ORIGINAL ARTICLE

Hemoadsorption Therapy for Calcium Channel Blocker Overdose at a Tertiary-level Intensive Care Unit: A Retrospective Study

Shahed Omar[1], Varadaben Shukla[2], Ayesha B Khan[3], Ziyaad Dangor[4]

Received on: 27 November 2024; *Accepted on:* 13 January 2025; *Published on:* 31 January 2025

Abstract

Objective: To describe the burden of calcium channel blocker (CCB) overdose at a tertiary intensive care unit (ICU).

Design and setting: Retrospective study of patients admitted to the ICU with CCB overdose from 2020 to 2022.

Participants: Adult participants with clinically confirmed CCB overdose.

Main outcome: Admission frequency, management strategies, and patient outcomes.

Results: A total of 1719 ICU admissions over the study period, 24 (1.4%) had CCB overdose with a case fatality rate of 12.5% (3/24). Interventions included mechanical ventilation (MV) (71%), vasopressors (92%), high-dose insulin euglycemic therapy (HIET) (71%), calcium (42%), methylene blue (4%), and fluid therapy (100%). Thirteen patients (54%) received hemoadsorption therapy (HA), and eleven received standard of care (SoC) based on current guidelines. The resin hemoadsorption group had a higher SAPS II score ($p = 0.002$), and a greater total maximal vasopressor dose ($p = 0.001$) than SoC group. The HA group also had a lower admission mean arterial pressure (MAP), ($p = 0.014$), a greater MAP increase at 48 hours ($p = 0.044$), and a longer ICU length of stay (LOS) ($p = 0.004$) compared to the SoC group. There was one death in the HA group (7.7%) and two in the SoC group (18.2%).

Conclusion: Calcium channel blocker overdose is an important and life-threatening cause of toxicology admissions in the ICU. Modern resin HA may contribute to improved hemodynamic stability providing a safe and important rescue therapy in cases with refractory shock. Well-designed studies are required to confirm its role in enhancing drug clearance thereby improving the hemodynamic state and clinical outcomes.

Keywords: Calcium channel blocker overdose, Critically ill, Extracorporeal blood purification, Hemoadsorption, Hypotension, Toxicology.

Indian Journal of Critical Care Medicine (2025): 10.5005/jp-journals-10071-24906

Highlights

Modern resin hemoadsorption therapy (HA) was used in a critically ill population with greater severity of illness and vasopressor requirements compared to standard of care (SoC). Its use as a rescue therapy for refractory calcium channel blocker (CCB) overdose was found to be safe and associated with a greater improvement in mean arterial pressure (MAP) at 48 hours with the possibility of faster shock resolution vs SoC. Its effect on mortality needs further study.

Introduction

Essential hypertension is common with an estimated prevalence of 38 and 48% in South Africa and on the African continent, respectively, with CCB prescribed as a first-line agent for many patient groups.[1–3] Accessibility to medications accounts for a large proportion of overdoses in adults,[4] with CCBs accounting for over 35% of cardiac drug overdoses and an increased risk of death in the USA.[5]

Amlodipine, a dihydropyridine CCB, is one of the three most commonly prescribed antihypertensives in the South African public healthcare setting.[6,7] It has a higher affinity for smooth muscle L-type calcium channels than non-dihydropyridine CCBs. This specific affinity is lost at high doses, leading to peripheral vasodilation, reduced cardiac contractility, bradycardia or tachycardia, and shock.[8] These drugs are lipid-soluble, protein-bound, have a large volume of distribution, and cannot be removed by hemodiafiltration or charcoal hemoperfusion.[8,9] Further, CCB overdose may saturate the hepatic enzymes responsible for its metabolism and reduce the first-pass effects, increasing systemic concentrations of the active drug.[8]

Anecdotal evidence suggests that CCB overdose is a common cause of hospitalization and intensive care unit (ICU) stays, but recent data on its prevalence and outcomes in South Africa is lacking.[1,10,11] Since clinical outcomes depend on treatment strategies, detailing the therapies used in our setting would provide context to current ICU outcomes. Most of the evidence however is based on animal data outcomes, human case series, and observational studies with physiological endpoints.[12] There are currently no clinical studies on

[1–3]Department of Critical Care, University of the Witwatersrand, Johannesburg, South Africa

[4]Vaccines and Infectious Diseases Analytics Research Unit (VIDA)/ University of Witwatersrand/Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa

Corresponding Author: Shahed Omar, Department of Critical Care, University of the Witwatersrand, Johannesburg, South Africa, Phone: +0027835695363, e-mail: shahedicu@gmail.com

How to cite this article: Omar S, Shukla V, Khan AB, Dangor Z. Hemoadsorption Therapy for Calcium Channel Blocker Overdose at a Tertiary-level Intensive Care Unit: A Retrospective Study. Indian J Crit Care Med 2025;29(2):130–136.

