Recent Advances In the Prevention Of Hypotension During Hemodialysis

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Korea
Agenda

- Definition of Intradialytic Hypotension (IDH)
- Pathophysiology of IDH
- Strategies and Maneuvers to Prevent IDH
  - Pharmacological
  - Na and UF profiling
  - BVM and Automatic Biofeedback
  - BTM and Cooling
  - HDF
- Review of major clinical studies
- Conclusion
Intra-dialytic hypotension (IDH)

- **Definition:**
  Decrease in systolic BP by ≥20 mmHg or decrease in MAP by 10 mmHg in combination with hypotensive symptoms and need for nursing intervention.
  
  Nadir-based IDH, cut-off SBPs of 90 and 100 mmHg

  
  

- One of the most frequent complications of hemodialysis
  
  20~30% of all hemodialysis sessions
Concerns about IDH

- Symptomatic discomfort
- Chronic fluid overload: HTN and LVH
- Reduced solute clearance
- Myocardial ischemia, Repeated
  - Perfused during diastole
  - Increased mortality
Determinants of Arterial Pressure during hemodialysis

\[ BP = CO \times TPR \]

- **Dialysis dependent**
  - UFR
  - CD
  - Osmotic solutes
  - Circulating BV
  - Vascular tone

- **Patients dependent**
  - Cardiac efficiency
  - Hydration status

- **Autonomic Nervous System efficiency**

- **Nitric Oxide**
- **Thermal balance**
- **Cathecolamine Interleukine**
Fluid removal during dialysis

Volume distribution

- Extracellular compartment = 20% of body weight
- Intracellular compartment = 40% of body weight

5% of body weight in the vessels
15% of body weight between the cells
40% of body weight in the cells
Factors affecting plasma refilling rate during dialysis

- Hydration
- Extracellular osmolarity
- Vascular tone
- Proteins concentration

UF
Principles of fluid removal

Blood volume change and refilling

Factors affecting refilling:
- Overhydration
- Plasma osmolarity
- Protein concentration
- UF rate
- Patient’s refill capability
5. Stratified approach to prevent IDH

**First-line approach**
- Dietary counseling (sodium restriction).
- Refraining form food intake during dialysis.
- Clinical reassessment of dry weight.
- Use of bicarbonate as dialysis buffer.
- Use of a dialysis temperature of 36.5°C.
- Check dosing and timing of antihypertensive agents.

**Second-line approach**
- Try objective methods to assess dry weight.
- Perform cardiac evaluation.
- Gradual reduction of dialysate temperature from 36.5°C downward (lowest 35°C) or isothermic treatment (possible alternative: convective treatments).
- Consider individualized blood volume controlled feedback.
- Prolong dialysis time and/or increase dialysis frequency.
Pharmacological Maneuvers for IDH

- Midodrine
  - 10mg, single oral dose 5-30min before HD
  - Safe and effective, but variable results
- Arginine vasopressin
  - A relative AVP deficiency during HD
  - Continuous IV infusion or Intranasal DDAVP
- Adenosine A1 receptor antagonists
Technical Maneuvers for IDH

- Objective assessment of dry weight: BCM®, S10®
- Handling dialysis treatment time, dialysis frequency & Ultrafiltration rate
- Sodium profiling & UF profiling
- Cold dialysate
- Blood volume monitoring
- Using biofeedback technology: Hemocontrol®/BTM® to control blood volume reduction during dialysis
Bioimpedance Spectroscopy (BIS)

Outer electrodes (red): Apply electrical current
Inner electrodes (blue): Measure voltage

Impedance = \frac{\text{voltage}}{\text{current}}
Effect of BIS-guided volume assessment on IDH

- IDH was more common among patients with hypovolemia assessed by M-BIA. M-BIA readily identified patients where IDH could be prevented by increasing dry weight. Kalainy S et al. *Can J Kidney Health Dis* 2015; 2

- The frequency of IDH was not decreased despite the use of M-BIA in conjunction with adjustment of UFR. Hur E et al. *Am J Kidney Dis* 2013; 61
Dialysis treatment time, dialysis frequency and UFR

