University of Missouri

Hypotension in Peritoneal Dialysis

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Disclosures

- none

Overview

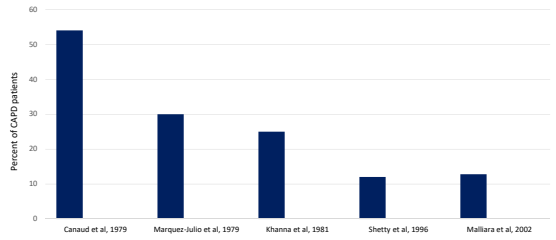
- Epidemiology
- Pathophysiology
- Outcomes
- Treatment

The Patient

68 year old male with DM, CHF, COPD on CAPD for 2 years.

- Hypertensive prior to starting dialysis
- Progressively declining blood pressures since month 5
- Orthostatic symptoms for past 6 months
- Stopped all anti-hypertensive medications
- 1.5% for all exchanges
- Progressive increase in weight with 2 admissions for CHF exacerbations

Prevalence of Hypotension in CAPD



Hypotension in HD vs PD

- 10-50% of HD treatments
- Most Common Causes:
  - Hypovolemia
  - Autonomic insufficiency
- 12-25% of CAPD patients
- Most Common Cause:
  - Hypovolemia

Orofino, Am J Nephrol 1990; Khanna, Perit Dial Bull 1981; Menon, Nephrol Dial Transplant 2001

Epidemiology of Hypotension in PD

TABLE I Causes of hypotension in chronic peritoneal dialysis patients [81 of 633 patients (12.8%)]

Group	*Patients [n (%)]*	*Age (years)*	*Months on PD*	*Months to hypotension*
Hypovolemia	32 (39.5)	62.7±14.8	58.8±35.8	32.1±26.8
Congestive heart failure	15 (18.5)	66.3±11.8	40.6±28.6	32.1±28.3
Antihypertensive treatment	11 (13.6)	61.6±17.5	38.7±20.8	16.4±14.9
Unknown cause	23 (28.4)	64.6±13.7	47.7±22.8	35.6±21.3
Total hypotensive patients	81 (100.00)	63.8±14.2	49.3±30.1	30.9±24.7

Malliara, Adv Perit Dial, 2002

Volume Status and Blood Pressure

- ISPD guidelines recommend frequent assessment of volume and holding anti-hypertensive medications until volume is optimized

Volume overload:
- Clinical evaluation: 25% volume overload
- Bioimpedance spectroscopy: 36-72% volume overload; 20-25% severe
- Lung Ultrasound: 46% volume overload in asymptomatic patients

Hypovolemia:
- No predictive clinical markers – physical exam, spot UNa, hemodynamic monitoring

Tzamaloukas et al, JASN 1995; Van Biesen et al, PLoS One 2011; Guo et al, PLoS One 2013; Kwan et al, Perit Dial Int 2014; Panuccio et al, Nephrol Dial Transplant 2012; Stephan et al, Brit J Anesth 2001

Volume Status and Blood Pressure in PD

- Volume and blood pressure not highly correlated in PD patients
- Total peripheral resistance is the most important determinant of blood pressure

Cheng et al, Perit Dial Int 2008; Tian et al, Perit Dial Int 2008

Volume Status and Outcomes in PD

- Fluid overload worsens CV mortality in PD patients
- Both overhydration and dehydration associated with loss of residual renal function

Siriopol et al, Nephrol Dial Transplant 2013; O'Lone et al, Nephrol Dial Transplant 2014;Konings et al, KI 2003; Davies et al, JASN 2003

Physiology of Arterial Hypotension

Decreased Cardiac Output	Nervous System Disorders
• Contractile Dysfunction Heart failure LVH Diastolic dysfunction Myocardial Infarction Myocarditis • Decreased Preload Hypovolemia Venous Dilation	• Autonomic Neuropathy • Sympathetic Dysfunction Decreased sensitivity to catecholamines • Impaired Pressure Control Mechanisms Baroreceptor and chemoreceptor feedback CNS Ischemia RAS impairment

Passadakis et al, Int J Art Organs 2002.

Autonomic Dysfunction in (hemo)Dialysis

- Chronic autonomic dysfunction due to uremia ?
- 23 chronic HD patients – 7 hypotension-prone and 16 non-hypotensive
- Direct measurement of volume changes, heart rate, vascular resistance, and peripheral blood flow
- Discontinued all anti-hypertensive medications prior to study
- All same dialysate

