Use of Dialysis and Hemoperfusion in the Treatment of Poisoning

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- Introduction
- DIALYSIS AND HEMOPERFUSION
- Choice of therapy
- Complications
- MANAGEMENT OF POISONING WITH SELECTED AGENTS

INTRODUCTION

Hemodialysis, hemoperfusion, and peritoneal dialysis (PD), particularly the first two procedures, can be useful in the management of drug overdose and poisoning.

However, these treatments should be applied selectively, as part of the general approach to the poisoned patient, include supportive therapy, decontamination,elimination enhancement, and antidotes

TABLE 20.1 Criteria for Consideration of Dialysis or Hemoperfusion in Poisoning

1. Progressive deterioration despite intensive supportive therapy
2. Severe intoxication with depression of midbrain function leading to hypoventilation, hypothermia, and hypotension
3. Development of complications of coma, such as pneumonia or septicemia, and underlying conditions predisposing to such complications (e.g., obstructive airways disease)
4. Impairment of normal drug excretory function in the presence of hepatic, cardiac, or renal insufficiency
5. Intoxication with agents with metabolic and/or delayed effects (e.g., methanol, ethylene glycol, and paraquat)
6. Intoxication with an extractable drug or poison, which can be removed at a rate exceeding endogenous elimination by liver or kidney

DIALYSIS AND HEMOPERFUSION

Any procedure used in poisoning treatment should have a greater effect on drug elimination than that which occurs spontaneously.

The decision to institute dialysis or hemoperfusion must be made on an individual basis.

In addition to providing extracorporeal drug elimination, dialysis can provide essential supportive care to poisoned patients with multiorgan or kidney injury.

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Choice of therapy

Peritoneal dialysis

Is not very effective in removing drugs from the blood, with maximal poison clearance rarely above 15 mL/min.

When hemodialysis is difficult to institute quickly, such as in small children,a prolonged session of PD can be a valuable adjunctive treatment for poisoning.

Under certain conditions, such as in the hypothermic-poisoned patient, PD maybe useful.

Hemodialysis

Hemodialysis is the therapy of choice for water-soluble drugs, especially those of low molecular weight along with a low level of protein binding, as such compounds will diffuse rapidly across the dialyzer membrane.

Examples are:

ethanol, ethylene glycol, lithium, methanol, and salicylates. Water-soluble drugs that have high molecular weights (amphotericin B and vancomycin) diffuse across dialyzer membranes more slowly and are less well removed.

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Hemodialysis is not very useful in removing lipid-soluble drugs (e.g., amitriptyline) with large volumes of distribution or drugs with extensive protein binding.

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Hemoperfusion

Hemoperfusion is a process whereby blood is passed through a device containing adsorbent particles.

Most commonly, the adsorbent particles are activated charcoal or some sort of resin. Although hemoperfusion may be more effective than hemodialysis in clearing the blood of many protein bound drugs

Hemoperfusion will remove many lipid-soluble drugs from the blood much more efficiently than hemodialysis.

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If a drug is equally well removed from the blood by hemoperfusion and hemodialysis, then hemodialysis is preferred:

- Potential problems of cartridge saturation are avoided.
- The incidence of hemoperfusion complications such as thrombocytopenia and leukopenia is reduced.
- With hemodialysis, any coexisting acid–base or electrolyte disturbances can be treated.

Continuous hemodiafiltration, hemoperfusion

Prolonged continuous treatment is potentially useful in drugs with moderately large volumes of distribution (VD) and slow intercompartmental transfer times, because post therapy rebound of plasma drug levels is avoided.

Continuous hemoperfusion has been used successfully in theophylline and phenobarbital toxicity, and continuous hemodiafiltration has been used in ethylene glycol and lithium toxicity

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Toxicokinetics

The following factors will influence poison dialyzability:

Molecular weight:

- Techniques that use diffusion such as hemodialysis usually have an approximate cutoff of 5,000 Da.
- Convection- and adsorption-based techniques are capable of removing poisons that are in excess of 50,000 Da in size.
- Plasmapheresis can remove poisons that are up to 1,000,000 Da in size.

Protein binding:

Since the poison–protein complex cannot freely pass through dialyzers or hemofilters.

Only poisons that are largely unbound (or free) can be removed by these techniques.

Volume of distribution:

VD is the theoretical volume into which a drug is distributed.

Heparin a drug confined to the blood compartment, has a VD of approximately 0.06 L/kg. Drugs distributed primarily in the extracellular water (e.g., salicylates) will have a VD of approximately 0.2 L/kg.

