INTRADIALYTIC HYPOTENSION

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Intradialytic Hypotension

- Definition
- Acute management
- Clinical Impact of Intradialytic Hypotension
- Epidemiology
- Etiology
- Clinical Significance
- Ultrafiltration Rate
- Physiology of BP maintenance
- Plasma volume in dialysis
- Na model
- Ultrafiltration model
- Dry weight
- Predicting Intradialytic Hypotension
  - Clinical
  - Advanced Technologies
- Different Patterns of Intradialytic Hypotension
- Effect of volume shifts
- Medication options for mitigating intradialytic hypotension
How do we define it?

- Intradialytic hypotension?
  - Clear when we see one.
  - More difficult to define as a single, objective definition.
Intradialytic Hypotension

• Calvo, 2002:
  • Fall in SBP below 100mmHg and a fall in DBP by 20mmHg with symptoms.

• Sulowicz, 2006:
  • Acute: sudden drop to below 90mmHg or of at least 20mmHg with symptoms.
  • Chronic: persistent if interdialytic SBP is maintained less than 90-100mmHg.
  • Recurrent: Minimal of 50% of treatments.

Calvo, C. Clinical Autonomic Research, 12(2), 84–7, 2002
Sulowicz, W. Kidney International, 70(S104), S36–S9, 2006
Intradialytic Hypotension

- **Standard Definition (NKF K-DOQI)**
  - Decrease in SBP by $\geq 20$mmHg or decrease in MAP by 10mmHg
    - Associated with symptoms or clinical events to require intervention.
      - Potential symptoms: Abdominal discomfort, yawning, sighing, nausea, vomiting, cramps, restlessness, dizziness, anxiety.
Acute Management

- Decrease or stop the Uf rate
- Patient position: Trendelenburg with leg raised by 15-30°
- Saline Bolus IV: 200-500ml usually adequate
- Oxygen to maintain end-organs perfusion

As the immediate measures are taken, evaluate for other acute problems.
- Sepsis? Fever, chills, new coughs, wounds
- Hemolysis? Acute back/chest/abdominal pain
- Pericardial effusion? Distant heart sounds, pericardial rubs
- Worsened cardiac function? Recent MI, chest pains, severe AS
- Bleeding? Melena, CGE, BRBPR
- Air Emboli?
- Dialyzer reaction?
- Medication overdose?
Clinical Impact?

- Intermittent drops in BP often without immediately visible harm.

- Is it harmful?
- Or just “one of those things” that happen?
Subclinical Negative Impact

- **Brain Ischemia**: MRI have shown pathologic changes with dialysis, worse with intradialytic hypotension (IDH)
  - Brain white matter ischemic injury from loss of axons and myelin (McIntyre, Seminars in Dialysis, 2010)

- **Cardiac Stunning**: Echo during dialysis confirms the presence of LV regional wall motion abnormality (Chesterton, Hemodialysis International, 2010)
  - Episodic IDH is thought to exacerbate evolving myocardial injury.
  - Cardiac muscles receive coronary flow during diastole and most HD patients have a widened pulse pressure.

- **Gut Stunning**: Non-occlusive mesenteric ischemia is associated with frequent IDH. (Daugirdas, AJKD, 2001)
  - Mesenteric ischemia may also allow bacterial endotoxins to be introduced into the circulation, causing vasodilation and reduced cardiac contractility. (McIntyre, Seminars in Dialysis, 2010)
Apparent Negative Impact

• Severe episodes with actual stroke, MI, bowel ischemia.

• AVF thrombosis rate is higher with IDH.
  • In patients with IDH >30% of all Rx had 2x risk of AVF thrombosis

• Substandard Dialysis Treatments

• Negative Perception of Dialysis/Health Care

• Negative Psychological Impact and Quality of Life
Epidemiology

- 75% of all patients have had at least 1 episode in a study.
- Occurs in 5 to 30% of all dialysis treatments.
- In some patients, 50% of treatments are affected.

- Older patients
- Longer dialysis vintage
- Diabetes
- Lowe pre-dialysis blood pressure
- Higher Uf goal
Etiology

• In essence, the BP depends on:
  • 1) Cardiac reserve
  • 2) Intravascular volume and fluid removal rate
  • 3) Vascular tone
Clinical Significance

- In 17% of all treatments, intradialytic hypotension seen.
- 25% are free of intradialytic hypotension
- 75% of all patients has had at least 1 episode.
  - 16% of all patients had more than 1x/week on average.
    - These patients had higher mortality rate, higher admission rates and longer hospital stays.
- Dialysis facility was an independent predictor.
  - Older patients
  - Longer dialysis vintage
  - Diabetes
  - Lowe pre-dialysis blood pressure
  - Higher Uf goal

In essence, the BP depends on:
1) Cardiac reserve
2) Intravascular volume and Uf rate
3) Vascular tone

Fluid removal and hypotension

Fair statement?

