td>27</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

- Lower IDWG, anti-hypertensive use and intradialytic hypotension with volume control; SIMILAR BP LEVELS

Kayikcioglu M et al. Nephrol Dial Transplant 2009; 24: 956-62
To steer away from salt use this helpful guideline

**Read Labels!**

Choose foods where the mgs of sodium are close to the number of calories (1 to 1 ratio)

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### Nutrition Facts

**Serving Size:** 1 slice

<table>
<thead>
<tr>
<th>Amount Per Serving</th>
<th>% Daily Value*</th>
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</thead>
<tbody>
<tr>
<td><strong>Calories</strong> 60</td>
<td></td>
</tr>
<tr>
<td>Calories from Fat 4</td>
<td></td>
</tr>
<tr>
<td><strong>Total Fat</strong> 0.5 g</td>
<td>1%</td>
</tr>
<tr>
<td>Saturated Fat 0 g</td>
<td>0%</td>
</tr>
<tr>
<td>Trans Fat 0 g</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Cholesterol</strong> 0 mg</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Sodium</strong> 130 mg</td>
<td>5%</td>
</tr>
<tr>
<td>Potassium</td>
<td></td>
</tr>
<tr>
<td><strong>Total Carbohydrate</strong> 13 g</td>
<td>4%</td>
</tr>
<tr>
<td>Dietary Fiber 0 g</td>
<td>0%</td>
</tr>
<tr>
<td>Sugars 2 g</td>
<td></td>
</tr>
<tr>
<td>Sugar Alcohols</td>
<td></td>
</tr>
<tr>
<td>Protein 2 g</td>
<td></td>
</tr>
<tr>
<td>Vitamin A</td>
<td></td>
</tr>
<tr>
<td>Vitamin C</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td></td>
</tr>
<tr>
<td>Iron</td>
<td></td>
</tr>
</tbody>
</table>

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### Whole Grain Honey Wheat Bread

**Nutrition Facts**

Amount per Serving (serving size) = 1 slice

- **Calories 100**
- Fat Calories 15
- Total Fat 1.5g
- Sat. Fat 0.5g
- Trans Fat 0g
- Polyunsat. Fat 1g
- Monounsat. Fat 0.5g
- **Cholesterol 0mg**
- **Sodium 115mg**
- Total Carb. 21g
- Dietary Fiber 4g
- Sugars 4g
- Protein 4g
SALT SUCKS

* SALT sucked the water out of this fish and made it dry

* SALT will suck the water out of your cells and make you thirsty

  Avoid the thirst by avoiding the salt
  Control blood pressure by controlling the thirst
  Salt makes you thirsty
Once IDWG are within normal limits post weights can be reduced 0.2 -0.3kg per treatment (0.6-0.9kg /week)

Post weights can be reduce sooner but its not as effective and it is limited.

Time to decrease blood pressure varies from patient to patient depending how much they are overloaded and how well the control their IDWG.
Are staff convinced?

- Do they remind their patients in every session that “salt is a poison for them”?
- Do they warn their patients that “hypotensive episodes and cramps in this session is because of too much interdialytic weight gain resulting from dietary salt intake”?
- Is it mentioned to patients about EXCELLENT results (someone who has normal blood pressure without pills after reducing salt intake and interdialytic weight gain)?
### Conclusion

- Longer dialysis, utilization of additional ultrafiltration sessions and salt restriction facilitate to achieve euvolemia and normal blood pressure.

- Dietary salt restriction is an absolute requirement to limit exposure to hypervolemia in the interdialytic period (reduction of interdialytic weight gain)

- Dietary salt restriction can be accomplished, usually in the long term.
Ask for current “dry” weights to be reviewed and changed if necessary because the NEW DRY WEIGHT is to become the actionable target weight for future prescriptions

- RATIONALE: Many dry weights have not been updated for extended periods of time. In most instances they should be close to the current lowest post dialysis weight

Adjust this new target weight, USING A STANDING ORDER, by decreasing the dry weight by APPROXIMATELY 0.3Kg to 0.6 Kg per week. Standing orders are written by the physician to guide the staff

- RATIONALE: Up to now, most dry weights have not been reduced and therefore many patients have remained hypertensive.
* Maintain dry weight at the same level once pre-dialysis systolic blood pressure is lower than 140mmHg
  * RATIONALE: While many patients may safely have their systolic blood pressures lower than 140, some diabetic patients may have blood pressure drops on standing so caution is necessary. This is due to autonomic dysfunction
* Use an Ultrafiltration model which removes fluid more quickly at the beginning and more slowly at the end of the treatment. Programming mode in the HD machine is probably the best option. This will require your order.
  * RATIONALE: This will significantly reduce hypotensive episodes and cramping and will help to maintain blood pressure and reduce cramping.
* Set BTM at 36.5 degrees Celsius
  * RATIONALE: This slight degree of cooling will maintain blood pressure and increase patient comfort through vasoconstriction.
6). Consideration should be given to reducing doses of antihypertensive medicines as soon as a reduction in blood pressure is observed.