- Limit Interdialytic weight gain (IDWG) : ≥ 3kg or ≥ 3% of estimated dry weight occurs more frequently among patients with IDH.
  - Counsel patient regarding salt intake and habitual drinking
  - Prevent hyperglycemia in diabetes
  - Utilize diuretics at high doses in patients with residual renal function

- Some experts recommend that when prescribing dialysis time, it is important to consider that the maximum UFR should not exceed 10 mL/kg/h

- More frequent or longer treatments that allow for lower UFR likely lessens the risk of IDH, but may result in more frequent episodes of IDH, if total ultrafiltration exceeds the target, if the target weight is underestimated.
Sodium Profiling Hemodialysis

- Time-dependent profile of high ~ low $D_{Na}$
  - period to maintain plasma tonicity ~ to compensate Na load

High $D_{Na}$ to increase plasma Na & tonicity

Plasma refilling = ↓ IDH

Low $D_{Na}$ to compensate sodium gain
SPHD + UF Profiles is Essential

SPHD with constant UF

- Constant UF rate
  - low plasma volume
  - low $P_{Na}$/oncotic pressure
  - high risk for IDH

SPHD with UF profiles

- High UF rate
  - high plasma volume
  - high $P_{Na}$/oncotic pressure

- Low UF rate
  - low plasma volume
  - low $P_{Na}$/oncotic pressure
  - ↓ high for IDH
Problem of SPHD: Sodium Load

- Dialysate sodium up to 138~140 mEq/L

**Diffusive Sodium Gain**

- **Intradialytic period**
  - ↓IDH & its related morbidities

- **Interdialytic period**
  - ↑Cx d/t sodium gain (thirst, weight gain, Hypertension)

Just shifting the time of dialysis discomforts?
<table>
<thead>
<tr>
<th>Ultrafiltration profile</th>
<th>Control</th>
<th>PS</th>
<th>NS</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>IDH↓, Na gain ↑</td>
<td>No effect</td>
<td>No effect</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>IDH↓, Na gain ↑</td>
<td>IDH↓, Na gain ↓</td>
<td>IDH↓, Na gain ↓</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions**

1) Na balance positive SPHDs is effective but result in Na gain
2) Na balance neutral SPHDs is effective without Na gain
   if UFP is combined

Song JH *JASN* 2005, Vol 16
Principle of Blood Volume Monitor (BVM)

Plasmatic Volume
RBC Volume
Blood Volume

Arterial line (expansion chamber)

Emitter
Receiver
Sent light
Not absorbed light

Optical Hemoglobin measurement

\[ Hgb = f(I_0 - I) \]

\[ BV\%(t) = \frac{Hgb(0)}{Hgb(t)} - 1 \]
Changes in blood volume during hemodialysis

Initial period
- Plasmatic refilling
- Higher hypotensive risk

Time (min)

BV (%)
“Fuzzy” logic control system for regulating changes in relative blood volume (BVM).

![Diagram showing the control system for BVM changes during hemodialysis.]

**Hemodialysis International** 2011 Oct; 15: S37-S42
Automated blood volume regulation during hemodialysis (Biofeedback)

Clinical prescription

desired BV → △ BV → Controller → measured BV → Blood Volume monitor → Dialysis machine → DELIVER UF rate conductivity

SET UF rate Conductivity

measuring + automated actions
Leading blood volume along the optimal trajectory

- Total UF
  - 0 to 3
  - 0 to 2
  - 0 to 1
  - 0 to 0

- Na^+ concentration
  - 17 to 13

- ΔBV (%)
  - Time (min) graph
    - 0 to 210 min
    - Upper tolerance
    - Lower tolerance
    - Target value
    - Actual value

- Blood Volume
  - -7.6%
Cold Dialysate

- ↓Plasma volume
  → cutaneous vasoconstriction
  → ↑core temperature
    (impaired thermal balance)
  → peripheral vasodilatation *in critical level*
  → IDH

- 36.5 ~ 38 °C → 35~35.5°C : ↓ IDH
Blood Temperature Monitor (BTM)

Close-Loop Control System
BTM & BVM in feedback loop

Heat control

UF control

Dialyzer

Hydraulic system
Landmark-Reports of Each Maneuver (profiling HD)

