IN THE NAME OF GOD

HEMODIALYSIS COMPLICATIONS

Intradialytic Hypotension-(Etiology)

Patient related factors :

- Impaired plasma volume refilling (too high ultrafiltration, autonomic dysfunction)
- Decreased cardiac reserve (diastolic or systolic dysfunction)
- Impaired venous compliance
- Autonomic dysfunction (diabetes, uremia)
- Arrhythmias
- Anemia
- Drug therapy (vasodilators, ß blockers, calcium channel blockers)
- Alteration of vasoactive substances in blood (low NO, high endothelin-1 and angiotensin-2)
- Eating during treatment (increased splanchnic blood flow)
- Too low target weight estimation

Procedure related factors

- Rapid decrease in plasma osmolality (relatively large surface area membrane, high starting BUN)
- Excess absolute volume and rate of fluid removal (for fluid overload)
- Change in serum electrolytes (hypocalcemia, hypokalemia)
- Dialysate – acetate, warm dialysate
- Membrane blood interaction
- Hypoxia (partially patient related

Other less common causes

- Pericardial tamponade
- Myocardial infarction
- Aortic dissection
- Internal or external hemorrhage
- Septicemia
- Air embolism
- Pneumothorax
- Hemolysis

Pathogenesis

- Vascular instability during dialysis is a multifactorial process in which procedure and patient related factors may influence the decrease in plasma volume and induce an impairment of cardiovascular regulatory mechanisms. An awareness of the risk factors and by identifying those patients who are most susceptible may significantly improve cardiovascular stability during dialysis. Among high-risk patients, monitoring and biofeedback of the various hemodynamic variables, together with an extensive use of convection, can prevent the appearance of symptomatic hypotension and help in averting its onset

Treatment

- Stop or reduce ultrafiltration
- Place patient in Trendelenburg position
- Administration of saline and hypertonic agents. However, excess fluid replacement should be avoided to prevent sodium overload.
- Continuous infusion of pressor agents (meteraminol, norepinephrine) are very rarely neede

Prevention

Patient end strategy

- Reduce intradialytic weight gain (dietary and treatment compliance)
- Avoid anti-hypertensive medication on the morning of the dialysis day
- Avoid missing dialysis and stay the entire dialysis time for treatment
- Avoid eating during dialysis

Procedure related strategy

- Dialysate sodium- sodium profiling and sodium gradient protocol but maintaining zero sodium balance to the extent possible
- Modeling fluid removal- sequential ultrafiltration and dialysis, blood volume controlled hemodialysis
- Cool dialysate- isothermic dialysis is well tolerated and clearly reduces the incidence of hypotension
- Reduction of the ultrafiltration rate with prolongation of treatment time
- Accurate estimation of dry weight (segmental bioimpedance, and others)
- Judiciously increasing dialysate calcium while avoiding hypercalcemia
- Medications

-Midodrine given approximately 30 min before dialysis significantly reduces the incidence of hypotension. It has been considered safe and well tolerated.

-Carnitine has been recommended in-patients with frequent hypotensive episodes

Intradialytic Hypertension(Etiology)

- Genetic predisposition
- Pre existing hypertension
- Extracellular volume excess
- Increased renin- angiotensin system activity (possibly in the presence of increased sodium overload)
- Increased sympathetic activity
- Increased endothelin-1 to nitric oxide ratio
- Uremic toxins (ADMA)
- Blood hyperviscosity
- Correction of hypoxia- induced vasoconstriction
- Increased dialysate sodium
- Secondary hyperparathyroidism

Treatment and Prevention

- Lifestyle modifications such as weight reduction, dietary modification, sodium restriction, physical activity and moderation of alcohol consumption can reduce systolic blood pressure from 2-14 mm Hg
- Adjustment of target weight on a regular basis. Gradual reduction of interdialytic weight gain over a few weeks using zero sodium balance, salt restriction, longer dialysis or extra dialysis sessions may yield a significant benefit
- Reducing erythropoeitin dose in patients with severe hypertension and withholding of anti-hypertensive medications on the day of dialysis
- Nephrectomy in resistant cases
- Renal transplantation or conversion to PD

Diagnosis

Type A reaction

- Severe and rapid in onset
- Rare (7.0 per 1000 patient year)
- Established by three major criteria or two major and one minor criterion
- Etiology- Use of ethylene oxide (ETO) for sterilization of dialyzer and polyacrylonitrile membranes (PAN) membranes, especially AN69 in patients on ACE-inhibitors