7). Consideration should be given to replacing dialyzable beta blockers with Carvedilol (non dialyzable).

Final Aim: Normal systolic blood pressure 120-140 mmHg in all patients previously hypertensive.
What about the Hypotensive Patient?

- Bringing down IDWGs to gains appropriate to their size is most important.
- Hearts are weak
- Less fluid and the heart can work easier. sBP will increase to normal limits.
- It's not clear if decreasing post weights are beneficial. Blood pressure may increase.
- NICaS is a great non invasive device to determine how much fluid should be removed.
Gradual (about 0.6 Kg a week) but persistent reduction in post dialysis weight is necessary to achieve euvoilema and NORMAL blood pressure while minimizing symptoms and hypotension.

Dietary salt restriction is an absolute requirement to limit exposure to hypervolemia in interdialytic period (reduction of interdialytic weight gain).

Dietary salt restriction is essential and it can be accomplished (not in short term but in long term).
The father of this therapy

In memory of
Professor
Evert J Dorhout Mees
1925 - 2016
In 1972...
Congress extends Medicare coverage to all patients with end stage renal disease.
<table>
<thead>
<tr>
<th>Group</th>
<th>Blood Flow</th>
<th>Time</th>
<th>Molecules Removed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>High</td>
<td>Prolonged</td>
<td>Small and middle</td>
</tr>
<tr>
<td>2</td>
<td>High</td>
<td>Short</td>
<td>Only small</td>
</tr>
<tr>
<td>3</td>
<td>Low</td>
<td>Prolonged</td>
<td>Only middle</td>
</tr>
<tr>
<td>4</td>
<td>Low</td>
<td>Short</td>
<td>Neither middle or small</td>
</tr>
</tbody>
</table>
K Clearance of urea (volume of fluid eg plasma water from which urea has been removed, It is a measure of efficiency)

t Time on dialysis in minutes

Kt Represents the volume of fluid cleared of urea(ml) during a single tx (in minutes)

V Volume of water in a patient’s body (liters)
Dialyzer clearance = 300 mL/min

Time = 180 min

Kt = 54,000 ml = 54L

V = 70 kg x 0.60 = 42 L

Kt/V = 54/42 = 1.3
What is URR

* Urea reduction ratio is the urea reduction as a result of dialysis.

Ex. 50 mg/dl – 15 mg/dl = 35 mg/dl
35/50 = 70/100 = 70%

* URR does not take into account the urea generated by the body during dialysis
* Or extra urea removed during dialysis along with excess fluid
  Or the effect of volume removal which affects the concentration of urea
Urea Kinetics (Kt/V)

\[
\text{Kt/V}_{sp} = -\ln (R - 0.008 \times T) + (4 - 3.5 \times R) \times \text{UF/W}
\]

Urea Reduction Ratio (R)

\[
R = \frac{C_{\text{post}}}{C_{\text{pre}}}
\]

Daugirdas
Figure 8.4 The effect of blood flow on solute clearance. The data are the same as for Figure 8.2 but graphed in order to demonstrate the declining rate of increase in solute clearance as higher blood flows are achieved. Note that maximal vitamin B12 clearance is achieved at a relatively modest blood flow (100 ml/min). The data were obtained in vitro and aqueous flow was used to simulate blood flow to the dialyzer.
Japanese Registry, 1992

N = 42,341

DIALYSIS DOSE AND MEMBRANE FLUX IN HEMODIALYSIS


Kt/V = 1.3

- Standard dose
- High dose

Kt/V = 1.7

Patients Surviving (%)

Mo. of Follow-up

No. at Risk
Standard dose
High dose

854  759  630  524  451  382  315  253  197  149
857  753  637  538  470  399  327  266  219  166
Time to death by Flux groups
Duration of Dialysis < 3.7 Years (573 Deaths)

Adjusted RR for High Flux: 1.05 (0.89 - 1.24), p = 0.55
Time to death by Flux groups

Year on dialysis > 3.7 Years (298 Deaths)

Adjusted RR for High Flux: 0.68 (0.53 - 0.86), p = 0.001
Why do some patients have poor Kt/Vs