• IDH prone patients \((NDT, 2006)\)
  • Control : 25% (16/64) IDH
  • Na profile (LD) : 23% (15/65) IDH
  • UF profile (LD) : 31% (19/61) IDH
  • Na + UF profile (LD) : 10% (7/73) IDH

• IDH prone patients \((JASN, 2005)\)

<table>
<thead>
<tr>
<th>%</th>
<th>Control</th>
<th>PS</th>
<th>PS+U</th>
<th>NS+U</th>
<th>NA+U</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intradialytic discomfort</td>
<td>51.5</td>
<td>21.2</td>
<td>24.2</td>
<td>24.2</td>
<td>30.3</td>
</tr>
<tr>
<td>Interdialytic discomfort</td>
<td>18.2</td>
<td>45.5</td>
<td>36.4</td>
<td>15.2</td>
<td>21.2</td>
</tr>
</tbody>
</table>

• A meta-analysis of sodium profiling techniques \((Hemo Int, 2017)\)
  • Stepwise profiling was more effective than other profiling methods
  • Linear profiling had no evidence to be any more effective than conventional HD
A meta-analysis of sodium profiling techniques and the impact on intradialytic hypotension

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**Hemodialysis International**
2017; 21:312-322 DOI: 10.1111/hdi.12488
Landmark-Reports of Each Maneuver (Hemocontrol® or BTM®)

• IDH prone patients (KI, 2002) : Hemocontrol® HD
  • Conventional HD vs BVC HD : 30% reduction of IDH in BVC HD

• IDH prone patients (NDT, 2006) : Hemocontrol® HD
  • Symptomatic IDH : 8% BVC feedback, 16% standard HD, 14% Na profile HD, 17% DC-controlled feedback

• IDH prone patients (Plos One, 2015) : Hemocontrol® HD
  • 2-fold increase in plasma AVP at 30 minutes into biofeedback session

• IDH prone patients (AJKD, 2002) : Isothermic feedback
  • Conventional HD vs Isothermic HD : 50% reduction of IDH in Isothermic HD

• 2 RCT (CJASN, 2015) ; Programmed cooling to 0.5°C below BT
  • 1 year use can reduce the progression of cardiomyopathy and protect against ischemic brain damage
Clinical benefits in dialysis patients

Efficacy of Hemocontrol Biofeedback System in Intradialytic Hypotension-Prone Hemodialysis Patients

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Accepted: 31 March 2014

We conducted a study to determine whether the hemocontrol biofeedback system (HBS) can improve intradialytic hypotension (IDH) in hypotension-prone hemodialysis (HD) patients compared with conventional HD. In this multicenter prospective crossover study, 60 hypotension-prone patients were serially treated by conventional HD for 8 weeks (period A), by HD with hemoscav blood volume monitoring for 2 weeks (period B0), and by HBS HD for 8 weeks (period B1). The number of sessions complicated by symptomatic IDH during 24 HD sessions (14.9 ± 5.8 sessions, 62.1% in period A vs. 9.2 ± 7.2 sessions, 38.4% in period B1, P < 0.001) and the number of IDH-related nursing interventions in a session (0.96 ± 0.66 in period A vs. 0.56 ± 0.54 in period B1, P < 0.001) significantly decreased in period B1 than in period A. Recovery time from fatigue after dialysis was significantly shorter in period B1 than in period A. The patients with higher post-dialysis blood pressure, lower difference between pre- and post-dialysis blood pressure, less frequent HD, and higher pre- and post-dialysis body weight in period A responded better to HBS in period B1 in regard to the reduction of IDH. In conclusion, HBS may improve the patient tolerability to HD by reducing the IDH frequency and promoting faster recovery from fatigue after dialysis.