Source of support: Nil

Conflict of interest: None

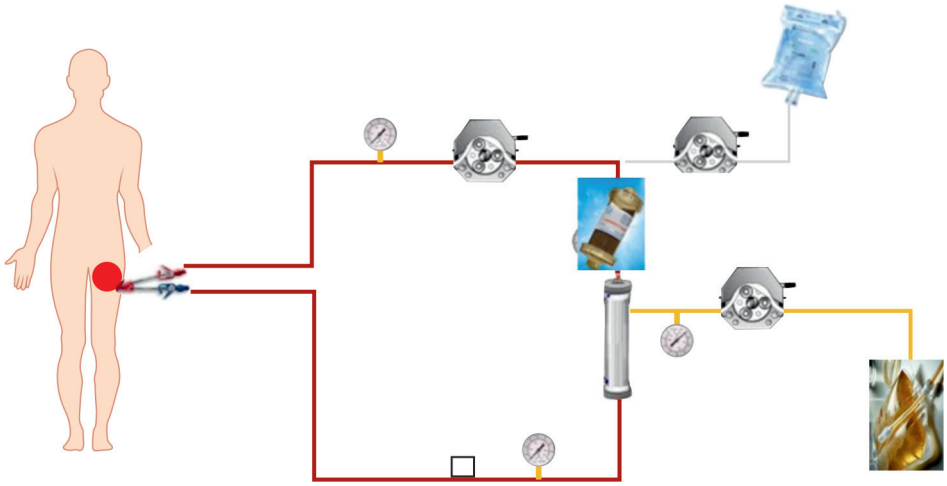

Fig. 1: Circuit configuration. Pump speed: 150–180 mL/min. Predilution (bicarbonate buffer) at 500 mL/h. Heparin load: 20 U/kg body weight. Heparin infusion into the circuit: 15 U/kg/h × 6 hours. Cycle 1 duration: 6 hours. Interval 12–18 hours. Cycle 2 duration 6 hours

the effects of modern resin HA in ICU patients with CCB overdose, especially concerning its impact on platelet counts.[13] Therefore, in this retrospective study, we describe the admission frequency, and outcomes and explore management strategies, including HA therapy in patients admitted to our ICU for CCB overdose over a 3-year study period.

Materials and Methods

Study Design and Setting

We performed a retrospective observational study to describe the admission frequency, management strategies employed, and ICU outcomes of CCB overdose admissions to a tertiary-level academic adult ICU from January 1, 2020 to December 31, 2022 at the Chris Hani Baragwanath Academic Hospital in Johannesburg, South Africa. This hospital serves 1.5 million people in Soweto and acts as the tertiary referral center for much of Gauteng, North West, parts of the Northern Cape, and informally to most of South Africa. We followed the STROBE guidelines/checklist for observational studies.

Inclusion Criteria

Clinical features of CCB overdose (hypotension, bradycardia/compensatory tachycardia, signs of heart failure, hyperglycemia) and confirmation by family members of the drugs ingested (amlodipine) by providing empty packaging of the ingested drug which in our setting is done with suicidal intent.

Exclusion Criteria

Polypharmacy patients with a predominant other toxidrome, e.g., cholinergic, adrenergic etc. Family confirmation of the CCB was not recorded.

Data Collection

Clinical data, laboratory information, and blood gas lactate levels from the first 48 hours were extracted from patient records into an electronic database. Intensive care unit management information and ICU survival were documented.

ICU Management Strategies for CCB Overdose

Standard of Care

Standard of care comprised fluid optimization, intravenous calcium (Ca), vasopressor therapy (noradrenaline and/or adrenaline), and high-dose insulin euglycemic therapy (HIET), while rescue therapies included methylene blue.[1,4] Supportive management was applied as per usual care.

