

The Role of Hemodialysis in Toxicology including neonates: A Systematic Review

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ABSTRACT

Background: The management of poisoned patients often is complicated by the need for renal replacement therapies, particularly hemodialysis, to effectively address acute poisonings complicated by renal dysfunction.

Objective: This systematic review synthesizes current literature concerning the use of hemodialysis in toxicology, assessing its effectiveness at toxin clearance and its association with complications.

Methods: A literature search was conducted across major databases, including PubMed, Embase, Cochrane Library, and Web of Science, focusing on articles published from January 2000 to October 2023 that analyze hemodialysis for toxic substance removal. Data extraction prioritized toxin types, patient demographics, hemodialysis specifics, and clinical outcomes.

Results: Hemodialysis is most effective for water-soluble and minimally protein-bound toxins like acetaminophen, lithium, salicylates, methanol, and ethylene glycol. Its effectiveness decreases with highly protein-bound substances, those with a high volume of distribution, and volatile compounds. Inborn errors of metabolism can cause toxic metabolite buildup, affecting neonatal brain development. A study of 20 cases showed that timely hemodialysis improved clinical outcomes in 85% of patients. Common complications include hypotension, infections, and electrolyte imbalances, which require close monitoring and tailored interventions.

Conclusion: Hemodialysis is an important tool in the management of toxicological emergencies. However, the success of hemodialysis is dependent on many factors, including the characteristics of the toxin and the patient's health status. Recent advances in dialysis membranes and Continuous Renal Replacement Therapy have improved its use in such cases. However, there are limitations to its use, and alternative treatment strategies must be considered for some poisonings. This review discusses kidney replacement therapy options, challenges for infants, and the importance of informed catheter use by interventional radiologists.

Keywords: Toxicology, Nephrology, Hemodialysis, poisons

1. INTRODUCTION

The management of poisoned patients often involves the initiation of renal replacement therapies, and most commonly includes hemodialysis, particularly in the context of acute poisonings complicated by intrinsic renal dysfunction.

Several clinical scenarios make the consideration of hemodialysis mandatory in the case of poisoning. Acute Kidney Injury, especially of nephrotoxic etiology, impairs renal clearance, resulting in an accumulation of potentially toxic metabolites.

Thus, the treatment for such patients can only be effectively achieved with the aid of hemodialysis. ²⁻³Additionally, even when it is a matter of a critical overdose of substances such as salicylates or lithium, the established regimens fail to suffice and require the administration of hemodialysis.

This review will synthesize and analyze current literature on the use of hemodialysis in the field of toxicology but with an emphasis on a critical assessment of its effectiveness in the clearance of different toxic agents. Currently, the efficiency of hemodialysis is reliant on the physiochemical properties of the toxin in question, molecular weight, volume of distribution, and protein-binding affinity. Small, water-soluble, and minimally protein-bound toxins tend to have higher clearance rates during dialysis. Besides the assessment of hemodialysis effectiveness in toxin removal, the complications of the treatment should also be considered. Adverse effects may occur with patients undergoing hemodialysis, including hypotension, which may be more significant in a volume-depleted intoxicated patient.^{4,5} There is also the risk of infectious complications and electrolyte imbalances, like hyperkalemia or hypocalcemia, that need to be accounted for in an all-inclusive treatment plan.

In addition to these, some patient-related factors can influence the success of managing toxicological emergencies with hemodialysis. This includes baseline renal function, comorbid conditions, age, and overall physiological status, and can significantly alter the response of the patient and the potential occurrence of complications due to treatment. In conclusion, this review brings attention to the essential role of hemodialysis in the acute management of poisoned patients. It will be most appropriate to emphasize its use in specific cases, giving light to complications and challenges that go with it in clinical toxicology. Continued research may help refine protocols in treatment and optimize outcomes for patients facing toxicological crises.

2. METHODOLOGY

A systematic review was carried out based on the PRISMA guidelines to understand the role of hemodialysis in toxicology. The search for literature was done in major databases, namely PubMed, Embase, Cochrane Library, and Web of Science. The inclusion criteria included articles from peer-reviewed journals published in the English language from January 2000 to October 2023, with special reference to the use of hemodialysis in the removal of toxins.

Data extraction focused on several key parameters, including the types of toxins involved, the demographics of the patient populations, specific aspects of the hemodialysis procedures employed, and the resulting clinical outcomes.

This methodological approach ensured that the overall picture of existing evidence regarding the effectiveness of hemodialysis as a therapeutic intervention in cases of different toxic exposures would be drawn. We thus intended to outline, through a systematic review of literature, the contexts in which hemodialysis is most effective, identify variables influencing its success, and evaluate risks and complications associated with the treatment.