Converse et al, J Clin Invest 1992

Table II. Hemodynamic Responses to Hemodialysis

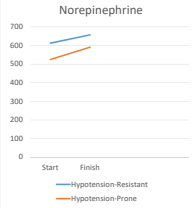
	Baseline	Volume removed during dialysis 33 % of total	67 % of total	100 % of total
A. Hypotension-resistant patients (n = 16)				
Volume removed, *liters*	0	0.8±0.1	1.9±0.2	2.8±0.3
Mean arterial pressure, *mmHg*	105±5	104±4	101±5	101±5
Heart rate, *beats/min*	74±4	72±4	75±4	76±5
Calf blood flow, *ml/min per 100 ml*	3.3±0.4	2.7±0.3	2.5±0.3*	2.3±0.3*
Calf vascular resistance, *U (dyn·s·min^{-5})*	37±4	44±4	49±5*	54±5*

	Baseline	Volume removed during dialysis 33 % of total	67 % of total	95 % of total	100 % of total
B. Hypotension-prone patients (n = 7)					
Volume removed, *liters*	0	0.9±0.3	1.9±0.5	2.5±0.5	2.7±0.5
Mean arterial pressure, *mmHg*	116±6	115±3	116±6	99±5*	60±6*
Heart rate, *beats/min*	71±4	74±3	78±3*	86±4*	74±5
Calf blood flow, *ml/min per 100 ml*	3.0±0.3	2.5±0.3	2.0±0.2*	1.7±0.2*	1.7±0.2*
Calf vascular resistance, *U (dyn·s·min^{-5})*	42±6	51±7	66±12*	63±9*	38±7

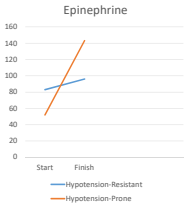
Data are mean±SE. * $P < 0.05$ vs. baseline.

Converse et al, J Clin Invest 1992

Autonomic Dysfunction in (hemo)Dialysis



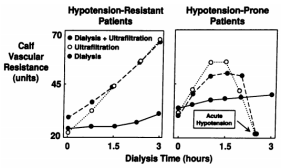
	Hypotension-Resistant	Hypotension-Prone
Norepinephrine (pg/ml)		
Start	613 +/- 117	525 +/- 68
Finish	657 +/- 140	591 +/- 23
Epinephrine (pg/ml)		
Start	83 +/-18	52 +/- 9
Finish	96 +/- 53	143 +/-53



Converse et al, J Clin Invest 1992

Autonomic Dysfunction In HD Is Due To Decreased Blood Volume

- Chronic autonomic dysfunction due to uremia ?
- Studies repeated on interdialysis day showed no difference between the two groups



Converse et al, J Clin Invest 1992

Autonomic Dysfunction in (hemo)Dialysis

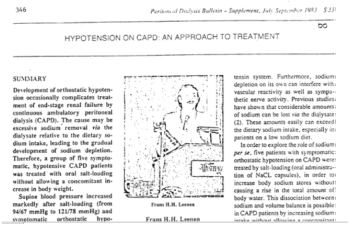
- Hypovolemia ⟶ Sympathetic inhibition ⟶ Vasodepressor effect
- Ventricular mechanoreceptors stimulated by excessive deformation of a nearly empty ventricle in forceful contraction

1 – Decreased catecholamines

2 – Paradoxical response to volume depletion

Converse et al, J Clin Invest 1992

Hypotension in Peritoneal Dialysis



346 Peritoneal Dialysis Bulletin - Supplement, July-September 1983 S 23

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HYPOTENSION ON CAPD: AN APPROACH TO TREATMENT

SUMMARY

Development of orthostatic hypotension occasionally complicates treatment of end-stage renal failure by continuous ambulatory peritoneal dialysis (CAPD). The cause may be excessive sodium removal via the dialysate relative to the dietary sodium intake, leading to the gradual development of sodium depletion. Therefore, a group of five symptomatic, hypotensive CAPD patients was treated with oral salt-loading without allowing a concomitant increase in body weight.

Supine blood pressure increased markedly after salt-loading (from 94/67 mmHg to 121/78 mmHg) and symptomatic orthostatic hypo-

From H.H. Leenen

From H.H. Leenen

tension system. Furthermore, sodium depletion on its own can interfere with vascular reactivity as well as sympathetic nerve activity. Previous studies have shown that considerable amounts of sodium can be lost via the dialysate (2). These amounts easily can exceed the dietary sodium intake, especially in patients on a low sodium diet.

In order to explore the role of sodium *per se*, five patients with symptomatic orthostatic hypotension on CAPD were treated by salt-loading (oral administration of NaCL capsules), in order to increase body sodium stores without causing a rise in the total amount of body water. This dissociation between sodium and volume balance is possible in CAPD patients by increasing sodium

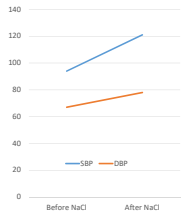
Leenen et al, Periton Dial Bull 1983

Sodium Supplementation in CAPD

- 5 patients
- NaCl tablets 5-10 g per day
- Dose titrated based on BP and tolerance
- Clinically-determined volume control maintained by adjusting dialysate