Keywords: Hypotension; Renal Dialysis; Clinical Trial; Dialysis Volume
Number of sessions IDH occurred during 24 sessions

- 61.4% in Conventional HD (15/24)
- 37.6% in HemoControl HD (9/24)

Statistical significance: \( P < 0.001 \)
Number of nursing interventions per session

- Conventional HD: 0.96
- HemoControl HD: 0.56

P < 0.001
Post-dialysis BP

**Systolic**
- **Con.**
- **Hemo**
  - P<0.0001

**Diastolic**
- **Con.**
- **Hemo**
  - P=0.004

**MAP**
- **Con.**
- **Hemo**
  - P=0.0002
Recovery of Fatigue After Dialysis

P = 0.048

Conventional HD

HemoControl HD

- By next HD
- Next morning
- At bed time
- When arriving home
- Within minutes
(a) Biofeedback HD versus conventional HD with constant dialysate conductivity and ultrafiltration rate; outcome: IDH. Relative treatment effect estimate (rate ratio).

Effect of low temperature dialysis on intradialytic hypotension. 95% CI, 95% confidence interval; BTM, biofeedback temperature monitoring.

<table>
<thead>
<tr>
<th>Source</th>
<th>Intervention</th>
<th>Cool Dialysis</th>
<th>Standard Dialysis</th>
<th>Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ayoub 2004</td>
<td>Fixed 35 C</td>
<td>0 / 30</td>
<td>0 / 30</td>
<td>1.00 [0.02, 50.40]</td>
</tr>
<tr>
<td>Beerenhout 2004a</td>
<td>BTM 35.2 C</td>
<td>0 / 12</td>
<td>0 / 12</td>
<td>1.00 [0.02, 50.40]</td>
</tr>
<tr>
<td>Chesterton 2009</td>
<td>Fixed 35 C</td>
<td>1 / 9</td>
<td>2 / 9</td>
<td>0.50 [0.05, 5.51]</td>
</tr>
<tr>
<td>Cruz 1999</td>
<td>Fixed 35.5 C</td>
<td>6 / 99</td>
<td>29 / 99</td>
<td>0.21 [0.09, 0.50]</td>
</tr>
<tr>
<td>Dheenan 2001</td>
<td>Fixed 35 C</td>
<td>0.375 / 30</td>
<td>0.937 / 30</td>
<td>0.40 [0.01, 17.66]</td>
</tr>
<tr>
<td>Jost 1993</td>
<td>Fixed 35 C</td>
<td>0 / 12</td>
<td>18 / 12</td>
<td>0.03 [0.01, 0.45]</td>
</tr>
<tr>
<td>Kaufman 1998</td>
<td>BTM 35.7 C</td>
<td>5 / 15</td>
<td>10 / 15</td>
<td>0.50 [0.17, 1.46]</td>
</tr>
<tr>
<td>Selby 2006</td>
<td>Fixed 35 C</td>
<td>1 / 9</td>
<td>1 / 9</td>
<td>1.00 [0.06, 15.99]</td>
</tr>
<tr>
<td>van der Sande 1999</td>
<td>Fixed 35.5 C</td>
<td>0 / 9</td>
<td>1 / 9</td>
<td>0.33 [0.01, 8.18]</td>
</tr>
<tr>
<td>van der Sande 2009</td>
<td>BTM 0.5C below body</td>
<td>1 / 21</td>
<td>3 / 21</td>
<td>0.33 [0.03, 3.20]</td>
</tr>
<tr>
<td>Yu 1995</td>
<td>Fixed 35 C</td>
<td>0 / 18</td>
<td>0 / 18</td>
<td>1.00 [0.02, 50.40]</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td>0.32 [0.16, 0.56]</td>
</tr>
</tbody>
</table>

Test for heterogeneity for pooled Rate Ratio: Chi² = 6.35, df = 10 (P=0.78), P=0%

Reem A. Mustafa et al. CJASN 2016;11:442-457
Hemofiltration and Hemodiafiltration Reduce Intradialytic Hypotension in ESRD (RCT)

Locatelli et al, *JASN* 2010 Oct; Vol 21
Take Home Messages

- All these developments have not been able to totally abolish hypotension
- Unlikely any single successful treatment option exists, but rather an integrated, multidisciplinary approach may need: Biofeedback technologic combination (Hemocontrol® plus BTM®)
- To create an individual patient dialysis profile may prove more successful
- Attention needs to reduce interdialytic weight gains, so reducing UF requirements: technology can not alone compensate for excessive weight gains
- Ultimately, these maneuvers need to demonstrate a mortality and morbidity benefit