Extracorporeal Therapy for Poisoning

A workgroup has developed guidelines for the use of hemodialysis treatments for common toxicities

Editor's note: This article is a summary of a presentation Dr. Goldfarb is scheduled to give at the 2016 Kidney Week conference in Chicago, November 15, 1:30 to 2:00 p.m.

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HEMODIALYSIS (HD) has been used for the treatment of poisoning since the 1940's. Despite this long history, its utility generally has not been demonstrated by randomized controlled trials. The application of extracorporeal treatments (ECTR), including hemodialysis (HD) and charcoal hemoperfusion (HP), in the treatment of poisoning, therefore, has proceeded without underlying data confirming its appropriate use. Without data, consensus cannot easily be achieved and guidelines cannot be formulated.

In 2011, Marc Ghannoum, MD, a nephrologist on the faculty of the University of Montreal, decided to apply the principles of evidence-based medicine to the field. He heads the EXTRIP (EXtracorporeal TReatments In Poisoning) workgroup (www.extripworkgroup.org). The EXTRIP workgroup developed a detailed methodology for formulating recommendations, which begins with a thorough literature review of ECTR use in the setting of poisoning. Each member of the group reviews the available evidence and voices an anonymous opinion. This results in a robust discussion regarding the evidence and the final statements. The votes are tallied and recommendations developed.[1]

The result of this concerted effort has been the publication of a wealth of reviews and recommendations, to date regarding 13 potential toxins: acetaminophen, barbiturates, carbamazepine, digoxin, lithium, metformin, methanol, phenytoin, salicylates, thallium, theophylline, tricyclics, and valproic acid. Here we highlight a few of the recent publications and controversies.

Tricyclic antidepressants

Tricyclic antidepressants (TCAs) remain in widespread use, although they are not considered first-line agents due to their side effect profile and the development of superior agents. Though reviews have suggested a benefit of ECTR, EXTRIP recommended against its use ECTR in TCA poisoning. The evidence was based on 77 studies (a majority are case reports and 1 observational study), which included a total of 108 patients. TCAs are extensively protein bound and lipophilic, resulting in low dialyzability. They may appear to be dialyzable because they are small molecules (200-400 Daltons) that can freely cross HD membranes. But due to their large volume of distribution, there is no significant effect of ECTR on the total body burden. The treatment of severe TCA poisoning should instead be focused on aggressive supportive care and reversal of sodium channel blockade with sodium salts, particularly sodium bicarbonate.[2]

Acetaminophen

Acetaminophen (APAP) is one of the most common drug poisonings among adults and children. APAP is metabolized by the liver to an active and toxic metabolite, N-acetyl-p-benzoquinone imine (NAPQI). This toxin requires glutathione to be conjugated and inactivated. Sizable ingestions deplete glutathione stores, leading to accumulation of NAPQI and hepatotoxicity and liver failure. The standard of care is administration of N-acetylcysteine (NAC), which acts as a source of glutathione. Fatalities are rare and mostly occur in patients who experience a delay or interruption in NAC administration. APAP has a low molecular weight of 151.2 Daltons and is 25% protein bound with a low volume of distribution. Based on EXTRIP criteria, APAP is considered to have moderate dialyzability (10%–30% removal of total dose in a 6-hour ECTR session), although recent reports show rates of APAP extraction over 50% of total ingested dose). EXTRIP published recommendations based on 24 articles (1 randomized controlled trial, 1 observational study, and 22 case reports, including 23 fatalities). The conclusion was that ECTR is indicated only when NAC cannot be administered and in rare cases where patients develop signs of mitochondrial injury early after ingestion as manifested by acidemia and high lactate levels.[3] ECTR should be followed with further NAC administration, as the antidote is itself dialyzable.

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Aspirin

Acetylsalicylic acid (aspirin, ASA) is another medication responsible for many poisonings and deaths. It is an organic acid with a molecular weight 180 Daltons, 90% protein bound (as low as 30% in the setting of an overdose), and a small volume of distribution. Salicylates interfere with adenosine triphosphate generation leading to lactic acidosis and ketoacidosis. The drop in systemic pH increases entry of salicylates into the brain, resulting in cerebral edema and death. Treatment includes bowel decontamination and the administration of sodium bicarbonate to alkalinize the plasma relative to the brain and the urine relative to the plasma, and to facilitate excretion by the kidneys. EXTRIP's recommendations were based on 84 articles (1 randomized control study, 80 case reports/series, and others). They concluded that salicylates are dialyzable and that ECTR was recommended for severe poisonings (varying salicylate levels with different thresholds for preserved and impaired renal function, altered mental status, acute respiratory distress syndrome, acidemia and failure of supportive therapy. ECTR not only removes salicylates but serves as a source of bicarbonate.[4]

Conclusion

ECTR for poisoning represents a complicated clinical scenario. The group hopes that future case reports will be detailed in regards to patients' clinical presentations and the interventions utilized, and be thorough with respect to data collection throughout the case. A checklist of 114 items that should be included in a case report was developed. This checklist should be consulted when ECTR is employed so that the appropriate variables will be observed and toxicokinetic calculations will be accurate, leading to a higher quality and more useful publication.[5] n

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