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Thus, even if a hemodialysis or hemoperfusion treatment extracts most of the drug present in the blood.

Flowing through the extracorporeal circuit, the amount of drug removed during a single treatment session will represent only a small percentage of the total body drug burden.

Endogenous clearance:

Extracorporeal removal usually is not indicated when endogenous clearance by metabolism and elimination is expected to exceed the rate of exogenous elimination.

This explains why hemodialysis is not indicated for poisons like cocaine or toluene.

TABLE 20.2 Serum Concentrations of Common Poisons in Excess of Which Hemodialysis (HD) or Hemoperfusion (HP) Should Be Considered

Drug	Serum Concentration[a] (mg/L)	Serum Concentration[a] (mcmol/L)	Method of Choice
Phenobarbital	100	430	HP, HD
Glutethimide	40	180	HP
Methaqualone	40	160	HP
Salicylates	800	4.4 mmol/L	HD
Theophylline	40	220	HP, HD
Paraquat	0.1	0.4	HP > HD
Methanol	500	16 mmol/L	HD
Meprobamate	100	460	HP

Vascular access for hemodialysis or hemoperfusion in poisoning:

In patients without permanent vascular access in place, percutaneous cannulation of a large central vein using a dialysis catheter is required.

Choice of hemodialyzer

High-flux, high-efficiency dialyzers with high urea clearances should generally be used.

The development of high-cutoff hemodialysis membranes (with increased pore size of 8 to 10 nm) may allow clearance of larger toxins and molecules as large as 50 to 60 kDa.

Choice of a hemoperfusion cartridge

- Typical sorbents are activated carbons (charcoals), ion exchange resins, or nonionic exchange macroporous resins.

- Sorbent particles have been rendered biocompatible by coating the surface with a polymer membrane.

The hemoperfusion circuit:

The hemoperfusion circuit is similar to the blood side of a hemodialysis circuit and includes an air detector and a venous air trap.

Standard hemodialysis blood pumps and machines (without use of dialysis solution) are often used to drive the blood through the tubing and cartridge.

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- Setup and priming with saline or dextrose differ depending on the brand of cartridge used, and the manufacturer’s literature should be consulted in all instances.

- The hemoperfusion cartridge must be primed in a vertical position with the arterial (blood inlet) side facing downward.

Heparinization during hemoperfusion.

- Once the cartridge has been primed, a bolus dose of heparin (usually 2,000–3,000 units) is administered into the arterial line.

- As a rule, because of some adsorption on the sorbent, more heparin may be required for a hemoperfusion treatment (e.g., approximately 6,000 units or10,000 units for charcoal and resin, per session)

- Heparin should be given in amounts sufficient to maintain the patient's (ACT) or partial thromboplastin time at about twice the normal value.

Duration of hemoperfusion.

A single 3-hour treatment will substantially lower the blood levels of most poisons for which hemoperfusion is effective.

More prolonged use of a hemoperfusion cartridge is inefficient, because the charcoal tends to become saturated.

Any rebound in blood drug concentrations consequent to tissue release can be treated with a second hemoperfusion session.

Complications.

All extracorporeal techniques require vascular access through a central line, and this procedure itself is subject to complications.

Hemodialysis

- Hypophosphatemia.
- Alkalemia.
- Disequilibrium syndrome in acutely uremic patients.

Hemoperfusion.

Mild transient thrombocytopenia and leukopenia can occur, but cell counts usually return to normal within 24 to 48 hours following a single hemoperfusion.

Adsorption or activation of coagulation factors has also been observed rarely and may be clinically significant in patients with liver failure.

TABLE 20.3 Some Available Hemoperfusion Devices (May Vary by Country)

Manufacturer	Device	Sorbent Type	Amount of Sorbent	Polymer Coating
Asahi[a]	Hemosorba	Charcoal	170 g	Poly(2-hydroxyethyl methacrylate) (poly-HEMA)
Gambro	Adsorba 150/300c	Charcoal	150/300 g	Cellulose acetate
Braun[a]	Haemoresin	Resin XAD-4 Amberlite	350 g	None

MANAGEMENT OF POISONING WITH SELECTED AGENTS

Acetaminophen:

Activated charcoal should be given to patients presenting within 4 hours of ingestion.

If serum acetaminophen levels are above 150 mg/L (1.0 mmol/L) at 4 hours, the likelihood of toxicity is high and NAC (PO or IV) should be given.