Modern Resin Hemoadsorption Therapy

Modern resin HA is available for toxicology cases in our ICU and is being increasingly utilized. Hemoadsorption therapy therapy was defined as the SoC plus modern resin HA. Hemoadsorption therapy therapy was applied using the HA-230 Jafron filter, in Zhuhai City, China. It consisted of two therapies each of 6 hours duration using an extracorporeal renal circuit with 500 mL of predilution therapy. The two cycles were performed on separate consecutive days, beginning during the first 48 hours. A continuous renal replacement circuit and hemofilter (ST-150 set) were used with the Prismaflex system (Baxter). Our selected mode was continuous veno-venous hemofiltration (CVVH) with predilution and no postdilution. The HA-230 filter was positioned in series between the access limb of the circuit and the hemofilter. The blood pump speed was set between 150 and 180 mL/minute. Heparin 20 units/kg body weight was administered into the circuit as a bolus and then continued at 15 mL/kg/hour for the 6-hour hemoadsorption duration. Figure 1 illustrates the circuit setup used. The predilution rate of 500 mL/hour was intended to enhance circuit patency. Amlodipine is almost completely protein-bound and there was no expectation of drug removal using convection/hemofiltration. This decision to initiate HA therapy was made by the on-call Intensivist based on severe disease not responding to all available first and second-line therapies as described in the available standard care.

Sample Size and Statistical Analysis

The primary outcome was to describe the admission frequency, management strategies, and outcomes [length of stay (LOS) ICU and ICU mortality] of suspected CCB overdose. The management strategies included a description of the utilized in the ICU, clinical evolution (hemodynamic and lactate profiles during the first 48 hours, maximum and minimum platelet counts, durations of vasopressor therapy, mechanical ventilation (MV), and HIET.

Descriptive statistics on baseline characteristics assumed a non-normal distribution (small sample size). Admission frequency was calculated as the proportion of CCB ICU admissions of all ICU

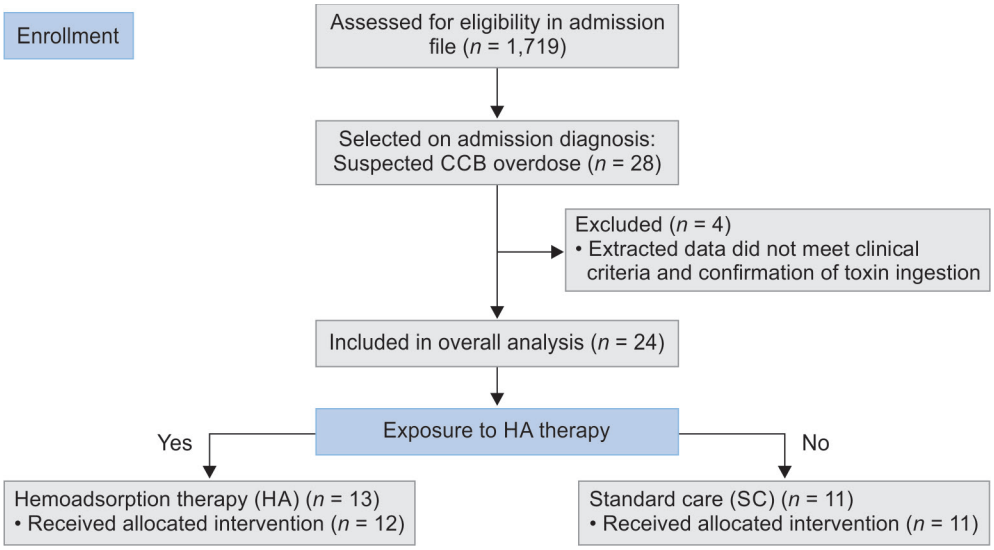

Fig. 2: Study flow diagram

Table 1: Baseline data

Variable	*All (n = 24)*	*HA (n = 13)*	*SoC (n = 11)*	*p*
Age years, Median (IQR)	19 (18–26.6)	18 (18–26)	25 (19–28)	0.28
Weight kg, Median (IQR)	68.4 (60–74.5)	60 (60–70)	71 (62–90)	0.07
Female gender *n* (%)	23/24 (95.8%)	11/12 (91.7%)	11/11 (100%)	1.0
Co-morbidities present, *n* (%)	6/24 (25%)	5/12 (41.7%)	1/11 (9.1%)	0.15
SAPS II, Median (IQR)	30 (24–32)	32 (30-35)	24 (18–27)	0.002*
Maximum total pressor dose (µg/kg/min)	1.18 (0.81–2.25)	2 (1.25–2.9)	0.75 (0–1.1)	0.001*
Insulin dose ≥100 U/h	8/24 (33.4%)	8/13 (61.5%)	0/11	0.002*
Time to peak total pressor (h)	22.5 (5.5–37)	28 (11–37)	3 (0–37), *n* = 7	0.12
Acute kidney injury	10/24 (41.7%)	7/13 (53.8%)	3/11 (27.3%)	0.19
Renal replacement therapy	8/24 (33.4%)	7/13 (53.8%)	1/11 (9%)	0.03*
Platelet count high (cells × 10^9/L)	286 (234–362)	297 (238–384)	279 (230–319)	0.6
Platelet count low (cells × 10^9/L)	156 (90–180)	121 (69–158)	173 (153–252)	0.06

*Significant $p < 0.05$

admissions during the study period. Independent medians were compared using the Mann-Whitney *U* test. Proportions were compared using the Chi-squared test/Fisher exact test. Logistic regression was used to determine independent predictors of HA therapy. Statistical analysis was conducted using Statistica version 13.3 (TIBCO, USA). A 0.05 level of significance was assumed for all analyses.

