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Hemoperfusion

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INTRODUCTION

Hemoperfusion is an extracorporeal blood purification modality that consists of the passage of anticoagulated whole blood through a device, usually a column, that contains adsorbent particles [1]. It is used for the removal of toxins in poisonings and has been used for the removal of cytokines in septic patients in some centers [2-5].

However, although hemoperfusion is effective for removing toxins, it is rarely used in the treatment of poisoning [6,7] and is among the least available extracorporeal modalities for detoxification [8].

An overview of hemoperfusion, including the clinical settings in which this technology may be used, is reviewed here. A general introduction to the treatment of poisoning as well as a discussion of the use of other technologies for poisoning, such as hemodialysis and peritoneal dialysis, are presented separately. (See "Enhanced elimination of poisons" and "General approach to drug poisoning in adults".)

MECHANISM

In hemoperfusion, whole blood is passed through a column that contains fixed adsorbent particles [1]. Toxins with molecular weights ranging from 100 to 40,000 daltons bind to the particles and are removed as blood exits the column. Higher-molecular-weight solutes are adsorbed less efficiently [9].

There are two major types of adsorbent particles, including activated charcoal and resins (such as the hydrocarbon polymer, polystyrene). Charcoal has greater affinity for water-soluble molecules, while

resins have greater affinity for lipid-soluble molecules. Although available in Europe, resin columns for hemoperfusion are not available in the United States, because of a limited market.

The adsorbent may be modified to provide selective removal of endotoxin, cytokines, or antibodies. (See 'Sepsis' below and 'Other' below.)

INDICATIONS

The major accepted indication for hemoperfusion is the removal of lipid-soluble, highly protein-bound toxins (ie, poisoning) that are not easily removed with standard hemodialysis. Hemoperfusion has also been used in some centers for the removal of cytokines in septic patients; the removal of antibodies and antibody-antigen complexes in autoimmune and other disorders; and the removal of hepatic toxins in liver failure.

Poisoning — Hemoperfusion is preferred to hemodialysis alone for paraquat poisoning. Hemoperfusion provides better clearance compared with high-flux hemodialysis and is associated with increased survival among individuals who have ingested paraquat [10-13]. Concomitant hemodialysis may be required in patients with reduced kidney function, although this has not been clearly shown to add a survival benefit to hemoperfusion alone [14,15]. (See "Paraquat poisoning", section on 'Indications for extracorporeal therapies'.)

Other indications for hemoperfusion are less clear. Hemoperfusion used to be preferred to hemodialysis for the removal of many toxins including barbiturates [16], theophylline [17], valproic acid [18], carbamazepine [19], amanita mushrooms [20,21], and aluminum after chelation with deferoxamine [22,23]. However, this initial preference for hemoperfusion was based on older data that compared hemoperfusion with standard dialysis with cuprophane membranes (ie, prior to the advent of high-flux [large-pore] dialyzers) [24]. High-flux hemodialysis, which is used today, appears to provide equivalent or better clearance [25-27], although, except for paraquat, there are few studies that have directly compared hemoperfusion to high-flux hemodialysis. Even if high-flux hemodialysis and hemoperfusion are comparable with respect to toxin removal, the increased availability, decreased cost, familiarity, and lower complication rate favors the use of hemodialysis (table 1) [28].

Another advantage of hemodialysis is that it corrects concurrent metabolic or acid-base disturbances that may be present and increases body temperature in the severely hypothermic patient [1].

Sepsis — Hemoperfusion devices containing either the antibiotic polymyxin B or a polystyrene divinylbenzene copolymer have been specifically developed for removing cytokines from patients with sepsis or endotoxemia. These devices have been approved for use in Europe and Japan but are not available in the United States.

- Polymyxin B – An adsorbent column containing resin bound to the antibiotic polymyxin B removes endotoxins that activate the inflammatory cascade [29]. Endotoxin levels decrease within minutes after starting hemoperfusion [29]. Some studies have shown improvements in hemodynamic measures (mean arterial pressure, catecholamine dose), respiratory function, and the sepsis-related organ failure (SOFA) scores [30].