Its efficacy in preventing liver failure declines if started more than 10 hours after ingestion, but NAC is still recommended even after 24 hours.

Aspirin

In adults, severe aspirin poisoning is usually accompanied by metabolic acidosis with respiratory alkalosis, whereas in children, isolated metabolic acidosis is often encountered. aspirin is well removed by hemodialysis.

Hemodialysis should be considered :

- the serum level exceeds 90 mg/dL
- there is evidence of marked acidemia.
- neurologic involvement (neurologic symptoms, hyperthermia, seizures)
- noncardiogenic pulmonary edema.

Digoxin

The probabilities of digoxin-induced arrhythmias are 50% and 90% at serum levels of 2.5 and 3.3 ng/

The drug is 25% proteinbound. For these reasons, only 5% of the body load will be removed by a 4-hour hemodialysis treatment.

Hemoperfusion is more effective and has been shown to improve symptoms, it is not routinely recommended in the treatment of digoxin.

In dialysis patients, Fab therapy remains preferred over hemoperfusion or plasmapheresis.

Ethylene glycol

- The first phase of toxicity due to ethylene glycol begins <1 hour after ingestion and is characterized by CNS depression similar to ethanol intoxication.
- The second phase is due to the toxic effects of the metabolite, glycolic acid, on the cardiopulmonary 12 hours after ingestion. A severe metabolic acidosis commonly occurs

- 24 to 48 hours, renal failure often supervenes as a result of oxalate precipitation in the kidney, delaying the excretion of the poison.

TABLE 20.5 Indications for Hemodialysis in Patients with Severe Ethylene Glycol or Methanol Poisoning

1. Severe metabolic acidosis (pH <7.25–7.30)
2. Renal failure
3. Visual symptoms/signs
4. Deteriorating vital signs despite intensive supportive care
5. Ethylene glycol or methanol levels >50 mg/dL unless fomepizole is being administered and patient is asymptomatic with a normal pH[a]

Isopropanol

Isopropanol is a common cause of poisoning but is only

occasionally fatal.

Gastrointestinal and CNS symptoms, including confusion, ataxia, and coma, occur in 1 hour. Hypotension due to cardiac depression and vasodilatation.

Hemodialysis might be considered:

✓ if the isopropanol levels are >400 mg/dL

✓significant CNS suppression

✓ renal failure

✓hypotension exists

Lithium carbonate

- Mild (serum Li 1.5–2.5 mmol/L)
- Moderate (serum Li 2.5–3.5 mmol/L) lithium toxicity are characterizedby neuromuscular irritability, nausea, and diarrhea.
- Severe toxicity (serum Li >3.5 mmol/L) can result in seizures, stupor, and permanent neurologic deficit.

As lithium is 0% protein-bound it is removed very well by dialysis. Hemodialysis should be considered:

- serum Li >3.5 mmol/L
- serum Li >2.5 mmol/L in patients with appreciable symptoms or in patients with renal insufficiency,
- when serum Li is between 2.5 and 3.5 mmol/L in asymptomatic patients but when levels are expected to rise

Paraquat

Delayed toxicity with pulmonary fibrosis and renal and multiorgan failure can occur following ingestion of more than 10 mL of paraquat concentrate.

Survival is dependent on the amount ingested and the plasma levels with respect to time of ingestion .Plasma levels of above 3 mg/L regardless of when they are measured are usually fatal.

Initial management includes gastric lavage with administration of activated charcoal.

Hemoperfusion is effective in drug removal and should be considered when the plasma paraquat level is 0.1 mg/L or above.

Phenothiazines and tricyclic antidepressants.

- These agents are highly protein-bound and have extremely large volumes of distribution.
- The total amount of these drugs removed by either hemodialysis or hemoperfusion is small.
- Treatment of intoxication with these agents is largely supportive, including bicarbonate therapy for widened QRS complex.

Dabigatran

Is an oral direct thrombin inhibitor for prophylaxis of thromboembolism in patients with nonvalvular atrial fibrillation.

Recent publications have confirmed that dialysis removes the anticoagulant.

The kinetics seem to follow first-order elimination during dialysis.

Metformin

The condition, which if severe can be fatal, is termed metformin-associated lactic acidosis (MALA).

Metformin is absorbed from the gut relatively rapidly and is not metabolized.

MALA is defined as a venous serum lactate level >5 mmol/L with serum bicarbonate <22 mmol/L. The mainstay of therapy is supportive, including bicarbonate administration, hemodialysis for correction of acidosis and removal of lactate and metformin.