Results

Of the 1719 ICU admissions over the study period, 292 (17%) had toxin ingestion, and 28 admissions were referred with CCB overdose (Fig. 2). Four participants did not meet the clinical criteria of CCB overdose and were excluded from the analysis. The admission frequency of CCB overdose was 1.4% (95% confidence interval: 0–3.8%) of all admissions. The median age was 19 (IQR: 18–26.6) and 23 [95.8% were female (Table 1)]. The median LOS in the ICU was 8 days (5–10) and 3 of the 24 (12.5%) were demised.

Management Strategies in the ICU

The frequency of different interventions is provided in Table 2. All patients required intravenous fluid therapy administered based on volume responsiveness. Although not always statistically significant, the HA group had greater utilization of MV, vasopressor support, and HIET therapy (Table 2). The duration of cardiovascular and ventilatory support is provided in Table 3. The median LOS in the ICU was significantly longer in the HA group 9 days

Table 2: Frequency of interventions

Variable, Median (IQR)	*All (n = 24)*	*HA (n = 13)*	*SC (n = 11)*	*p*
MV, *n* (%)	17/24 (71%)	13/13 (100%)	5/11 (45%)	0.003*
Vasopressor, *n* (%)	22/24 (92%)	13/13 (100%)	9/11 (82%)	0.1
Adrenaline, *n* (%)	22/24 (92%)	13/13 (100%)	9/11 (82%)	0.1
Noradrenaline, *n* (%)	11/24 (46%)	7/13 (54%)	4/11 (36%)	0.39
Calcium, *n* (%)	10/24 (42%)	6/13 (46%)	4/11 (36%)	0.68
HIET, *n* (%)	17/24 (71%)	11/13 (85%)	6/11 (55%)	0.1
Methylene blue *n* (%)	1/24 (4%)	1/12 (8%)	0/11 (0%)	0.34

MV, mechanical ventilation. *Significant $p < 0.05$

(IQR 8–12) compared to 5 days (IQR 4–8) in the SoC group, $p = 0.004$. Although mortality in the ICU was lower in the HA group (1/13, 7.7%) compared to the SoC group (2/11, 18.2%); this did not reach statistical significance, $p = 0.44$. Platelet counts were not significantly different between the HA and SoC groups (Table 1).

Clinical Evolution: Hemodynamic Profile over the First 48 Hours of Admission

There was a significantly lower admission MAP1 and a significantly greater increase at 48 hours in the HA group. Maximum total vasopressor dose (noradrenaline + adrenaline) was significantly higher in the HA group compared to the SoC group and the time to peak vasopressor dose trended later in the HA group (28 hours vs 3 hours). See Tables 1 and 4.

Table 3: Duration of organ support

Variable, Median (IQR)	*All*	*HA (n = 11)*	*SC (n = 11)*	*p*
Vasopressor duration, Median (IQR)	4.5 (3–6)	6 (4–10)	3 (2–5)	0.008*
MV duration, Median (IQR)	5 (0–7)	7 (5–11) *n* = 10	0 (0–5)	0.006*
HIET days, Median (IQR)	1.25 (0–4)	1.25 (0–3)	3 (0–5) *n* = 10	0.76

*Significant $p < 0.05$

Clinical Evolution: Changes in Lactate (mmol/L) over the First Day of ICU Admission

There were no significant differences in lactate levels on admission to ICU ($p = 0.93$). The median lactate in the HA group peaked at 14 hours post-admission and was significantly higher than the SoC lactate ($p = 0.028$). Lactate levels in the SoC group peaked at 3 hours and reached a nadir at 14 hours, while levels in both groups were similar again at 22 hours ($p = 0.11$) (Fig. 3).

Predictors of Use of HA Therapy

We selected three variables (eight events per variable to avoid overfitting) that were significantly associated with HA therapy on univariate analysis ($p < 0.05$) and entered them into a logistic regression model. These were the SAPS II score (severity of illness at baseline), initial MAP, and the use of RRT. SAPS II score independently predicted HA utilization, OR = 1.43 (95% CI: 1.03–1.99).