Diagnosis

-Type B reaction

- Primary symptoms are chest and back pain
- Occurs 20-40 minutes into the dialysis treatment
- Disappears or lessens dramatically during the subsequent hours of dialysis
- Pathogenesis of type B reaction is not clear

-May be related to complement activation

- Current data do not support the role of membrane biocompatibility in development of type B reactions

Treatment

- Symptomatic and supportive
- Discontinue HD and discard the blood, oxygen, anti-histamines, epinephrine and corticosteroids
- HD can be initiated after stabilization with a more biocompatible membrane and a hemodialyzer not sterilized with ETO (ethylene oxide)

Prevention

- Avoid combination of PAN membrane and angiotensin converting enzyme inhibitor (ACEI) use
- Use of ARBs (angiotensin receptor blockers) and dialysate with 3.5 mEq/L calcium may lower the risk

Disequilibrium Syndrome

- The full blown syndrome is rarely seen now. Disequilibrium syndrome most commonly occurs in:

- First few dialysis sessions
- Elderly and pediatric patients
- Patients with pre-existing CNS lesions (recent stroke, head trauma) or conditions characterized by cerebral edema (malignant hypertension, hyponatremia, hepatic encephalopathy)
- High pre-dialysis BUN
- Severe metabolic acidosis

Etiology

- Cerebral edema resulting from urea removal from the blood more rapidly than from the CSF and brain tissue generating a urea osmotic gradient responsible for water moving into brain cells.
- HD generates a CO2 gradient between plasma and CSF lowering the pH in the CSF and brain tissue. This change will promote an increase in brain cell osmolality due to the rise in H+ concentration and the in-situ generation of osmols (acid radicals from protein metabolism) resulting in brain edema

Treatment

- Usually self-limited. However, for severe symptoms HD should be stopped.
- If seizures occur, glucose, diazepam, phenytoin loading followed by infusion
- Osmotically active agents in dialysate have been tried- albumin, glycerol, mannitol)

Prevention

- Identify high risk patients
- Reduce dialysis efficacy and limit urea reduction to 30% (smaller dialyzer, decreasing blood flow, sequential dialysis increasing dialysis time), however, a recent small series found tolerance to higher urea reduction
- Prophylactic administration of osmotically active agents (mannitol, glucose, fructose) and using high sodium dialysate
- IV mannitol 20% at 50 ml/hr with intravenous diazepam- simplest way to prevent DDS in high risk patients

Cramping(Etiology)

- Approximately 20% of dialysis sessions are accompanied by muscle cramps
- Cramps are more pronounced in patients who require high ultrafitration rates and are possibly dialyzed below their dry weight. They are presumably related to reduction in muscle perfusion that occurs in response to hypovolemia. Compensatory vasoconstrictive responses may shunt blood centrally during treatment, and could play a role in promoting muscle cramps.
- Changes in intra or extracellular balance of potassium and concentration of ionized calcium can disturb neuromuscular transmission and produce cramps.
- Peripheral vascular disease, although common in dialysis patients, may not be associated with increased prevalence of intradialytic cramps which confirms that processes related to the dialytic treatment are responsible for the cramps.

Differential Diagnosis

While the majority of cramps are associated with dialysis treatment, the differential diagnosis is extensive and includes the following conditions:

- Changes in intra or extracellular balance of potassium and concentration of ionized calcium can disturb neuromuscular transmission and produce cramps
- Idiopathic cramps
- Contractures (occurring in conditions such as metabolic myopathies, and thyroid disease)
- Tetany (due to hypocalcemia or alkalosis)
- Dystonias (occupational cramps, anti-psychotic medications)
- Other leg problems such as restless leg syndromes and periodic leg movements, must be distinguished from cramps

Treatment and Prevention

- Many of the treatment strategies are similar to those used to treat intradialytic hypotension
- Physical maneuvers such as massage of the calf muscles and dorsiflexion of the foot are not very helpful
- Immediate treatment is to increase intravascular volume by interrupting or slowing ultrafiltration and administering saline, mannitol or glucose. In addition to effecting an intravascular shift of water, hypertonic solutions may directly improve blood flow to the muscles.
- Use of dialysate sodium, potassium or calcium modeling. The concept of individualization of dialysate composition seems to be a good preventive method.
- Careful reassessment of the dry weight, counseling the patient to reduce interdialytic weight gain and using bicarbonate dialysis
- Carnitine4, quinine5, prazocin, vitamin E, vitamin C and Japanese herbal extract have been tested with variable results.