Intradialytic hypotension usually does not occur if no fluid is ever removed from the patient in the absence of an acute illness.
Safe Ultrafiltration Rate?

- HEMO Study data: Data from 1846 patients.

- Compared by Uf rates:
  - up to 10 ml/h/kg
    - 70kg patient, 3.5hrs = <2.45 Liter target
  - 10–13 ml/h/kg
    - 70kg patient, 3.5hrs = 2.45~3.18 Liter target
    - Higher risk of CHF without mortality risk increase seen from this point
  - over 13 ml/h/kg:
    - 70kg patient, 3.5hrs = >3.18 Liter target
    - Increased risk of mortality. All cause mortality 1.59, CV mortality 1.71

Physiology of BP maintenance

Estimated plasma volume = 3.4 Liters, if 70kg and Hct 30
= 0.07x weight(kg)x(1-Hct)

Intracellular 28L

Interstitial 10.6L

Plasma 3.4L

Uf Goal: 3L
Plasma volume in dialysis

• Plasma refilling:
  • Almost 1 entire plasma volume is removed with HD but actual blood volume decrease is only 5-20%. Fluid moves in from the extracellular space.
  • Using high Na profile hastens the fluid movement from intracellular to extracellular.
  • Similarly, albumin IV, hypertonic saline, 20% Dextrose
Na model

• Clinically useful
• Excess thirst and fluid gains
• Increased BP
Ultrafiltration Profile

• Rationale that when the patient are move volume overloaded, earlier in the treatment, it’s much faster to refill the plasma volume.

• Higher Uf at the start of dialysis with reduction over time appear to provide best hemodynamic stability.

• Then constant profile
Dry weight

- Setting of accurate dry weight
- Usually determined by trial and error.
- The only way to clinically know:
  - Symptomatic development: Cramps, hypotension, nausea.
  - Other measures, Blood Volume Monitoring, bioimpedance, inferior vena cava ultrasound of uncertain value. More studies are needed.

- If the patient’s weight is below the dry weight, need to inform the physicians to adjust the dry weight or assess for acute/unresolved illnesses. Any new reasons for volume depletion?
Predicting Intradialytic Hypotension

- The first line of defense against IDH:
  - Pausing of ultrafiltration
  - Placing the patient in a reclined position
  - Possible administration of Saline IV

- Patients have individual MAP values which remain constant when well.
  - MAP = SBP x 0.33 + DBP x 0.66
  - BP1: 110/70 = MAP 82; BP2: 110/45 = MAP 66

- Decreasing MAP can precede IDH
  - MAP < 70 mmHg or decrease by 30 mmHg from pre-dialysis value
  - Pre-emptive pause in Uf for 10 minutes; Uf resumed if MAP improved to 70 mmHg or if MAP returned “close to starting MAP.”
  - This pre-emptive maneuver reduced the risk of IDH by 61%.

Blood Volume Monitoring

- Using real-time Hct data, provides information on plasma volume removal and refill balance.
- No predetermined threshold level of plasma volume reduction to predict impending hypotension.
- But BVM may be helpful in predicting the fluid removal limit per individual patient.
- Mixed data.

Bioimpedance Spectroscopy

High frequency current can go through all water space

Low frequency current can only pass through extracellular space

Differentiate:
• Lean Body Mass,
• Adipose Tissue Mass
• Excess water

Collective data on usefulness in preventing IDH remain to be seen.

Some promise in better defining the excess water volume in dialysis patients noted.
Intradialytic Hypotension Patterns

• If the BP is related to plasma refilling and preload and the volume is being removed slowly and consistently, why does the BP often drop suddenly?

• There is usually no sudden removal of volume immediately before the hypotensive episode.
Sudden BP Drops at Dialysis

- Much of the 3L of plasma volume is in the skin and splanchnic venous system which can alter their tone and the venous capacitance significantly.
Physiology of BP maintenance
Physiology of BP maintenance

Blood vessels relax

Cells

Blood Pressure Drops
Sudden vasodilatation

• During dialysis, sympathetic tone ramps up to maintain the BP.
  • In HD patients with sudden drops in BP, these episodes were preceded by increased levels of inosine and hypoxanthine in the blood. Then the sympathetic tone suddenly drops along with calf vascular resistance and HR (Converse, et al, 1992).