Discussion

The most important finding of this observational study was that amlodipine CCB accounts for 1.4% of ICU admissions, coupled

Table 4: Mean arterial pressure

Variable, Median (IQR)	*All (n = 21)*	*HA (n = 12)*	*SoC (n = 9)*	*p*
MAP 1 hour, mm Hg	63 (62–70)	62 (57.5–65)	72 (63–74)	0.014*
MAP 48 hours, mm Hg	73 (68–82)	73 (67–82) *n* = 13	74.5 (70–84) *n* = 8	0.65
MAP change at 48 hours, mm Hg	14 (5–16)	16 (12–20) *n* = 13	7 (–2 to 14) *n* = 8	0.044*

*Significant $p < 0.05$

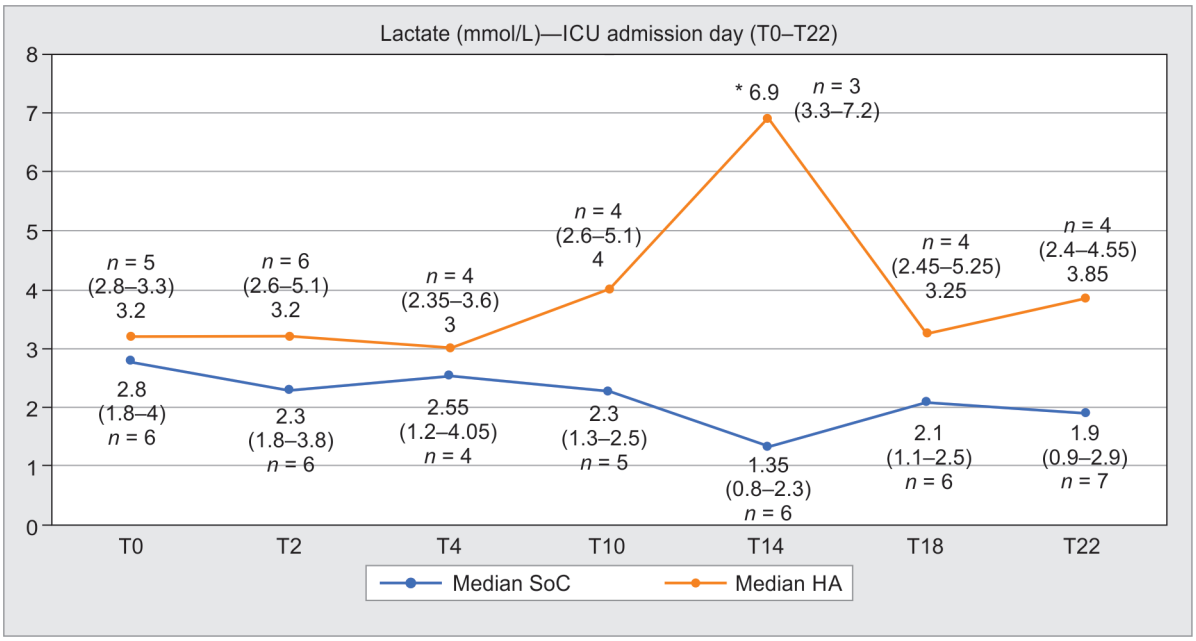

Fig. 3: Changes in median lactate levels (mmol/L) over the first day. *X*-axis: *T* = time in hours. *Y*-axis. Median lactate concentration in mmol/L. IQR in parenthesis. *Significant difference between median HA and SC groups. Median lactate levels were similar at admission ($T = 0$ hour, $p = 0.93$) and at all time points during the first 24 hours except for $T = 14$ hours, $p = 0.028$. Median lactate levels in the SoC group peaked at $T = 3$ hours, while in the HA group, they peaked at $T = 14$ hours. Peak lactate in the SoC group decreased over the next 11 hours to reach a nadir, while in the HA group, it decreased over the next 6 hours to reach its lowest at $T = 20$ hours. At this point, there was no significant difference between the two groups, $p = 0.66$

with a high mortality rate. A recent review indicated a lack of data on the frequency of CCB in South Africa.[1] Outside of case reports, we could not find any specific local ICU data in the literature, and our data provides the first published estimate of the burden of amlodipine overdose in an ICU setting. Data from the Danish poison information center (DPIC) indicated that amlodipine accounted for 71% of all CCB inquiries, supporting the significance of our finding.[14] Furthermore, the American Association of Poison Control Centers' National Poison Data System reported 6,132 cases of CCB overdose in the United States of America.[5] This 2020 report detailed a 2.4% major adverse event rate including death. According to the DPIC data from 5 years in the past decade, the 30-day hospital mortality rate from intentional CCB overdose was 2% and amlodipine was involved in 29% of fatalities.[14] The mortality rate in our study was about six-fold higher (12.5%) likely reflecting the mortality in a critically ill population requiring ICU care.