Thallium

Thallium is a highly toxic metal originally used for the treatment of ringworm infestation, and then as a rodenticide, but because of toxicity it is now relegated to industrial use.

Thallium mimics potassium, as these two elements are similar in ionic size.

Thallium inhibits critical metabolic enzymes such as pyruvate kinase and succinate dehydrogenase.

The usual findings of thallium poisoning are alopecia and painful ascending peripheral neuropathy

Continue:

Hourly thallium removal by hemodialysis and charcoal hemoperfusion appears superior to removal by normal kidney function

TABLE 20.8 Drugs and Chemicals Removed with Hemodialysis

Antimicrobials/ Anticancer

Cefaclor
Cefadroxil
Cefamandole
Cefazolin
Cefixime
Cefmenoxime
Cefmetazole
(Cefonicid)
(Cefoperazone)
Ceforamide
(Cefotaxime)
Cefotetan
Cefotiam
Cefoxitin
Cefpirome
Cefroxadine
Cefsulodin
Ceftazidime
(Ceftriaxone)
Cefuroxime
Cephacetrile
Cephalexin
Cephalothin
(Cephapirin)
Cephradine
Moxalactam
Amikacin
Dibekacin
Daptomycin
Fosfomycin
Gentamicin
Kanamycin
Neomycin
Netilmicin
Sisomicin
Streptomycin
Tobramycin
Bacitracin
Colistin
Amoxicillin
Ampicillin
Azlocillin
Carbenicillin
Clavulinic acid
(Cloxacillin)
(Dicloxacillin)
(Floxacillin)
Mecillinam
(Mezlocillin)
(Methicillin)
(Nafcillin)
Penicillin
Piperacillin
Temocillin
Ticarcillin
(Clindamycin)
(Erythromycin)
(Azithromycin)
(Clarithromycin)
Linezolid
Metronidazole
Nitrofurantoin
Ornidazole
Sulfisoxazole
Sulfonamides
Tetracycline
(Doxycycline)
(Minocycline)
Tinidazole
Trimethoprim
Aztreonam
Cilastatin
(Dapsone)
Doripenem
Imipenem
(Chloramphenicol)
(Amphotericin)
Ciprofloxacin
(Enoxacin)

(continued)

(Norfloxacin)
Ofloxacin
Isoniazid
(Vancomycin)
Capreomycin
PAS
Pyrizinamide
(Rifampin)
(Cycloserine)
Ethambutol
5-Fluorocytosine
Acyclovir
(Amantadine)
Didanosine
Foscarnet
Ganciclovir
(Ribavirin)
Vidarabine
Zidovudine
(Pentamidine)
(Praziquantel)
(Fluconazole)
(Itraconazole)
(Ketoconazole)
(Miconazole)
(Chloroquine)
(Quinine)
(Azathioprine)
Bredinin
Busulphan
Cyclophosphamide
5-Fluorouracil
(Methotrexate)
Barbiturates
Amobarbital
Aprobarbital
Barbital
Butabarbital
Cyclobarbital

(Calcium channel blockers)
Captopril
(Diazoxide)
Carbromal
Chloral hydrate
(Chlordiazepoxide)
(Diazepam)
(Diphenylhydantoin)
(Diphenylhydramine)
Ethiamate
Ethchlorvynol
Ethosuximide
Gallamine
Glutethimide
(Heroin)
Meprobamate
(Methaqualone)
Methsuximide
Methyprylon
Paraldehyde
Primidone
Topiramate
Valproic acid

Cardiovascular Agents
Acebutolol
(Amiodarone)
Amrinone
Atenolol
(Digoxin)
Enalapril
Fosinopril
Lisinopril
Quinapril
Ramipril
(Encainide)
(Flecainide)

Tocainide

Alcohols
Ethanol
Ethylene glycol
Isopropanol
Methanol

Analgesics, Antirheumatics
Acetaminophen
Acetophenetidin
Acetylsalicylic acid
Colchicine
Methylsalicylate
(D-Propoxyphene)
Salicylic acid

Antidepressants
(Amitriptyline)
Amphetamines
(Imipramine)
Isocarboxazid
MAO inhibitors
Moclobemide
(Pargylline)
(Phenelzine)
Tranylcypromine
(Tricyclics)

Solvents, Gases
Acetone
Camphor
Carbon monoxide
(Carbon tetrachloride)
(Eucalyptus oil)
Thiols
Toluene
Trichloroethylene

