SALT AND WATER MANAGEMENT: A CRITICAL CONSIDERATION IN HD AND PD PRESCRIPTIONS

OPTIMAL DIALYSIS – IN SEARCH OF THE HOLY GRAIL
PART 1: VOLUME AND BP MANAGEMENT

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CONFLICT OF INTEREST

• ASSOCIATE CMO OF FRESENIUS KIDNEY CARE
OPTIMAL DIALYSIS – THE HOLY GRAIL – PART 1

DEFINE THE TRUE TOXIN

UREA – KT/V: IMPROVE CARE WITH INCREASED UREA CLEARANCE AND REMOVAL OF MYSTERY TOXINS

VERSUS

SALT AND WATER: IMPROVE CARE THROUGH VOLUME, BLOOD PRESSURE AND CARDIOVASCULAR CARE

YOU MUST CHOOSE

BUT CHOOSE WISELY
I CHOSE VOLUME

Put the patient first

The problem is salt and water

Can we improve volume BP control at home?
CURRENT CHALLENGES FOR DIALYSIS MODALITIES: CARDIOVASCULAR DISEASE AND THERAPY TOLERANCE

- The hallmark of morbidity and mortality of dialysis populations is cardiovascular disease and substantial patient fatigue.

- PD and HHD can be used to address efficacy of managing CVD and patient choice of dialysis therapy over time.

- But conventional HD and PD longer term face complications from persistent volume overload, uncontrolled hypertension, with resultant LVH, heart failure & arrhythmias.
THE PROBLEM: DIALYSIS IS ASSOCIATED WITH PRESSURE, VOLUME, AND CV-RELATED MORBIDITY

Approximately 4 in 5 dialysis patients have diagnoses of diabetes, heart failure, or cardiac arrhythmia.

Any 1 of 3 conditions: 1.7–2.0 times higher risk of CV death

Any 2 of 3 conditions: 2.5–3.6 times higher risk of CV death

All 3 conditions: 5.0 times higher risk

PREVALENCE & HAZARD RATIO

21%
HR = 1.0

27%
HR = 1.7

14%
HR = 3.2

16%
HR = 5.0

7%
HR = 2.5

5%
HR = 2.0

5%
HR = 3.6

4%
HR = 1.9

14% HEART FAILURE

5% DIABETES

7% CARDIAC ARRHYTHMIA

SPECIAL DATA ANALYSES: 2016 USRDS ESRD DATABASE AND MEDICARE CLAIMS DATA.
ASSOCIATED MORTALITY: UFR VS. INTERDIALYTIC FLUID LOAD

High UFR is not good, but persistent fluid overload is worse!

Intradialytic UFR and Mortality Risk

<table>
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<tr>
<th>UFR (mL/hour/kg)</th>
<th>Hazard Ratio</th>
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<tr>
<td>0-5</td>
<td>1.00</td>
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<tr>
<td>6-7</td>
<td>1.03</td>
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<td>8-9</td>
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<td>10-11</td>
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<tr>
<td>12-13</td>
<td>1.23</td>
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<tr>
<td>14+</td>
<td>1.43</td>
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</tbody>
</table>

Total Volume Loading and Mortality Risk

1 year cumulative FO-based analysis

- Overhydrated
- Nonoverhydrated


Volume loading creates markedly abnormal cardiac pressure.

The loading between treatments create high wall stresses, LVH, and systolic and diastolic dysfunction.
PATHOPHYSIOLOGY AND OUTCOMES: HEMODIALYSIS

- Fluid & Na Overload
  - Uncontrolled Hypertension
  - Left Ventricular Hypertrophy
  - Heart Failure
  - Hospitalizations and Death

- High Ultrafiltration Rate
  - Intradialytic Hypotension
  - Cramping, Dizziness, Nausea, etc.
  - "Early Sign-Offs" and "No-Shows"

- Organ Stunning
  - Long Post-Dialysis Recovery Time
  - Poor QOL

- Chronic between treatment fluid loading

- Intra-treatment fluid removal
PATHOPHYSIOLOGY AND OUTCOMES:
PERITONEAL DIALYSIS (PD)