Another striking finding from our data was the female preponderance (95% female gender). The DPIC data also reflected a majority of female cases (61%).[14] The gender paradox in suicidology has been well described with a greater frequency of nonfatal suicide attempts in females compared to males. In addition, drug or toxin use in females has been reported to be more common than violent methods.[15]

The frequency of interventions in the ICU used to treat CCB overdose reflects current guidelines.[12,16–18] All patients required fluid therapy (IV), over 90% required vasopressor support with noradrenaline, adrenaline, or both, about 70% required HIET, and 42% required ongoing calcium in ICU. These measures are indicative of first-line treatment published in consensus guidelines.[17,19] Rescue therapy availability is limited in our setting. Methylene blue is intermittently available, intralipid therapy and extracorporeal membrane oxygenation (veno-arterial) are unavailable.[20] Lipid therapy has been noted to be ineffective in CCB overdose involving dihydropyridines.[21]

In addition to SoC, modern resin HA is available and used for protein and lipid-bound toxins in severe poisoning. Based on the physical characteristics of CCBs modern resin hemoadsorption devices could be useful to enhance the elimination of these drugs.[22] Data from an *ex-vivo* model demonstrated the effective removal of amlodipine using a modern resin adsorption filter similar to the one available in our setting.[23] Removal of amlodipine in a clinical setting, using a styrene resin adsorption filter with associated shock resolution and good clinical outcome has also been suggested.[24] Current EXTRIP guidelines recommend against the use of extracorporeal therapy for CCB overdose.[25] However, this guideline is based on hemodiafiltration and older charcoal adsorption filter technology.[26] Consideration of the affinity for protein-bound substances that modern resin adsorption filters possess may have been overlooked.[22]

Patients receiving modern resin HA had a significantly higher SAPS II score indicating greater severity of illness and higher predicted mortality compared to standard care SoC. The total maximum vasopressor dose (adrenaline and noradrenaline) was also significantly higher in the group receiving resin HA group. This reflects the use of HA therapy in patients who were refractory to standard care. Despite a significantly lower MAP, there was a greater recovery in the HA group's 48-hour MAP profile. It is plausible that HA therapy may have contributed to the hemodynamic recovery.

Due to the greater hemodynamic instability, initiation of HIET therapy was more frequent in the HA group (85 vs 55%) and significantly higher doses were administered. Despite this, we noted a trend toward a shorter duration of HIET in the HA group compared to the SC group (about 1 day vs 3 days). There is scarce data on modern HA and amlodipine overdose. We postulate that HA enhanced the clearance of amlodipine, potentially contributing to a shorter duration of HIET therapy and improved hemodynamic stability, despite initially higher vasopressor doses.[23,24] We further speculate that additional potential benefits of less HIET therapy could be due to the limitation of adverse effects of this therapy. These are hypoglycemia, hypokalemia, hypomagnesemia, hypophosphatemia, and volume overload related to glucose and electrolyte replacement.[27–29]

Important data from our study reinforces the greater severity of disease in the modern resin hemoadsorption group compared to the SC group with longer durations of vasopressors, MV, and length ICU of stay. Despite this greater severity of disease and the higher predicted mortality in the modern resin hemoadsorption group, there was only one death in the HA group (1/13) 7.7% and two in the SoC group (2/11) 18.2%. This possible mortality benefit of HA therapy needs further exploration.

Our study provides important detail regarding the changes in lactate during the first day of shock from CCB overdose. Median lactate levels were similar at ICU admission. Median lactate levels in the SoC group peaked early, at 3 hours, and cleared slowly over the next 11 hours to reach a low at 14 hours, coinciding with the peak of the HA group. The HA peak lactate decreased to its 24-hour nadir within the next 6 hours, corresponding to approximately half the time of the SoC group. If the reduction of lactate over time is an estimate of lactate clearance this may indicate a faster resolution of a global oxygen delivery deficit (shock) in the HA group.[30] Improved lactate clearance has also been shown to affect mortality independent of its effect on organ support.[31] The potential higher lactate clearance in the HA group needs to be further explored as it may indicate faster shock resolution, increased extracorporeal lactate removal, or both.