Plants, Animals,

TABLE 20.9 Drugs and Chemicals Removed with Hemoperfusion

Barbiturates
Amobarbital
Butabarbital
Hexabarbital
Pentobarbital
Phenobarbital
Quinalbital
Secobarbital
Thiopental
Vinalbital

Nonbarbiturate Hypnotics, Sedatives, and Tranquilizers
Carbamazepine
Carbromal
Chloral hydrate
Chlorpromazine
(Diazepam)
Diphenhydramine
Ethchlorvynol
Glutethimide
Meprobamate
Methaqualone
Methsuximide
Methyprylon
Phenytoin
Promazine
Promethazine
Valproic acid

Analgesics, Antirheumatic
Acetaminophen
Acetylsalicylic acid
Colchicine
D-propoxyphyene
Methylsalicylate
Phenylbutazone
Salicylic acid

Antimicrobials/ Anticancer
(Adriamycin)
Ampicillin
Carmustine
Chloramphenicol
Chloroquine
Clindamycin
Dapsone
Doxorubicin
Gentamicin
Ifosfamide
Isoniazid
(Methotrexate)
Pentamidine
Thiabendazole
(5-Fluorouracil)
Vancomycin

Antidepressants
(Amitryptiline)
(Imipramine)
(Tricyclics)

Plant and Animal Toxins, Herbicides, Insecticides
Amanitin
Chlordane
Demeton sulfoxide
Dimethoate
Diquat
Endosulfan
Glufosinate
Methylparathion
Nitrostigmine
(Organophosphates)
Phalloidin
Polychlorinated
biphenyls
Paraquat
Parathion

(continued)

TABLE 20.9 Drugs and Chemicals Removed with Hemoperfusion *(continued)*

Cardiovascular
Atenolol
Cibenzoline succinate
Clonidine
Digoxin
(Diltiazem)
(Disopyramide)
Flecainide
Metoprolol
N-acetylprocainamide
Procainamide
Quinidine

Miscellaneous
Aminophylline
Cimetidine
(Fluoroacetamide)
(Phencyclidine)
Phenols
(Podophyllin)
Theophylline