Fluid Overload

Driven by volume issues

Uncontrolled Hypertension

Driven by dialytic volume issues

Left Ventricular Hypertrophy

Heart Failure

Hospitalizations and Death

50% of PD patients persistently volume overloaded upon incidence

Over time RRF and membrane UF decline adding to PD volume loading

Fluid overload is predictive of early PD Technique failure
FLUID OVERLOAD

• HOW DO WE DECIDE DRY WEIGHT
  • PHYSICAL EXAM
  • CARDIAC BIOMARKERS
  • LUNG ULTRASOUND
  • ECHOCARDIOGRAM
  • BIOIMPEDANCE
39,566 INCIDENT PATIENTS OVER 5 YEARS

18,371 (46%) PATIENTS WERE OVERHYDRATED AT BASELINE.

Volume status of PD patients at initiation and 3 year follow up (iPOD PD)
28 countries – 135 centers. N = 1092 incidents pts

- Overload: 56.4% (Relative Volume Overload > 7%)
- Mean overload: 1.9 ± 2.4 L
(3.3 ± 2.08 L in the overload group)\(^1\)

- Relative Volume overload > 7%
  was 48%, 49%, and 53%
after 1, 2, and 3 years\(^2\)

Fluid overload associated with death and technique failure
Fluid overload did not preserve Residual Renal Function

FLUID OVERLOAD IN PERITONEAL DIALYSIS AND INCREASED RISK OF DEATH\(^1\)

\(^1\)VAN BIESEN WV ET AL, FOR THE IPOD-PD STUDY GROUP. EVOLUTION OVER TIME OF VOLUME STATUS AND PD-RELATED PRACTICE PATTERNS IN AN INCIDENT PERITONEAL DIALYSIS COHORT. CJASN JUN 2019; 14 (6) 882-893.
BIOMARKERS IN PD

• SIGNIFICANTLY ELEVATED NT PROBNP IN ESRD IS ASSOCIATED WITH:
  • VOLUME OVERLOAD\(^1\)
  • HYPERTENSION\(^1\)
  • ATRIAL FIBRILLATION\(^2\)

1. Surachet Vongsanit · Andrew Davenport Journal of Nephrology
   https://doi.org/10.1007/s40620-019-00633-y Received: 14 May 2019 / Accepted: 30 July 2019

LUNG ULTRASOUND – U/S GUIDED VS USUAL CARE

LIMITATIONS: EXPLORATORY STUDY; SMALL SAMPLE SIZE
*NOT APPROVED FOR SALE IN THE US

• US-GUIDED STRATEGY VS “USUAL CARE” FOR DRY WEIGHT REDUCTION:
  1. DECREASED CARDIAC CHAMBER DIMENSIONS
  2. DECREASED LV FILLING PRESSURE
  3. NO DIFFERENCE IN SYSTOLIC PERFORMANCE

GAP BETWEEN CLINICALLY ASSESSED AND BIOIMPEDANCE MEASURED HYDRATION STATUS

*PLEASE NOTE THAT BCM DEVICE IS NOT APPROVED FOR SALE IN THE UNITED STATES*

- CLINICAL ASSESSMENT CRITERIA, INCLUDING INCREASED BLOOD PRESSURE, WAS NOT RELIABLE ENOUGH TO GUIDE TREATMENT DECISIONS
  - 15% OF OVERHYDRATED PATIENTS EXHIBITED NORMAL OR LOW BLOOD PRESSURE
- OVERHYDRATED STATUS WITH NORMAL OR LOW BLOOD PRESSURE MAY BE A BETTER INDICATION OF CARDIAC DYSFUNCTION

**BCM data showed clinicians incorrectly judged participants to be normohydrated or dehydrated, despite similar eGFRs across groups**