Air Embolism(Etiology)

- Can be venous or less commonly, arterial
- Three vulnerable areas of air entry in dialysis patients:

- Between patient and blood pump, due to high negative pressure and leaks in the circuit in this segment

- Air in the dialysate fluid (uncommon, mostly gets trapped in venous chamber)

- During central venous catheter insertion or removal

- Upright body position and hypovolemia, both by reducing venous pressure, are significant contributing factors

Treatment

- Prevent further air entry by clamping and disconnecting the circuit
- Flat supine position may be better over traditionally advocated left lateral (Duran's position) and Trendelenburg position
- Oxygen with FiO2 100%
- Hyperbaric oxygen (prevents cerebral edema)
- Use of Luer-lock syringes for blood draw from catheters

Prevention

- Test machine prior to use to ensure that the air detector alarm system is working effectively
- Catheter insertion or removal should be in a head low position (insertion site 5 cm below right atrium). Patient can assist by holding their breath or doing a Valsalva maneuver that will increase central venous pressure.

Hemolysis(Etiology)

-Mechanical

- High blood pump flow
- Single-needle dialysis
- Small gauge cannula
- Kinked blood lines
- High negative arterial pressure
- Offset blood pump
- Failure of rinsing
- Hydrogen peroxide

Hemolysis(Etiology)

-Contamination with

- Hypochlorite
- Formaldehyde

-Priming error

- Hypotonic saline

-Dialysate error

- Hyper or hypotonic dialysate
- Overheated dialysate

-Dialysate contamination

- Chloramines
- Nitrates
- Copper

Treatment

- Stop blood pump, clamp venous bloodline and discard the blood
- Provide oxygen to the patient
- Type and cross of blood transfusion if needed
- Resume HD as soon as patient is stabilized, since hyperkalemia accompanies hemolysis

Prevention

- Test machine prior to use to ensure that the air detector alarm system is working effectively
- Avoid chemical contaminants that can damage RBC's
- Oxidants such as chloramines, copper, zinc
- Reducing agents such as formaldehyde, hypo or hypertonic dialysate
- Overheated dialysate
- Avoid small needles
- Highly negative arterial pressure alarms
- Ensure correct positioning of tubing in the roller pumps
- Avoid accidental compression of lines

Cardiac Arrhythmias

-Risk Factors

- Left ventricular hypertrophy
- Heart failure
- Ischemic heart disease
- High risk in those with reduced heart rate variability and increased QT dispersion

Risk Factors

- Other factors
  - Age
  - Respiratory failure
  - Rapid reduction of extra-cellular volume
  - Electrolyte and acid-base derangement
  - Cardiac and major vascular surgery
  - Digoxin therapy
  - Sympathetic dysfunction
  - Increased phosphate and PTH

Diagnosis and Treatment

- Draw blood samples for electrolytes, bicarbonate and glucose levels
- EKG, oxygen, IV fluids
- May need to discontinue HD. Correct electrolyte disturbance (especially potassium, calcium and magnesium)
- Cardioversion with AED (automated external defibrillator) in case patient is hemodynamically unstable and has a treatable rhythm

Diagnosis and Treatment

- Digoxin can be used to control ventricular rate in SVT.

-Patients on digitalis might need increase of the dialysate potassium to 3- 3.5 mEq/L to prevent hypokalemia.

- Amiodarone can be used in usual dose for ventricular arrhythmias
- Intracellular shift of potassium can be minimized by reducing dialysate glucose (from 200 to 100 mg/dl), and when acid base status permits, bicarbonate level

Prevention

- Avoidance of low hemoglobin levels and hypoxia during dialysis. Maintenance of optimal calcium, phosphate and PTH levels
- Oxygen use

Hemorrhage(Risk Factors)

- Platelet dysfunction
- Ineffective platelet-vessel wall interaction and heparin induced thrombocytopenia (HIT)
- Use of anti-coagulation during HD
- Co-morbid conditions

-Uncontrolled hypertension

-Liver disease, sepsis, certain medication (especially anti-platelet drugs)

- Access site kept covered
- Venous needle falling out or catheter connection disrupted (venous pressure may fall too little to cause an alarm)

Risk Assessment

- Very high - Active bleeding during HD
- High - Surgical/traumatic wound within 3 days
- Low - Surgical/traumatic wound > 7 days