• Mechanism: Decreased cell perfusion increases ATP consumption. This leads to accumulation of AMP, adenosine, then inosine and hypoxanthine. Adenosine receptor activation leads to sudden drops in vascular resistance.

• Bezold-Jarisch reflex: Even in normal subjects, when the lower-body is subjected to a negative pressure, the BP is maintained for a while but suddenly will drop along with bradycardia development. Afferent nerve to inferior myocardium implicated; Unproven but though to play a role.
Circulatory Blood Redistribution

Sudden BP drops: Caffeine

• Caffeine:
  • Raises the BP transiently through sympathetic activity.
  • Also blocks the adenosine-receptor to minimize sudden onset hypotension. Does not seem to help with gradual onset hypotension.  (Shinzato, JASN, 1994)
  • 2006 study by Imai supports the role of adenosine A1 receptor

Change in the incidence of intradialytic hypotension  Imai, Kidney International, 2006
Dialysate Temperature

- A reduction in dialysate temperature from 36.7 to 34.4 decreased the frequency of IDH from 0.58 to 0.05 episodes per treatment in a study of 7 patients with frequent IDH. (Sherman, 1985)
- Temperature setting of at least 1 degree from the actual body temperature seem to help.
- Multiple similar study results in the efficacy of lower dialysate temp.
Zoloft (sertraline)

- SSRIs are used in the treatment of idiopathic orthostatic hypotension and neuro-cardiogenic syncope.
- Retrospective study:
  - 9 ESRD patients with HD-associated hypotension on sertraline for depression.
  - Data comparison on sertraline for 6 weeks vs. off medication for 6 weeks.
- Number of hypotensive episodes:
  - On sertraline (0.6 ± 0.2 episodes/session)
  - Off sertraline (1.4 ± 0.3 episodes/session).
- Therapeutic interventions for IDH (saline bolus, albumin infusion, decreased UF, and Trendelenberg positioning)
  - Off sertraline 11.0 ± 3.0 interventions
  - On sertraline 1.7 ± 0.8 interventions
- Speculated that sertraline attenuates the paradoxical sympathetic withdrawal.
- Limitations: 9 patient, non-randomized, retrospective
  - In 4 of 9 patients with similar nadir MAP
  - In 7 of 9 patients with the same post-dialysis MAP on or off sertraline.
Midodrine

• The prodrug achieves peak levels in 60-90 minutes.
  • Excretion of the drug is primarily renal with a half-life of 3 hours for desglymidodrine. In patients with ESRD, however, the half-life is increased.

• In a single-dose, randomized, placebo-controlled, blinded pharmacokinetic study in 16 ESRD patients with IDH.
  • The half-life of desglymidodrine, which was 3.5 hours on HD, increased to 9 hours on nondialysis days.

• Blowey et al described treatment with midodrine in a single patient for pharmacokinetic data.
  • The half-life was 10 hours on nondialysis days, but decreased to 1.4 hours with HD, confirming that HD effectively removes both the prodrug and active metabolite.
Midodrine Effect

![Graph showing blood pressure changes with and without midodrine]

- **SBP/without**
- **DBP/without**
- **MAP/without**
- **SBP/with**
- **DBP/with**
- **MAP/with**

*P<0.001, †P<0.01, ‡P<0.05

**Axes:**
- Y-axis: Blood Pressure (mm Hg)
- X-axis: Pre-HD BP, Lowest IDBP, Post-HD BP
Prevention of Recurrent Episodes

• Reassessing Dry Weight
  • Trial and error
  • Blood volume monitoring
  • Bioimpedance spectroscopy

• Avoiding Food: Peripheral vascular resistance drops, up to 2 hrs following the ingestion

• BP medication adjustments
Acute problems leading to IDH

- Sepsis
- Hemolysis
- Bleeding
- Pericardial effusion
- Worsened cardiac function: MI, aortic stenosis
- Medication overdose, interaction
- Air emboli
- Dialyzer reaction
Summary

- Safe Uf rate is <13 ml/kg/hr.
  - Remind patients to drink less liquids.
  - Discuss with the patient/physician to increase dialysis time.
- Low dialysate temperature in place?
- Monitor for changes in MAP.
  - Pre-emptive holding of Uf for 10 minutes until MAP better?
  - Saline, hypertonic saline, 20% dextrose, albumin as per local procedures and physician orders.
- Na profiling: Pros vs. Cons
- Uf profile review
- Holding BP medications pre-dialysis
- Discuss with physicians re: midodrine, caffeine, Zoloft
- Role of Blood Volume Monitoring?
- Always think of acute issues
- Is Peritoneal Dialysis an option?