RESIDUAL RENAL FUNCTION

• PERITONEAL DIALYSIS
  • WHAT WE KNOW –
    • RRF IS VOLUME WHICH HELPS WITH UF IN THE PD PATIENT
    • RRF IN PD IS ASSOCIATED WITH IMPROVED TECHNIQUE SURVIVAL AND PATIENT SURVIVAL
    • ISPD SUPPORTS EFFORTS TO MAINTAIN RRF IN PD
      • MINIMIZE NEPHROTOXINS – NSAID, IV CONTRAST, AMINOGLYCOSIDES
      • AVOID DEHYDRATION
      • MAXIMIZE UOP
        • HIGH DOSE FUROSEMIDE
          • US > 200 MG DAILY
          • EUROPE - 500 MG PO BID
      • MAINTAIN GFR
        • ACE INHIBITORS
RESIDUAL RENAL FUNCTION

• PERITONEAL DIALYSIS
  • WHERE DOES VOLUME PLAY A ROLE?
  • PRESCRIPTION FOR VOLUME CONTROL
    • SOME SAY KEEP PATIENT VOLUME OVERLOADED TO PROTECT RRF
      • THEY ARE WRONG. SEE PREVIOUS SLIDES.
    • HYPOVOLEMIA ASSOCIATED WITH DECLINE IN RRF
    • HYPERVOLEMIA DOES NOT PROTECT RRF
RESIDUAL RENAL FUNCTION

• HOME HEMODIALYSIS
  
  • WHAT WE KNOW –
    • RRF DECLINED FASTER IN FHN NOCTURNAL TRIAL WITH MFD
    • RRF IS PRESERVED AS WELL AS SEEN IN PD WITH THE KIHDENEY TRIAL IN EUROPE (MFD WITH DAILY DIALYSIS)
  
  • WHAT WE THINK – TRY TO PRESERVE RRF IS OK
    • MINIMIZE NEPHROTOXINS – NSAID, IV CONTRAST, AMINOGYCOSIDES
    • AVOID DEHYDRATION
    • FUROSEMIDE SEEMS REASONABLE

• WHAT WE DON’T KNOW
  • DOES RRF IMPACT SURVIVAL OR HOSPITALIZATION IN MFD/HHD
PRESCRIBING RRT FOR VOLUME CONTROL
SHORTER DWELL TIMES MAY LEAD TO INCREASED SERUM SODIUM, RESULTING IN INCREASED THIRST\textsuperscript{1}

- AQUAPORIN CHANNELS PRODUCE SODIUM FREE OR "FREE WATER" TRANSPORT DURING THE 1ST HOUR OF DWELL
- SODIUM DIFFUSION INCREASES AFTER 2 HOURS OF DWELL
- SODIUM SIEVING CAN CONTINUE \textgreater{}2 HOURS INTO DWELL DEPENDING ON TRANSPORT TYPE AND DEXTROSE CONCENTRATION

ULTRAFILTRATION VARIES BY DWELL TIME, MEMBRANE EFFICIENCY, AND DEXTROSE CONCENTRATION¹

- **USE AVERAGE TRANSPORTER STATUS FOR THE INITIAL PRESCRIPTION**
- **MAXIMUM UF IS BETWEEN 2 – 6 HOURS DEPENDING ON DEXTROSE CONCENTRATION**
- **NEGATIVE UF NOT LIKELY BEFORE 7 – 14 HOURS**
- **UF GOALS SHOULD BE BALANCED WITH LEVEL OF DEXTROSE EXPOSURE**

Average transporter status modeled from source.
KEYS FOR SODIUM AND VOLUME REMOVAL IN PD

GOALS OF THERAPY
• MINIMIZE SODIUM SIEVING
• MAXIMIZE ULTRA FILTRATION
• MAXIMIZE UOP AND RRF
• AVOID DRY DAYS
  • ESPECIALLY WITH LOSS OF RRF

PATHWAYS TO GOALS
• DWELL TIMES 2 – 5 HOURS
• ADEQUATE DWELL VOLUMES
• MEASURE PET
• DIURETICS, AVOID NEPHROTOXINS, ? ACE – INHIBITORS
• AVOID HYPO AND HYPER VOLEMIA
• WITH CYCLER CONSIDER DAYTIME EXCHANGE
• ICODEXTRIN FOR HIGH TRANSPORTERS
HHD - FHN studies: Significant **Cardiovascular** Benefits