The findings of this systematic review are aimed to improve clinical appreciation and guide best practice for clinical practitioners involved in the care of poisoned patients on hemodialysis, both focusing on the strength and limitations in this critical toxicology area. ⁷Thus, this review will benefit clinicians and researchers while providing a valuable resource to toxicologists interested in the use of hemodialysis in cases involving toxicological emergencies and providing a background for future studies concerning optimization of treatment protocols for affected patients.

3. RESULTS AND DISCUSSION

The success of hemodialysis in poisoned patients largely depends on the toxin used. In such a scenario, knowing the pharmacokinetics and characteristics of different toxins can guide one to understand the suitability of hemodialysis in a therapeutic manner.

Acetaminophen

Acetaminophen is also known as paracetamol toxicity and has been established as one of the medical emergencies commonly resulting from overdose in most patients. In cases of major intoxication, especially with liver dysfunction from acute liver failure, hemodialysis is very helpful in enhancing the removal of the toxic metabolite. N-acetylcysteine remains the first line of treatment in acetaminophen overdose. Hemodialysis is used as a form of treatment for those patients with established liver failure and those who show poor response to NAC therapy. Research proves that hemodialysis would decrease serum acetaminophen even when the hepatic function is compromised maximally, thereby decreasing the risk of further injury to the liver. ⁹⁻¹¹This intervention is very useful because it would offer rapid detoxification which is essential in reducing morbidity and mortality mainly associated with fulfilment hepatic failure.

Lithium and Salicylates

Hemodialysis is perhaps one of the technological advancements which can be used in clinical toxicology practice and especially in an emergency situation like the use of lithium and salicylates. Lithium is a mood stabilizer but has a very narrow therapeutic index, making the patient prone to toxicity, particularly in the context of renal failure. Hemodialysis is quite effective in the clearance of lithium, and significant decreases in serum lithium levels are observed within hours of starting dialysis. ^{12,13}The ability to rapidly clear lithium is important because toxicity can cause significant neurologic compromise

and cardiovascular instability.

Likewise, salicylate toxicity, a condition often ascribed to chronic use or an intentional overdose, requires aggressive approaches to treatment. Hemodialysis has been noted to be useful in the elimination of salicylates from the blood, particularly in patients displaying severe clinical manifestations such as metabolic acidosis and altered mental status. ¹⁴ The faster clearance rates of salicylates during dialysis highlight the necessity of hemodialysis in acute intoxications. This would contribute to better clinical outcomes and ultimately reduce the stay in the hospital.

Alcohols: Methanol and Ethylene Glycol

More recently, methanol and ethylene glycol have gained greater recognition as poisons capable of causing significant disturbances in metabolism, leading to multiple organ failure. Hemodialysis has emerged as a cornerstone therapeutic intervention for this toxicity because methanol and its toxic metabolite, as well as ethylene glycol with its own lethal metabolite, can be effectively removed through it. In the case of methanol ingestion, for example, dialysis removes effective amounts of the toxic metabolites formaldehyde and formic acid, which are known to cause severe metabolic acidosis and ocular toxicity.

The fact that hemodialysis can significantly decrease serum levels of these toxicants further supports its role as a life-saving intervention in the setting of severe intoxication. Early initiation of hemodialysis can prevent the progression to irreversible organ damage and improve survival. ¹⁵In addition, the effectiveness of hemodialysis in correcting metabolic acidosis due to glycolic acid from ethylene glycol metabolism underscores its utility in the treatment of this specific poisoning.

Determinants of Efficacy

The effectiveness of hemodialysis in removing toxins is found to be influenced by several key factors, both concerning the physicochemical properties of the toxins themselves and individual patient characteristics. From this understanding, clinical decisions on the utilization of hemodialysis for toxin clearance can be made.

Physiochemical Properties

The molecular weight and protein binding of toxins determine the effectiveness of hemodialysis. Water-soluble toxins with low molecular weights are cleared more efficiently during dialysis. For example, favorable characteristics of lithium and salicylates enable effective removal from plasma. In contrast, large molecules or high protein binding with low water solubility is harder to clear, which can lead to suboptimal hemodialysis effectiveness.

Understanding these properties allows for a better assessment whether hemodialysis should be employed as a treatment modality. Other factors include volume of distribution; certain substances which are heavily distributed into tissues will not be adequately removed by dialysis as the majority will not be present in the blood stream during a treatment session.

Patient Factors

Apart from toxin characteristics, patient-related factors also significantly determine the results of hemodialysis in toxicological settings. Genetic variations, pre-existing comorbidities, and the patient's baseline renal function could determine how effectively hemodialysis performs in clearing toxins from the body.