  Studies have yielded conflicting results on mortality [30-34]. A systematic review and meta-analysis including seven trials (n = 841) found that polymyxin hemoperfusion was associated with lower mortality (risk ratio 0.65, 95% CI 0.47-0.89) [33]. However, there was significant heterogeneity between studies that was only partly explained by the study venue and the baseline mortality rate. The quality of evidence was considered low overall.

- **Polystyrene divinylbenzene copolymer** — A polystyrene divinylbenzene copolymer column has been developed for use with intermittent hemodialysis, continuous renal replacement therapy (CRRT) machine, cardiopulmonary bypass, or extracorporeal membrane oxygenation (ECMO) blood circuit [35-37]. Improvements in hemodynamic status/vasopressor dose and organ dysfunction have been reported in patients with septic shock [35], acute respiratory distress syndrome (ARDS) [36], and systemic inflammatory response syndrome (SIRS) associated with cardiopulmonary bypass [37]. However, a small, randomized trial did not show significant differences in cytokine levels after hemoperfusion in patients receiving cardiopulmonary bypass [38]. A larger trial including patients with sepsis also showed no reduction in interleukin 6 (IL-6) levels or decrease in mortality with hemoperfusion [39]. Studies have similarly not shown a benefit on mortality of CRRT in sepsis. (See "Continuous renal replacement therapy in acute kidney injury", section on 'Indications'.)

Other — The removal of pathogenic antibodies and antibody-antigen complexes is used in multiple conditions including systemic lupus erythematosus, vasculitis, antiglomerular basement membrane disease, pemphigus, atopic dermatitis, Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy, myasthenia gravis, multiple sclerosis [40-44], and as a preconditioning protocol to allow for ABO-incompatible kidney transplantation [45]. (See "Therapeutic apheresis (plasma exchange or cytapheresis): Indications and technology" and "Kidney transplantation in adults: ABO incompatibility", section on 'Overview of desensitization'.)

Although the standard of care is plasmapheresis/therapeutic plasma exchange (TPE), a possible advantage of hemoperfusion/immunoadsorption is more specific immune modulation without the requirement of plasma product infusions. However, immunoadsorption is considered experimental for such conditions and has not supplanted apheresis alone for removal of pathogenetic antibodies [40-42].

The removal of hepatic toxins by some extracorporeal liver assist devices also involves adsorption. This issue is discussed elsewhere. (See "Acute liver failure in adults: Management and prognosis", section on 'Artificial hepatic assist devices'.)

PRESCRIPTION

Hemoperfusion is conducted using dialysis blood lines and a dialysis machine apparatus containing a blood pump and pressure gauges. The column generally contains between 100 and 300 g of activated charcoal or 300 to 650 g of resin. A list of some of the clinically available hemoperfusion devices and the contained sorbents is shown in the table (table 2).

Vascular access — We use a tunneled or nontunneled central venous hemodialysis catheter for most patients. If an arteriovenous fistula or graft is available when the poisoned patient also has end-stage kidney disease (ESKD), it is appropriate to cannulate this access for hemoperfusion.

Selection of cartridge — The choice of cartridge depends upon body size and drug involved. A small cartridge should be utilized for a child or a patient with a tiny habitus. In the US, the cartridge will contain polymer-coated charcoal. In Europe, where resin is available, the resin, XAD-4, can be used for a lipid-soluble drug.

Anticoagulation — Anticoagulation is typically required for hemoperfusion, either with systemic heparin or regional citrate. Heparin requirements are likely to exceed that necessary for hemodialysis due to heparin adsorption. The activated clotting time (ACT) should be maintained at approximately 2 to 2.5 times normal or an activated plasma thromboplastin time (APTT) of approximately 60 to 70 seconds. Regional citrate anticoagulation is used in some centers (see "Anticoagulation for the hemodialysis procedure"). Priming and flushing of the devices are achieved with normal saline.

Blood flow — The minimum blood flow for efficient drug removal is approximately 300 mL/min. Blood flow should be increased as possible to approximately 450 mL/min.