**FREQUENT HEMODIALYSIS ASSOCIATED WITH THE FOLLOWING 12-MONTH IMPROVEMENTS**

- **12%** Reduction in left ventricular mass\(^1,2\)
- **20%** Fewer hypotensive episodes\(^1\)
- **7%** Decrease in systolic blood pressure\(^1\)
- **36%** Less antihypertensives consumed\(^1\)

How to prescribe patient centered hemodialysis at home in 3 steps

1. Frequency
   Medical indications for increased time and duration

2. Treatment time
   Balancing ultrafiltration and volume status

3. Dialysate volume
   Small solute clearance and saturation
5+ DAYS PER WEEK
- Improved BP control & survival\(^1,4-8\)
- Reduced LVH & cardiovascular hospitalizations\(^4,7,8,10\)
- Reduced UFR, recovery time & hypotensive episodes\(^3-5,10-15\)
- Improvements in sleep quality, RLS & HRQoL\(^5,16-18\)

References at end
**STEP 2: TREATMENT TIME**

**Goal UFR 6.5 ml/kg/hr**

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**FREQUENCY □ HOURS PER TREATMENT**

1. **Treatment Frequency**
2. **Treatment Time**
3. **Goal UFR**

**INPUT**

- mL/wk ÷ Body Weight
  - (~950 mL/day x 7 days)
  - 6,650 mL/wk ÷ 68 kg
  - = 98 mL/kg/wk

**CALCULATE**

- UF Rate
  - 98 mL/kg/wk ÷ 6.5 mL/kg/hr
  - = 15 hrs/wk

**RESULT**

- hrs/wk ÷ sessions/wk
  - 15 hrs/wk ÷ 5 sessions/wk
  - = 3 hours/session

**PRESCRIBE**

- Most patients will control UF with 15 hours/week (15 – 18 hours seems reasonable for diurnal therapy)
STEP 3: DIALYSATE VOLUME
HOW MUCH VOLUME SHOULD MRS. C USE?

<table>
<thead>
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<th>Weight (kg)</th>
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Allows for UF of <1.5 L/day.
Minimum of 20L of dialysate per treatment. Minimum of 12 hours of treatment per week. 15 hours of treatment per week is typical.
Right prescription, right therapy every day
- Whether In-center, PD or HHD

- Assess adequate and optimal prescription every clinic (at least)
  - **Salt and water**, Kt/V, Nutrition, QOL
    - Patient and partner
  - Reasons for modifications
    - “Adequate” dialysis not achieved
    - Residual renal function declined
    - Cardiovascular decline
    - Sarcopenia, infections etc
    - Patient and/or partner depression, burnout
    - Telehealth / records with unacceptable adherence

- Is Prescription correct?
- Is Therapy correct?
  - Know when to change therapies and why
  - Modification of frequency, time, solo, nocturnal as needed
  - Consider Respite
OTHER MANAGEMENT

VOLUME CONTROL

• DIET
  • MUST RESTRICT SALT AND WATER IN
    • IN-CENTER
    • PD
    • HOME HEMODIALYSIS
    • TRANSPLANT

MEDICATIONS

• BETA BLOCKER
• ACE INHIBITOR
  • ALSO PRESERVE RRF
• CALCIUM CHANNEL BLOCKERS
• OUTCOMES OF MEDS (INTENSIVE BP CONTROL)\(^1\)
  • INCREASED NUMBER OF MEDS
  • DRY WEIGHT ROSE
  • INTRADIALYTIC SYMPTOMS INCREASED
  • NON STATISTICAL DIFFERENCE IN LVM
  • SMALL STUDY BUT MORE DEATHS

   https://doi.org/10.1681/ASN.2017020135
CLINICAL EVIDENCE FOR BENEFITS OF INCREASED FREQUENCY AT HOME

REFERENCES


CLINICAL EVIDENCE FOR BENEFITS OF INCREASED FREQUENCY AT HOME


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