For instance, patients with pre-existing renal impairment may have altered pharmacokinetics for specific toxins that may require adjustment to routine hemodialysis protocols. The effects on individual metabolism and elimination pathways may complicate a clinical picture. Recognizing such nuances is essential in tailoring hemodialysis strategies to maximize effectiveness while minimizing risks and complications.¹⁷

4. COMPLICATIONS

Although hemodialysis is one of the indispensable interventions in management of toxicologic emergencies, complications are not the exception. Thorough knowledge about these possible complications is very much essential for practicing clinicians caring for poisoned patients. ^{18,19}

Hypotension

Hypotension is one of the most frequent complications of hemodialysis. This condition is particularly concerning in patients who present with dehydration or volume depletion, commonly seen in cases of severe intoxication. The rapid fluid removal during dialysis may contribute to this, causing significant hemodynamic instability. Clinicians need to be on the lookout for blood pressure monitoring and adjust dialysis parameters appropriately to avoid making hypotensive episodes worse.

Infection

Infectious complications, especially access-related infections, are another challenge during hemodialysis processes. Central venous catheters used for hemodialysis access have increased vulnerability to infections, which may complicate the clinical management of already compromised patients. Strict aseptic protocols must be implemented during catheter insertion and its maintenance to minimize this risk. Early recognition of infections and prompt treatment are also very important in preventing

further morbidity.

Electrolyte Imbalances

Electrolyte imbalances, such as hyperkalemia and hypocalcemia, are major concerns in the hemodialysis process. While the removal of potassium from the blood is the primary aim in the treatment of some toxicities, excessive removal can cause hypokalemia, which also poses risks. Calcium levels may fluctuate in patients with metabolic disorders or on medications that alter calcium metabolism. Electrolyte levels during dialysis must be carefully monitored and supplementation or adjustment of treatment protocols initiated to reduce complications in these patients.

5. FROM THE RECENT LITERATURE

Improved Dialysis Membrane Technology: 20-25

Improvements in dialysis membrane technology have been a significant area of research, and it is demonstrated how the development of high-flux and biocompatible membranous materials can take place. This would permit a better removal of larger molecular weight toxins, previously difficult to eliminate, which can improve the treatment of hemodialysis for patients with polymer and protein-bound toxins. Research shows that these innovations do not only increase the clearance of toxins but also decrease the chance of inflammation and immune responses, thus making the treatment safer for patients with pre-existing conditions.

Role of Continuous Renal Replacement Therapy (CRRT):

Literature has started to focus on the use of Continuous Renal Replacement Therapy (CRRT), especially in critically ill patients with mixed presentations of intoxication and multi-organ dysfunction. CRRT provides for more gradual toxin removal and hemodynamic stability compared to the traditional intermittent hemodialysis method. This is most useful with the management of toxins in unstable hemodynamics or in patients recovering from acute kidney injury. CRRT offers the possibility of a safer and more stable toxin clearance, especially in patients with severe salicylate or ethylene glycol poisoning.

Pharmacological Enhancements:

The recent research has also looked into adjunctive pharmacological therapies that can be used with hemodialysis to enhance the removal of toxins. For instance, hemodialysis has been used in combination with novel chelating agents for specific toxicities such as heavy metals and certain drug overdoses. This approach may improve renal clearance while reducing the overall dose and duration of dialysis required, thus improving patient tolerance and outcomes.

Telemedicine and Decision Support Tools:

The recent literature has documented the current surge in the integration of telemedicine and advanced decision-support tools into the management of toxicology cases involving hemodialysis. The tools address real-time data analytics and artificial intelligence, guiding clinicians on toxin-specific treatment protocols-ideal dialysis settings and duration, depending on the specific profiles of individual patients and toxins. Such innovations support rapid clinical decision-making, ensuring timely and evidence-based management of intoxicated patients.

Personalized Medicine Approaches:

Increasing studies have been conducted on personalized medicine in relation to hemodialysis for toxicology. Using pharmacogenomics, researchers seek to find strategies for the application of dialysis that would comply with the genetic profile of the patients, which may improve individual responses to treatment and also minimize adverse effects. Personalized approaches may be the next significant stride in optimizing hemodialysis efficacy in managing toxic exposures.

Though generally used as the therapeutic modality for managing wide ranges of exposure to toxins, there are various situations and particular types of poisonings in which hemodialysis is not beneficial or effective in its use. It is such knowledge that gives clinicians a fair basis for which they can apply their treatment preferences.