Pressure gauges detect interior rises in pressure, which indicate clot formation occurring inside the device; this is rare if heparinization is controlled via adequate monitoring of the ACT.

Duration — Intermittent hemoperfusion is usually performed for approximately four hours. Longer treatment times for charcoal hemoperfusion are unlikely to provide additional clearance due to device saturation. Treatment duration of only two hours has been standard in trials for endotoxin removal with a polymyxin B column. Reuse of devices is not performed.

Repeat treatments may be necessary once the drug redistributes from tissues into the plasma following its removal from the plasma compartment (ie, "rebound"). This is associated with increased

signs of drug toxicity such as neurologic dysfunction or coma.

We do not use continuous hemoperfusion. Intermittent hemoperfusion is more efficient in addressing the rebound effect and reduces the hematologic side effects of prolonged hemoperfusion (see 'Complications' below). Intermittent therapies also allow the replacement of saturated devices with fresh devices, which restores maximal extraction ratio.

MONITORING

Drug levels should be monitored, if available. However, reporting of drug levels often takes too long to be clinically useful. In such cases, the patient is started on hemoperfusion based on the history of known or suspected poisoning, and the clinical response is used to guide therapy. Platelet levels should be regularly monitored, such as after each treatment, as decreases in platelet count are not uncommon. (See 'Complications' below.)

COMPLICATIONS

The most common side effect of hemoperfusion is thrombocytopenia [46-48]. The platelet count usually returns to normal within 24 to 48 hours following hemoperfusion [46,47]. Thrombocytopenia may be worse with resin than with charcoal.

Other side effects include hypocalcemia, hypoglycemia, and neutropenia [47]. These complications are usually minor and correct spontaneously or can be corrected. There is also a mild reduction of one to two degrees in body temperature.

Hypotension is infrequent but well described [48]. If needed, vasopressor agents should be administered distal to the sorbent devices to minimize their adsorption.

The frequency of side effects has been reduced by coating of absorbents with a polymer solution that reduces platelet adhesion and complement activation.

COMBINED HEMODIALYSIS/HEMOPERFUSION

Hemoperfusion does not remove fluid or correct electrolyte imbalances such as hyperkalemia. Among patients with acute kidney injury, hemodialysis may be also be required.

Hemodialysis may be performed first followed immediately by hemoperfusion, using the same bloodlines and apparatus. Alternatively hemoperfusion may be combined with continuous renal

replacement therapy (CRRT) with the hemoperfusion column placed in the blood circuit upstream from the hemofilter [29,35].

The indications for dialysis are discussed elsewhere. (See "Renal replacement therapy (dialysis) in acute kidney injury in adults: Indications, timing, and dialysis dose", section on 'Urgent indications'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Dialysis".)

SUMMARY AND RECOMMENDATIONS

- Hemoperfusion consists of the passage of anticoagulated blood through a device containing adsorbent particles. The most commonly available adsorbent particles are activated charcoal and resin. (See 'Introduction' above and 'Mechanism' above.)
- Hemoperfusion may be superior to high-flux hemodialysis for paraquat removal. For other lipid-soluble or highly protein-bound drugs, high-flux hemodialysis appears to work as well as hemoperfusion and is generally preferred. (See 'Mechanism' above and 'Indications' above.)
- Hemoperfusion devices containing either the antibiotic polymyxin B or a polystyrene divinylbenzene copolymer have been specifically developed for removing cytokines from patients with sepsis or endotoxemia. (See 'Sepsis' above.)
- Platelet depletion is the most important side effect of hemoperfusion. Other side effects include hypocalcemia, hypoglycemia, a transient fall in white blood cell count, and a mild reduction in body temperature. Hypotension is infrequent. (See 'Complications' above.)