Diagnosis and Treatment

- Screen for bleeding and activated clotting time
- Prolonged bleeding time - cryoprecipitate, DDAVP or conjugated estrogen acutely
- Prolonged PTT (heparin induced) - Protamine, FFP

Prevention

- Should never keep access site covered
- Review heparin dose
- Strategy based on risk assessment
- Low risk - low dose conventional heparin, low molecular weight heparin
- Very high/high risk - regional anticoagulation with heparin and protamine, heparin- free dialysis, regional citrate anticoagulation, Prostaglandin (PGI2), PD

Hypoxia

During hemodialysis, PaO_2 falls about 10-20 mmHg. This decrease has no clinical consequences in patients with normal oxygen tension, but in seriously ill patients with predialysis hypoxemia, the drop in PaO_2 can be catastrophic

Etiology

- Acetate dialysate (now obsolete). Can also be seen with use of bicarbonate dialysate
- Acetate causes hypoxemia by at least two mechanisms:

-Increased oxygen consumption in the metabolism of acetate to bicarbonate

-Intradialytic loss of CO_2

- Rapid correction of chronic metabolic acidosis

Etiology

- Bioincompatible membranes

-Activate complement

- Hypocapnea due to intradialytic loss of CO_2 and adaptation to chronic metabolic acidosis predisposes to periodic breathing and sleep apnea syndrome (SAS)
- SAS is also a cause of hypoxia in HD patients

-High prevalence in HD patients (54-80%) and has both obstructive and central components

-Can alter autonomic responses and cause arrhythmias, pulmonary hypertension, and systemic hypertension

Treatment and Prevention

- Dialysis-induced hypoxemia can be attenuated by interventions that increase the CO_2 content of the dialysate either by direct administration or by using bicarbonate buffered dialysate
- Use of biocompatible membranes might be helpful
- In critically ill patients who may already have some degree of predialytic hypoxia, it is necessary to increase the ventilated volumes and/or the percentage of FiO_2
- Improvement in SAS has been reported with the use of prolonged dialysis such as nocturnal and daily hemodialysis

Pruritus(Etiology)

- Common abnormalities in ESRD play a role in pathogenesis:
- Xerosis (dry skin)
- Peripheral neuropathy
- Hypercalcemia
- Hyperphosphatemia
- Hypermagnesemia
- Zinc depletion
- Hypervitaminosis A

Pruritus(Etiology)

- No correlation found between standard biochemical tests (blood urea nitrogen, creatinine, calcium, phosphate, parathyroid hormone) and uremic pruritus
- A possible role for chronic inflammation
- A possible relationship between pruritus and type of dialyzer is not clear

Treatment

- Empirical, individualized and often ineffective
- Skin emollients, capsaicin, H-1 receptor antagonist, phototherapy (UVB)
- Newer drugs: Thalidomide, nicergoline, lidocain, mexiletine, cholestyramine, cromolyn sodium and Gabapentin
- Other modalities: Acupuncture, electric needle stimulation and sauna, parathyroidectomy and renal transplantation in recalcitrant cases

Prevention

- Optimizing calcium, phosphate, magnesium, PTH and delivered dose of dialysis (greatly reduced at Kt/V > 1.5)
- Avoidance of dialysis related factors such as iodine, ethylene oxide. Find out any allergy to heparin.
- Biocompatible membrane can be used preferably
- Consider parathyroidectomy. Renal transplantation is the only definitive treatment.

Febrile Reactions

- Febrile reactions are defined as a rise in temperature during HD of at least 0.5° C or a rectal or axillary temperature during dialysis of at least 38.0 or 37.5° C respectively. The majority (70%) of febrile reactions are associated with preexisting infections (vascular access, urinary and respiratory)

Febrile Reactions

- HD related febrile reactions can be associated with localized infection of the vascular access site (especially catheters and grafts) or products from the dialysate and/or the apparatus used for HD treatment.

Diagnosis and Treatment

- Obtain blood cultures
- Begin broad spectrum antibiotics immediately
- Treatment largely supportive and empirical
- Cluster of similar cases should prompt a review of:

-Water used for reprocessing

-Dialysate

-Processing procedure

-Bicarbonate system

Prevention

- Reduce the use of catheters for HD
- Reduce the susceptibility to infections by:

-Provide adequate HD

-Prevent and/or treat malnutrition

-Optimize hemoglobin concentration

-Avoid iron overload

- Use biocompatible dialysis membrane5
- Reduce S. aureus infections by screening nasal carriers and treating with mupirocin or gentamicin topically

Metabolic Acidosis

- Can occur accidentally as a consequence of dialysate fluid containing improper ratios of acid and base concentrates in the form of acetate or bicarbonate.
- Can also develop as a result of the accidental use of an acidic concentrate instead of acetate or bicarbonate and due to computer software malfunction of the machine
- Severe metabolic acidosis has been reported during first 2 hours of HD using sorbent regenerative hemodialysis in mechanically ventilated patients.