The lactate peak was significantly greater in the modern resin hemoadsorption group vs the SoC group and occurred later. This is in keeping with ongoing slower amlodipine absorption from the gastrointestinal tract, possibly with higher doses and associated delayed peak hemodynamic effects as supported by the longer time to peak vasopressor dose in the HA group. Additionally, saturation of the hepatic enzymes may reduce the first pass effect and contribute to ongoing shock from an apparent prolonged $T_{1/2}$ and toxic effects with a delayed peak lactate.[8]

Lastly, an important complication of hemoadsorption/hemoperfusion therapy is thrombocytopenia. We found no significant difference in the maximum and minimum platelet counts between the HA and SC groups during the ICU stay. Previous utilization of this hemoadsorption filter also demonstrated no significant changes in platelet counts or transfusion requirements.[32] This finding provides much-needed safety information regarding HA therapy.

Limitations

This was an observational study with a small sample size. However, it is notable that current guidelines suggest first-line treatment strategies with low levels of evidence. Being retrospective, the study is open to bias and confounding. However, we have described both groups of patients in terms of their predicted risk using underlying physiology and organ function and support. We have also used

detailed chronological changes in important clinical parameters to improve the characterization of the groups. Finally, the study data was from a single center limiting the validity of findings even though it represents the only ICU description of CCB overdose that we are aware of.

Conclusion

Calcium channel blocker overdose is an important and life-threatening cause of toxicology admissions in the ICU. Modern resin HA may contribute to improved hemodynamic stability providing a safe and important rescue therapy in cases with refractory shock. Well-designed studies are required to confirm its role in enhancing drug clearance thereby improving the hemodynamic state and clinical outcomes.

Disclaimer

This manuscript was published as a preprint on Research Square (link: https://www.researchsquare.com/article/rs-5256785/v1) before its formal publication in the Indian Journal of Critical Care Medicine.

Orcid

Shahed Omar https://orcid.org/0000-0001-8494-1518
Varadaben Shukla https://orcid.org/0009-0003-3781-071X
Ayesha B Khan https://orcid.org/0000-0002-3105-3522
Ziyaad Dangor https://orcid.org/0000-0003-4089-147X

