EDITORIAL

Amlodipine Intoxication: Resin Revival or *Fait Accompli*

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Poisoning in clinical practice is associated with a complex interplay of factors such as toxidromes, dose and formulation, presence of coingestants, underlying comorbidities, route of administration and most importantly time to presentation. Despite the myriad permutation of above factors, the vast majority of poisoned patient respond well to supportive measures and timely institution of established principles of critical care. There are a limited number of specific antidotes available *vis* a *vis* an ever-increasing number of Xenobiotics capable of lethal toxidromes irrespective of the intent for ingestion. The challenges faced in reporting of these cases stem from inconsistent clinical data, lack of severity assessment, poor reporting of timing and duration of exposure, paucity of lethal dose (LD50 cut-offs) and therapeutic vs prophylactic usage of rescue measures. Extracorporeal treatment (ECTR) such as hemodialysis (HD), hemoperfusion (HP), therapeutic plasma exchange (TPE) and novel high cut-off (HCO) hemofilters as salvage options have been in vogue for more than 100 years and still remain a topic of considerable controversy, debate and uncertainty. The EXtracorporeal TReatment In Poisoning (EXTRIP) workgroup have tried to clarify the role of ECTR in clinical practice by compilation of evidence-based recommendations and expert opinion.[1,2]

The general characteristics of poisoning amenable to ECTR are based on physiochemical and toxicokinetic properties such as molecular weight (MW), volume of distribution (VD), hydrophilic vs lipophilicity, protein and tissue binding, endogenous clearance and 'dialyzability' or elimination from plasma by convection or hemoadsorption.[3,4] Based on the guidelines of EXTRIP workgroup – barbiturates, salicylates, lithium, methanol, valproate, theophylline and thallium intoxications should be managed with early institution of ECTR. There is conditional recommendation for the usage of extracorporeal therapies in acetaminophen and carbamazepine overdose, while these therapies are strongly discouraged in tricyclic antidepressants and digoxin toxicity. Most of the calcium-channel blockers (CCB) and especially amlodipine are characterized by high lipid-solubility, increased VD and high protein-binding which renders them poorly dialyzable or removed by charcoal HP.

The study in consideration, published in the current edition is notable for usage of ECTR (Resin-based hemoadsorption cartridge) in amlodipine intoxication which is associated with high baseline mortality in a predominantly young population admitted in the Tertiary Care ICU setting of South Africa.[5] Although, retrospectively conducted over 3 years at a single-center, it throws important light on the severity of CCB toxidrome and has done comparative evaluation of novel HA therapy (HA-230, Jafron filter) vs SOC (standard of care) which involved supportive care along with institution of HIET (high-dose euglycemic therapy), calcium infusion and hemodynamic optimization. Although, the standard EXTRIP guidelines recommend against ECTR for CCB poisoning, they have only studied intermittent HD and charcoal HF which are unlikely to be of any benefit in view of high protein-binding and poor free drug availability.[3] The dominant observation in present case-series is the reduction in mortality and faster hemodynamic stabilization despite higher severity of toxic symptoms (high SAPS-II score, lower MAP on admission, increased requirement of RRT support and prolonged LOS) in the hemadsorption arm. These beneficial effects can be theoretically attributed to faster clearance of Amlodipine from the vascular compartment. The positive observation in this study needs to be tempered in the light of inherent weakness of the study such as—single center, retrospective, observational nature with small numbers (although substantial enough for a low-prevalence, single subgroup of xenobiotic in a real-world scenario), patchy details on duration of exposure and lack of defined LD50 value or cut-off levels for the implicated drug.

Notwithstanding all the limitations, this is an important thought—trigger for further evaluation of this emerging vista of ECTR driven by usage of resin-based hemoadsorption cartridge and/or polymer-based drug adsorption columns for enhanced clearance of putative toxins.

To be or not to be, is no longer the question—to dialyze or adsorb in addition to standard of care could be the answer..!

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