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REFERENCES

1. Winchester JF, Boldur A, Oleru C, Kitiyakara C. Use of dialysis and hemoperfusion in treatment of poisoning. In: Handbook of Dialysis, 4th ed., Daugirdas JT, Blake PG, Ing TS (Eds), Lippincot t Williams & Wilkins, Philadelphia 2007. p.300.
2. MUIRHEAD EE, REID AF. A resin artificial kidney. J Lab Clin Med 1948; 33:841.
3. Hampel G, Crome P, Widdop B, Goulding R. Experience with fixed-bred charcoal haemoperfusion in the treatment of severe drug intoxication. Arch Toxicol 1980; 45:133.
4. Gelfand MC, Winchester JF, Knepshield JH, et al. Treatment of severe drug overdosage with charcoal hemoperfusion. Trans Am Soc Artif Intern Organs 1977; 23:599.
5. Verpooten GA, De Broe ME. Combined hemoperfusion-hemodialysis in severe poisoning: kinetics of drug extraction. Resuscitation 1984; 11:275.
6. Shalkham AS, Kirrane BM, Hoffman RS, et al. The availability and use of charcoal hemoperfusion in the treatment of poisoned patients. Am J Kidney Dis 2006; 48:239.
7. Gummin DD, Mowry JB, Spyker DA, et al. 2016 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 34th Annual Report. Clin Toxicol (Phila) 2017; 55:1072.
8. Bouchard J, Lavergne V, Roberts DM, et al. Availability and cost of extracorporeal treatments for poisonings and other emergency indications: a worldwide survey. Nephrol Dial Transplant 2017; 32:699.
9. Denti E, Luboz MP, Tessore V. Adsorption characteristics of cellulose acetate coated charcoals. J Biomed Mater Res 1975; 9:143.
10. Rao R, Bhat R, Pathadka S, et al. Golden Hours in Severe Paraquat Poisoning-The Role of Early Haemoperfusion Therapy. J Clin Diagn Res 2017; 11:OC06.
11. Wang HR, Pan J, Shang AD, Lu YQ. Time-dependent haemoperfusion after acute paraquat poisoning. Sci Rep 2017; 7:2239.
12. Li A, Li W, Hao F, Wang H. Early Stage Blood Purification for Paraquat Poisoning: A Multicenter Retrospective Study. Blood Purif 2016; 42:93.

13. Hong SY, Yang JO, Lee EY, Kim SH. Effect of haemoperfusion on plasma paraquat concentration in vitro and in vivo. Toxicol Ind Health 2003; 19:17.

14. Park S, Lee S, Park S, et al. Concurrent Hemoperfusion and Hemodialysis in Patients with Acute Pesticide Intoxication. Blood Purif 2016; 42:329.

15. Lin G, Long J, Luo Y, et al. Continuous venovenous hemofiltration in the management of paraquat poisoning: A meta-analysis of randomized controlled trials. Medicine (Baltimore) 2017; 96:e6875.

16. Mactier R, Laliberté M, Mardini J, et al. Extracorporeal treatment for barbiturate poisoning: recommendations from the EXTRIP Workgroup. Am J Kidney Dis 2014; 64:347.

17. Ghannoum M, Wiegand TJ, Liu KD, et al. Extracorporeal treatment for theophylline poisoning: systematic review and recommendations from the EXTRIP workgroup. Clin Toxicol (Phila) 2015; 53:215.

18. Ghannoum M, Laliberté M, Nolin TD, et al. Extracorporeal treatment for valproic acid poisoning: systematic review and recommendations from the EXTRIP workgroup. Clin Toxicol (Phila) 2015; 53:454.

19. Ghannoum M, Yates C, Galvao TF, et al. Extracorporeal treatment for carbamazepine poisoning: systematic review and recommendations from the EXTRIP workgroup. Clin Toxicol (Phila) 2014; 52:993.

20. Aji DY, Calişkan S, Nayir A, et al. Haemoperfusion in Amanita phalloides poisoning. J Trop Pediatr 1995; 41:371.

21. Monhart V. [Amanita poisoning and the importance of sorption hemoperfusion in its therapy]. Vnitr Lek 1997; 43:686.

22. Chang TM, Barre P. Effect of desferrioxamine on removal of aluminum and iron by coated charcoal haemoperfusion and haemodialysis. Lancet 1983; 2:1051.