Solvents, Gases
Carbon tetrachloride
Ethylene oxide
Trichloroethane
Xylene

Metals
(Aluminum)*
(Iron)*

Hemoperfusion

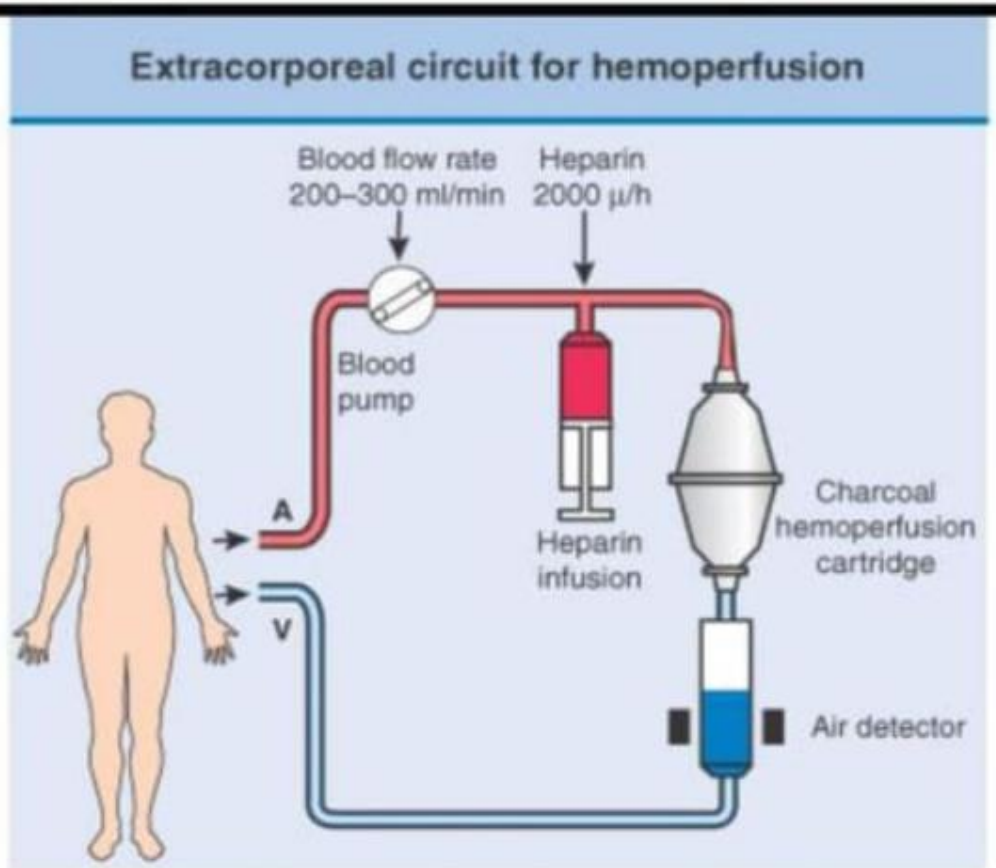
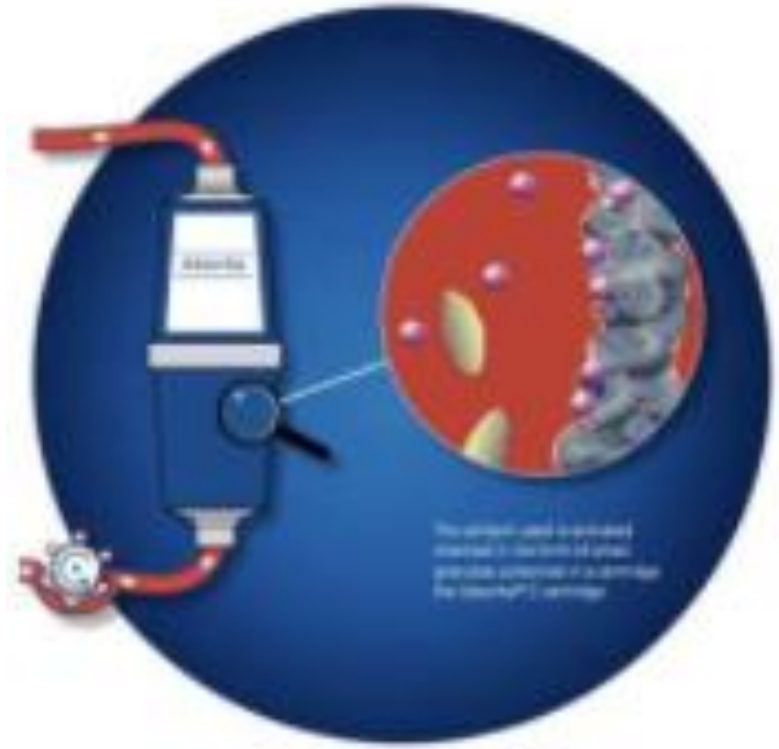


Figure 100.6 Extracorporeal circuit for hemoperfusion.

The Charcoal Hemoperfusion Filter



- Canister with 300g of activated charcoal
- Blood flow though the canister is driven by a normal dialysis machine
- There is no ultrafiltration, no fluid removal, no dialysis.

ochure from the "Adsorba C" range by Gambro, for the Prismaflex machines

TABLE 36.5 Factors to Be Considered When Choosing between Urinary Alkalinization, Hemodialysis, Hemoperfusion, and Continuous Renal Replacement Therapy (CRRT)

Urine Alkalinization	Hemodialysis	Hemoperfusion	CRRT
Toxin characteristics • Excreted unchanged by the kidney • Low degree of protein binding • Exist in a weakly acidic form • Have extracellular distribution	Toxin characteristics • Low molecular weight • Water solubility • Low protein binding	Toxin characteristics • High molecular weight • Lipid solubility • High protein binding • Low volume of distribution	Toxin characteristics • Slow release from tissues • Large volume of distribution
Patient characteristics • Normal renal function • Adequate urine output	Patient characteristics • Presence of kidney disease • Acid–base, electrolyte • Volume problems • Low platelet count	Patient characteristics • Hemodynamic instability	Patient characteristics • Critically ill • Hemodynamic instability
Examples • Tricyclic antidepressants • Phenobarbital • Salicylates	Examples • Lithium • Salicylate • Valproate • Theophylline • Methanol • Ethylene glycol	Examples • Theophylline • Phenobarbital • Glutethimide	Examples • Lithium • Salicylate • Valproate • Metformin • Acetaminophen • Ethylene glycol

Conclusion

Poisoning is a medical emergency and, in severe cases extracorporeal treatments may be urgently required to prevent or reverse major toxicity. The different options include IHD, intermittent HF, HDF, CRRT, hemoperfusion, TPE, exchange transfusion, and PD.


THANK
YOU


Thank
you