Leenen et al, Periton Dial Bull 1983

Sodium Supplementation in CAPD

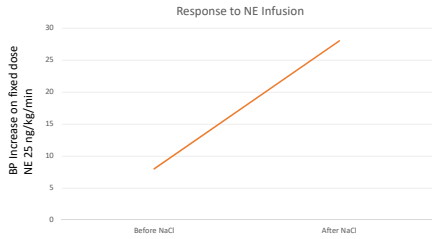


- Increased blood volume
- Increased extracellular volume

- Stable body weight

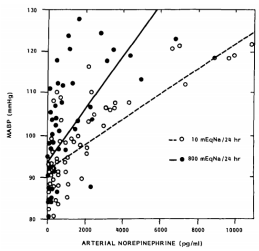
Leenen et al, Periton Dial Bull 1983

Sodium Supplementation in CAPD



Leenen et al, Periton Dial Bull 1983

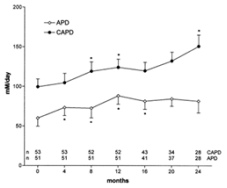
Sodium Balance Affects Sympathetic Responsiveness



Rankin et al, Hypertension 1981

CAPD vs APD

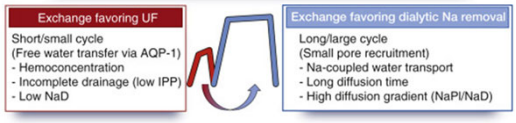
- Higher sodium removal in CAPD



Rodriguez-Carmona et al, AJKD 2004; Ortega et al, Am J Nephrol 2001; Davison et al, CJASN 2009; Davenport et al, Int J Artif Organs 2009;

CAPD vs APD

- Higher sodium removal in CAPD



Rodriguez-Carmona et al, AJKD 2004; Ortega et al, Am J Nephrol 2001; Davison et al, CJASN 2009; Davenport et al, Int J Artif Organs 2009;

CAPD vs APD

- Higher sodium removal in CAPD
- Volume control not significantly different between CAPD and APD
  - Bioimpedance spectroscopy :
    - ECF volume
    - Height-adjusted ECF volume
    - ECFV/TBW ratio

Rodriguez-Carmona et al, AJKD 2004; Ortega et al, Am J Nephrol 2001; Davison et al, CJASN 2009; Davenport et al, Int J Artif Organs 2009;

Outcomes for Hypotensive PD Patients

- Those who respond quickly have improved outcomes – mostly hypovolemia
- Overall survival: 3 years – 78%
  5 years – 54%

  * No difference based on etiology of hypotension

Malliara, Adv Perit Dial, 2002

Outcomes for Hypotensive CAPD Patients

- Decreased survival

Malliara, Adv Perit Dial, 2002

Outcomes for Hypotensive CAPD Patients

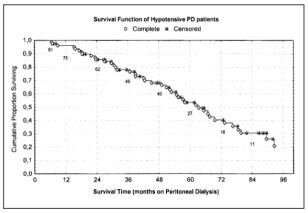


Fig. 2 - *Survival rates of all hypotensive PD patients. The numbers under the curve are the patients entering at that time interval.*

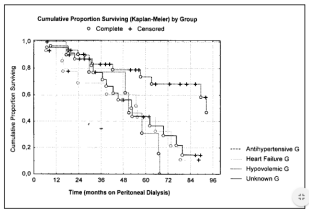


Fig. 3 - *Survival rates of hypotensive PD patients, by grou... Regardless of the etiology of hypotension all the patients had simi... probabilities for survival ($x^2 = 6.63$, $p = 0.08$).*

Malliara, Adv Perit Dial, 2002

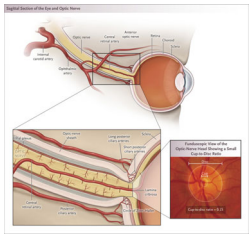
Outcomes for Hypotensive CAPD Patients

- Decreased survival
- Significant complications
  - Increased cardiovascular events
  - Anterior Ischemic Optical Neuropathy

Malliara, Adv Perit Dial, 2002

Anterior Ischemic Optic Neuropathy

- Acute blindness
- Usually bilateral
- Hypotension
- Adults and children
- PD is well-described risk in children



DiZazzo et al, Perit Dial Int 2015

Outcomes for Hypotensive CAPD Patients

- Unclear changes in survival
- Significant complications
  - Increased cardiovascular events
  - Anterior Ischemic Optical Neuropathy
  - Decreased quality of life

Malliara, Adv Perit Dial, 2002

Treatment of Hypotension in PD

- Salt loading
- Change prescription / modality
- Midodrine

Summary

- Causes of hypotension include hypovolemia, cardiac disease, altered autonomic response, and decrease in sympathetic activity
- Salt losses in PD likely contribute to hypotension
- Salt supplementation may be an effective treatment for chronic hypotension

- Research opportunities!!!