23. Weiss LG, Danielson BG, Fellström B, Wikström B. Aluminum removal with hemodialysis, hemofiltration and charcoal hemoperfusion in uremic patients after desferrioxamine infusion. A comparison of efficiency. Nephron 1989; 51:325.

24. Winchester JF. Dialysis and hemoperfusion in poisoning. Adv Ren Replace Ther 2002; 9:26.

25. Koh KH, Tan HH. High-flux haemodialysis treatment as treatment for carbamazepine intoxication. Med J Malaysia 2006; 61:109.

26. Tapolyai M, Campbell M, Dailey K, Udvari-Nagy S. Hemodialysis is as effective as hemoperfusion for drug removal in carbamazepine poisoning. Nephron 2002; 90:213.

27. Palmer BF. Effectiveness of hemodialysis in the extracorporeal therapy of phenobarbital overdose. Am J Kidney Dis 2000; 36:640.

28. Lavergne V, Nolin TD, Hoffman RS, et al. The EXTRIP (EXtracorporeal TReatments In Poisoning) workgroup: guideline methodology. Clin Toxicol (Phila) 2012; 50:403.

29. Shimizu T, Miyake T, Tani M. History and current status of polymyxin B-immobilized fiber column for treatment of severe sepsis and septic shock. Ann Gastroenterol Surg 2017; 1:105.

30. Cruz DN, Antonelli M, Fumagalli R, et al. Early use of polymyxin B hemoperfusion in abdominal septic shock: the EUPHAS randomized controlled trial. JAMA 2009; 301:2445.

31. Payen DM, Guilhot J, Launey Y, et al. Early use of polymyxin B hemoperfusion in patients with septic shock due to peritonitis: a multicenter randomized control trial. Intensive Care Med 2015; 41:975.

32. Iba T, Fowler L. Is polymyxin B-immobilized fiber column ineffective for septic shock? A discussion on the press release for EUPHRATES trial. J Intensive Care 2017; 5:40.

33. Terayama T, Yamakawa K, Umemura Y, et al. Polymyxin B Hemoperfusion for Sepsis and Septic Shock: A Systematic Review and Meta-Analysis. Surg Infect (Larchmt) 2017; 18:225.

34. Fujii T, Ganeko R, Kataoka Y, et al. Polymyxin B-immobilized hemoperfusion and mortality in critically ill adult patients with sepsis/septic shock: a systematic review with meta-analysis and trial sequential analysis. Intensive Care Med 2018; 44:167.

35. Kogelmann K, Jarczak D, Scheller M, Drüner M. Hemoadsorption by CytoSorb in septic patients: a case series. Crit Care 2017; 21:74.

36. Träger K, Schütz C, Fischer G, et al. Cytokine Reduction in the Setting of an ARDS-Associated Inflammatory Response with Multiple Organ Failure. Case Rep Crit Care 2016; 2016:9852073.

37. Träger K, Fritzler D, Fischer G, et al. Treatment of post-cardiopulmonary bypass SIRS by hemoadsorption: a case series. Int J Artif Organs 2016; 39:141.

38. Bernardi MH, Rinoesl H, Dragosits K, et al. Effect of hemoadsorption during cardiopulmonary bypass surgery - a blinded, randomized, controlled pilot study using a novel adsorbent. Crit Care 2016; 20:96.

39. Schädler D, Pausch C, Heise D, et al. The effect of a novel extracorporeal cytokine hemoadsorption device on IL-6 elimination in septic patients: A randomized controlled trial. PLoS One 2017; 12:e0187015.

40. Yamaji K. Immunoadsorption for collagen and rheumatic diseases. Transfus Apher Sci 2017; 56:666.

41. Stummvoll G, Aringer M, Handisurya A, Derfler K. Immunoadsorption in Autoimmune Diseases Affecting the Kidney. Semin Nephrol 2017; 37:478.