Metabolic Acidosis

- Treatment consists of intravenous administration of bicarbonate and dialysis with bicarbonate dialysate of a correct concentration (38-40 mEq/L)

- The mainstay of prevention is to fit all HD machines with a pH meter and alarms that will prevent the extreme acid load, which may be caused by an inappropriately prepared bicarbonate dialysate. Conductivity checks are vital.

Metabolic Alkalosis

- The most common cause is the loss of hydrochloric acid as a result of vomiting or nasogastric suction
- Less common causes:

-Technical errors during HD

-Malfunction of the dialysis machine's pH monitor and proportioning system (the reversed connection of bicarbonate and acid concentrate containers to the entry ports)

Metabolic Alkalosis

- Severe metabolic alkalosis may cause:
  - Tissue hypoxia
  - Arrhythmia
  - Seizure
  - Delirium
  - Stupor
- Applying HD therapy with specially formulated low-bicarbonate, low-acetate, or acid dialyses are safe and effective intervention for severe metabolic alkalosis. Severe metabolic alkalosis can be corrected rapidly and safely with bicarbonate concentrates dialysate between 25-28 mEq/L

Hypokalemia

- Severe intradialytic hypokalemia can occur even when the dialysate contained a higher potassium concentration than the predialysis serum potassium concentration1
- The cause of the hypokalemia is a rapid shift of potassium from the extracellular to the intracellular space secondary to correction of acidosis
- Dialysis induced hyperkalemia is rare.
- Reported causes include:

-History suggesting prolonged potassium loss

-Marked acidosis

-Baseline moderate hypokalemia

Prevention and Treatment

- Excess potassium removal during HD can prolong QTc interval on EKG preferentially and predispose to arrhythmia
- Try to keep post dialysis serum potassium 2-3 mEq/L
- Use dialysate with 3.0 mEq/l of potassium in patients with CAD and/or on digoxin, unless there is chronic, severe hyperkalemia
- Never use 0 mE/L potassium dialysate. Use of very low dialysate potassium (1 mEq/L) should be discouraged. Modelling of dialysate potassium could be helpful

Hyperkalemia

- Common in ESRD (around 10% of HD patients)
- Contributes to 3-5% of deaths

Etiology

- Excessive dietary potassium intake
- Metabolic acidosis
- Acute infection with marked catabolism
- Rhabdomyolysis
- Mineralocorticoid deficiency
- Medications
- Dialysis induced hyperkalemia (rare)

-High dialysate potassium concentration
-Hemolysis
-Accidental potassium infusions

Hyponatremia

- Hyponatremia can occur:

-At the start of dialysis if an error is made when connecting concentrate containers

-During dialysis if containers run dry and conductivity monitor fail

Treatment

- Clamp the bloodlines
- Discard the blood present in the dialysis tubing (as acute hyponatremia during HD is frequently associated with hemolysis and hyperkalemia)
- Anticonvulsants and blood transfusion may be needed
- Rapid correction of hyponatremia in HD patients may not be dangerous (except for one case report)
- Current recommendation would be to correct hyponatremia using the guidelines currently accepted for nonuremic patients

Prevention

- Dialysate sodium level should be higher than that in plasma

Hypernatremia

- Hyponatremia can occur when sodium concentration is high and the conductivity monitors of the dialysis machine are not functioning or the alarms are not set properly
- Dialysate conductivity can be incorrectly sensed as low by the coated conductivity cells (that gets coated by granules from less soluble batch of sodium bicarbonate powder)

-At the start of dialysis if an error is made when connecting concentrate containers

-During dialysis if containers run dry and conductivity monitor fai

Treatment

- Dialysis can be resumed with dialysate sodium

2 mEq/L lower than plasma sodium concentration while infusing isotonic saline. Use of dialysate sodium 3-5 mEq/L lower than plasma sodium might increase the risk of disequilibrium syndrome

Prevention

- Frequent check of conductivity monitors which can get coated with bicarbonate granules and can cause falsely low readings

THANK YOU