6. SPECIFIC INSTANCES²⁶ WHERE HAEMODIALYSIS IN TOXICOLOGY IS LESS USEFUL

1. Highly Protein Bound Toxins

The very first category that falls under that category for poisoning in which the use of hemodialysis fails is highly protein-bound toxins. Examples include drugs like phenytoin, warfarin, and some anti-depressives like amitriptyline. Hemodialysis removes almost all the toxins that are available in the unbound form. Thus, once a significant quantity of a drug is bound with plasma proteins, the effectiveness of hemodialysis in reducing its serum concentration declines significantly. Limited free drug amounts available for elimination result in limited clearance, a condition that promotes therapeutic failure. In such scenarios, other methods like activated charcoal therapy may be better alternatives for detoxification.

2. Slowly Distributed Substances

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Substances with a high volume of distribution (Vd) also make hemodialysis difficult. Some substances, like digoxin and certain local anesthetics, exhibit extensive tissue binding and distribution. Therefore, these drugs may not be present in the blood in substantial concentrations during dialysis. However, it has been realized that though hemodialysis may remove some toxin from circulation, it does not significantly affect overall body burden because much of the toxin resides in peripheral tissues. Thus, supportive care and observation may be more appropriate than immediate hemodialysis in such cases.

3. Substances with Minimal Renal Excretion

Some substances, like heavy metals (lead, mercury), have low excretion rates in the kidneys and accumulate through other mechanisms than filtration. Although chelation therapy is indicated for heavy metal poisoning, hemodialysis does not significantly enhance the clearance of these metals from the body. The chelating agents bind to the metals in the bloodstream, facilitating their excretion through the kidneys. Thus, relying solely on hemodialysis in these scenarios may not provide substantial benefits.

4. Volatile Substances

In poisoning involving volatile substances like hydrocarbons or some volatile anesthetics, hemodialysis is generally ineffective. Such compounds are very rapidly distributed within different body compartments and may also evaporate in the course of dialysis; thus, their removal becomes more difficult to attain therapeutic clearance. In addition, the main management for such poisonings is often supportive care with the prevention of aspiration.

Do the instructions differ in toxicology to technicians?

The dialysis technician must, therefore, manage patients in toxicological emergencies following specific protocols adapted to the types of toxins; they must know the clearance rates of the toxin and the needed adjustments in the treatment. A vigilant monitoring of vital signs and electrolyte levels is essential in cases involving altered mental status or significant metabolic derangements. ²⁷Proper management of access sites is of utmost importance in preventing infections secondary to central venous catheters, and fluid status must be closely monitored in order to avoid hypovolemia or overload. Collaboration with physicians and toxicologists is indispensable, allowing timely adjustments to be made in the treatment protocols to ensure the optimal safety and effectiveness of hemodialysis in such complex cases.

7. NEONATAL CONCERNS

Inborn errors of metabolism can lead to an accumulation of toxic metabolites and severe impairment of neonatal brain development. The study retrospectively presented 20 cases of metabolic intoxication from inborn errors of metabolism; with timely hemodialysis (HD), levels were significantly decreased and clinical results were improved in 85% of the patients. Although there were three deaths, HD ²⁸is considered safe when conducted by an experienced multidisciplinary team.

Hemodialysis plays a crucial role in addressing urgent metabolic complications and when peritoneal dialysis is contraindicated or ineffective. In infants, arteriovenous fistulas are seldom employed, with central venous catheter placements being the preferred method for hemodialysis. ²⁹Therefore, it is essential for interventional radiologists to be well-informed about the types of catheters available, appropriate catheter placement sites, and the associated potential complications to ensure safe and effective treatment.

Kidney replacement therapy (KRT) is critical for managing children and adults with acute kidney injury, fluid overload, kidney failure, inborn errors of metabolism, and severe electrolyte abnormalities. ³⁰Both peritoneal dialysis and extracorporeal hemodialysis can be tailored for various durations using either adult or infant-specific devices. This review addresses the challenges of delivering KRT in infants, highlights recent advancements and specific modalities, assesses newer devices, and examines ethical considerations and future research directions in KRT for this vulnerable population.

Conclusion

In summary, hemodialysis remains a key intervention in the management of various toxicological emergencies. However, it depends on a variety of factors such as the nature of the toxin, the characteristics of the patient, and their medical background. The new advancements in this area include improvements in dialysis membranes, Continuous Renal Replacement Therapy, and pharmacogenomics, all of which have further enhanced its role in toxicology. However, there are limitations for very highly protein-bound toxins, high volume of distribution substances, and volatile agents that require alternative treatments. Further research and clinical knowledge are necessary to optimize the protocols of hemodialysis to be both safe and effective in poisoned patients.

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