42. Kronbichler A, Brezina B, Quintana LF, Jayne DR. Efficacy of plasma exchange and immunoadsorption in systemic lupus erythematosus and antiphospholipid syndrome: A systematic review. Autoimmun Rev 2016; 15:38.

43. Meyersburg D, Schmidt E, Kasperkiewicz M, Zillikens D. Immunoadsorption in dermatology. Ther Apher Dial 2012; 16:311.

44. Oji S, Nomura K. Immunoadsorption in neurological disorders. Transfus Apher Sci 2017; 56:671.

45. Lo P, Sharma A, Craig JC, et al. Preconditioning Therapy in ABO-Incompatible Living Kidney Transplantation: A Systematic Review and Meta-Analysis. Transplantation 2016; 100:933.

46. Weston MJ, Langley PG, Rubin MH, et al. Platelet function in fulminant hepatic failure and effect of charcoal haemoperfusion. Gut 1977; 18:897.

47. Yang X, Xin S, Zhang Y, Li T. Early hemoperfusion for emergency treatment of carbamazepine poisoning. Am J Emerg Med 2018; 36:926.

48. Kittanamongkolchai W, El-Zoghby ZM, Eileen Hay J, et al. Charcoal hemoperfusion in the treatment of medically refractory pruritus in cholestatic liver disease. Hepatol Int 2017; 11:384.

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GRAPHICS

Drugs and chemicals removed with hemoperfusion

Barbiturates
Amobarbital
Butabarbital
Hexabarbital
Pentobarbital
Phenobarbital
Primidone
Quinalbital
Secobarbital
Thiopental
Vinalbital
Antidepressants
(Amitryptiline)
(Imipramine)
(Tricyclics)
Metals
Aluminum*
Cisplatin*
Iron*
Thallium
Miscellaneous
Aminophylline
Caffeine
Cimetidine
(Fluoroacetamide)
(Phencyclidine)
Phenols
(Podophyllin)
Theophylline
Solvents, gases
Carbon tetrachloride
Ethylene oxide
Trichloroethane

Antimicrobials/anticancer
(Adriamycin)
Ampicillin
Carmustine
Chloramphenicol
Chloroquine
Clindamycin
Dapsone
Doxorubicin
Gentamicin
Isoniazid
(Methotrexate)
Thiabendazole
Vancomycin
Pentamidine
Analgesics, antirheumatic
Acetaminophen
Acetylsalicylic acid
Colchicine
D-propoxyphyene
Methylsalicylate
Phenylbutazone
Salicylic acid
Tramadol
Cardiovascular
Digoxin
Diltazem
(Disopyramide)
Metoprolol
N-acetylprocainamide
Procainamide
Quinidine
Cibenzoline

Plant and animal toxins, herbicides, insecticides
Amanitin/*Amanita* mushrooms
Carbon tetrachloride
Chlordane
Demeton sulfoxide
Dimethoate
Diquat
Methylparathion
Nitrostigmine
Organophosphates¶
Phalloidin
Polychlorinated biphenyls
Paraquat
Parathion
Star fruit
Tetramine
Nonbarbiturate hypnotics, sedatives, anticonvulsants and tranquilizers
Carbamazepine
Carbromal
Chloral hydrate
Chlorpromazine
(Diazepam)
Diphenhydramine
Ethchlorvynol
Glutethimide
Meprobamate
Methaqualone
Methsuximide
Methyprylon
Phenytoin
Promazine
Promethazine
Valproic acid

( ): not well removed.
* Removed with chelating agent.
¶ With lipid emulsion.

Graphic 52887 Version 3.0

Available hemoperfusion devices

Manufacturer	Device	Sorbent type	Amount of sorbent	Polymer coating
Asahi	Hemosorba	Spherical charcoal	170 g	Polyhema
Gambro	Adsorba	Norit charcoal	100 or 300 g	Cellulose acetate
Toray Industries	Toraymyxin*	Toraymycin	?	None
Cytosorbents	Cytosorb*	Polystyrene divinylbenzene copolymer	300 g	None

*Only in Europe or Japan.

Graphic 79263 Version 4.0

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