- Prescription incorrect for Body V
- Poor accesses are tolerated
- Low K
- Patient end their treatment early
- Low t
- Prescription not followed
- Blood flow not correct from initiation
- t wrong
- Wrong dialyzer
- Wrong dialysate flow
- Access inadequate or recirculation
- Clotting of dialyzer
- Blood drawn incorrectly
- Increased hematocrit
How to Improve Kt/V

- **Increase blood flow rate**: the greater the quantity of blood is pumped through the dialyzer the higher the clearance. (>350mL/min).
- **Ultrafiltration rate**: more dialysate means more toxins can be removed (600-800 mL/min), this is impractical for this purpose because UFR determines how much fluid is to be removed.
- **Increasing time**
  - If Kt/V is 0.9 and goal is 1.2, then 1.2/0.9 = 1.33 times more Kt is needed. Increase time by 33% (from 3hrs to 4 hrs)
- **Bigger dialyzer with greater clearance.**
Kt/V is only one piece of the puzzle of treating ESRD
A Fable
The Hare and the Tortoise
(Aesop, 650 BC)

Aesop’s message: The slow but continuously moving turtle can travel as far and as quickly as the very much faster but intermittently sleeping rabbit.
In memory of
Frank Gotch
1926-2017
Strive for Optimal Dialysis
not just adequate dialysis
SYSTEMATIC REDUCTION OF INTERDIALYTIC WEIGHT GAIN AND POST HEMODIALYSIS WEIGHT LOWERS SYSTOLIC AND DIASTOLIC BLOOD PRESSURE: PRELIMINARY RESULTS OF A QUALITY IMPROVEMENT PROJECT.

Jochen G. Raimann, Caroline Williams, Surendra Gupta, Michelle Myers, Paul Parker, Alice Wei, Nathan W. Levin.

Background
Volume overload in hemodialysis (HD) patients is determined by the balance of Na\(^+\) and water during intra- and interdialytic periods. Reduction of dietary and dialytic Na\(^+\) intake has favorable effects on left ventricular mass and mortality as established from work in Tassin, and Izmir. We conducted a quality improvement project (QIP) which immersed Fresenius HD clinics in a culture of Na\(^+\) restriction supplemented by systematic and persistent post HD body weight (BW) reduction based on blood pressure (BP) assessments. This current retrospective analysis reports the success of the QIP on SBP and DBP, and investigates the relative effectiveness of the employed measures.

Methods
All patients in three HD clinics in this QIP received additional dietary intervention. In those with low (<120 mmHg) and high (>140 mmHg) SBP, respectively, post HD BW was reduced by 0.6 to 0.9 kg each week until a nadir of SBP was reached without intradialytic complications. BW, IDWG, SBP and DBP were compared over 4 months. Over periods of 2 to 9 months on an individual level, the effect sizes of IDWG and post HD BW reduction were quantitated using a linear mixed model (LMM) predicting BP (additionally adjusted for age, gender and race). Data are reported as mean ±SD or mean (95% CI).

Results
In 177 patients [63±13 years, 67% male, 62% white, 2.3±0.9 kg IDWG (3.1±1.2 IDWG% of BW), 76.6±19.6 kg post HD BW, 150±18 mmHg pre and 77±12 mmHg post HD BW] the intervention resulted in a borderline significant change of IDWG [-0.12 (-0.27 to 0.03) kg] and significant changes of pre [-3.9 (-6.5 to -1.2) kg] and post HD BW [-3.8 (-6.4 to -1.1) kg] in 151 subjects that completed 4 months of QIP. In a subset of 64 patients with SBP≥160 mmHg the intervention reduced the pre HD SBP and DBP by -15.7 (-20.2 to 11.2) and -7.2 (-9.8 to -4.5) mmHg, respectively. In those with low SBP (<120 mmHg; N=64) the intervention caused an increase of SBP and DBP by 11.2 (-1.2 to 23.5) and 4.4 (-2.9 to 11.6) mmHg, respectively. LMM identified ∆IDWG% and ∆post HD BW as having significant slope estimates in the prediction of SBP (∆SBP of 0.81 (P=0.04) and 0.09 (P=0.01) per 1 unit change of IDWG% and post HD weight, respectively) and DBP (ΔDBP of 0.40 (P=0.08) and 0.05 (P=0.02) per Δunit of IDWG% and post HD weight, respectively).

Discussion and Conclusion
In this QIP we have significantly reduced IDWG, pre and post HD weight and consequently pre HD SBP and DBP without increasing HD session times. Our data confirms the necessity of both IDWG and post HD BW reduction to effectively lower SBP and DBP in keeping with the methods and results of the Izmir group (Ok, E. and E. J. Mees (2010). "Unpleasant truths about salt restriction." Semin Dial 23(1): 1-3).