References

1. Stephen VS, Pluymers NA, Gauton SJ. Emergency management of calcium channel blocker overdose. S Afr Med J 2019;109(9):635–638. DOI: 10.7196/SAMJ.2019.v109i9.13704.
2. Kandala NB, Nnanatu CC, Dukhi N, Sewpaul R, Davids A, Reddy SP. Mapping the burden of hypertension in South Africa: A comparative analysis of the National 2012 SANHANES and the 2016 Demographic and Health Survey. Int J Environ Res Public Health 2021;18(10):5445. DOI: 10.3390/ijerph18105445.
3. Reddy SP, Mbewu AD, Williams DR, Harriman NW, Sewpaul R, Morgan JW, et al. Race, geographical location and other risk factors for hypertension: South African National Health and Nutrition Examination Survey 2011/12. SSM Popul Health 2021;16:100986. DOI: 10.1016/j.ssmph.2021.100986.
4. Veale DJH, Wium CA, Müller GJ. Toxicovigilance. I: A survey of acute poisonings in South Africa based on Tygerberg Poison Information Centre data. S Afr Med J 2013;103(5):293–297. DOI: 10.7196/SAMJ.6568.
5. Gummin DD, Mowry JB, Beuhler MC, Spyker DA, Bronstein AC, Rivers LJ, et al. 2020 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 38th Annual Report. Clin Toxicol (Phila) 2021;59(12):1282–1301. DOI: 10.1080/15563650.2021.1989785.
6. Onwukwe SC, Ngene NC. Blood pressure control in hypertensive patients attending a rural community health centre in Gauteng Province, South Africa: A cross-sectional study. S Afr Fam Pract (2004) 2022;64(1):5403. DOI: 10.4102/safp.v64i1.5403.
7. Hypertension Guideline Working Group, Seedat YK, Rayner BL, Veriava Y. South African hypertension practice guideline 2014. Cardiovasc J Afr 2014;25(6):288–294.
8. McKeever RG, Hamilton RJ. Calcium channel blockers. In: StatPearls [Internet]. Treasure Island: StatPearls Publishing; 2023.
9. Mirrakhimov AE, Barbaryan A, Gray A, Ayach T. The role of renal replacement therapy in the management of pharmacologic poisonings. Int J Nephrol 2016;2016:1–10. DOI: 10.1155/2016/3047329.
10. Ani JO, Ross AJ, Campbell LM. A review of patients presenting to accident and emergency department with deliberate self-harm, KwaZulu-Natal, South Africa. Afr J Prim Health Care Fam Med 2017;9(1):7. DOI: 10.4102/phcfm.v9i1.1275.
11. Matzopoulos R, Prinsloo M, Pillay-van Wyk V, Gwebushe N, Mathews S, Martin LJ, et al. Injury-related mortality in South Africa: A retrospective descriptive study of postmortem investigations. Bull World Health Organ 2015;93(5):303–313. DOI: 10.2471/BLT.14.149567.
12. St-Onge M, Dubé PA, Gosselin S, Guimont C, Godwin J, Archambault PM, et al. Treatment for calcium channel blocker poisoning: A systematic review. Clin Toxicol (Phila) 2014;52(9):926–944. DOI: 10.3109/15563650.2014.944977.
13. Mehta Y, Mehta C, Kumar A, George JV, Gupta A, Nanda S, et al. Experience with hemoadsorption (CytoSorb®) in the management of septic shock patients. World J Crit Care Med 2020;9(1):1–12. DOI: 10.5492/wjccm.v9.i1.1.
14. Christensen MB, Petersen KM, Bøgevig S, Al-Gibouri S, Jimenez-Solem E, Dalhoff KP, et al. Outcomes following calcium channel blocker exposures reported to a poison information center. BMC Pharmacol Toxicol 2018;19:78. DOI: 10.1186/s40360-018-0268-3.
15. Berardelli I, Rogante E, Sarubbi S, Erbuto D, Cifrodelli M, Concolato C, et al. Is lethality different between males and females? Clinical and gender differences in inpatient suicide attempters. Int J Environ Res Public Health 2022;19(20):13309. DOI: 10.3390/ijerph192013309.
16. Alshaya OA, Alhamed A, Althewaibi S, Fetyani L, Alshehri S, Alnashmi F, et al. Calcium channel blocker toxicity: A practical approach. J Multidiscip Healthc 2022;15:1851–1862. DOI: 10.2147/JMDH.S354645.
17. St-Onge M, Anseeuw K, Cantrell FL, Gilchrist IC, Hantson P, Bailey B, et al. Experts consensus recommendations for the management of calcium channel blocker poisoning in adults. Crit Care Med 2017;45(3):e306–e315. DOI: 10.1097/CCM.0000000000002087.
18. Lavonas EJ, Akpunonu PD, Arens AM, Babu KM, Cao D, Hoffman RS, et al. 2023 American Heart Association Focused update on the management of patients with cardiac arrest or life-threatening toxicity due to poisoning: An update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2023;148(16):e149–e184. DOI: 10.1161/CIR.0000000000001200.
19. Sircar M, Ghosh S. Calcium channel blocker overdose: Experience with amlodipine. Indian J Crit Care Med 2008;12(4):190–193. DOI: 10.4103/0972-5229.45080.
20. Sutar A, Murthy A, Chikkaswamy SB. Severe amlodipine toxicity: A case rescued with extracorporeal membrane oxygenation. Indian J Crit Care Med 2020;24(5):365–366. DOI: 10.5005/jp-journals-10071-23423.
21. Jović-Stosić J, Putić V, Zivanović D, Mladenov M, Brajković G, Djordjević S. Failure of intravenous lipid emulsion in treatment of cardiotoxicity caused by mixed overdose including dihydropyridine calcium channel blockers. Vojnosanit Pregl 2016;73(1):88–91. DOI: 10.2298/VSP150512090J.
22. Ankawi G, Fan W, Pomarè Montin D, Lorenzin A, Neri M, Caprara C, et al. A new series of sorbent devices for multiple clinical purposes: Current evidence and future directions. Blood Purif 2019;47(1–3): 94–100. DOI: 10.1159/000493558.
23. Capponi V, Young W, Chan P, Lavonas E. A novel adsorbent system rapidly clears amlodipine from human blood. In: Updates in ICU Medicine: Controversies, Challenges and Solutions. San Diego; 2017.
24. Omar S, Parris P, Gurke CR. Hemoadsorption therapy for calcium channel blocker overdose: A case report. J Emerg Med 2023; Available from: https://www.sciencedirect.com/science/article/pii/S0736467923005875.
25. Wong A, Hoffman RS, Walsh SJ, Roberts DM, Gosselin S, Bunchman TE, et al. Extracorporeal treatment for calcium channel blocker poisoning: Systematic review and recommendations from the EXTRIP workgroup. Clin Toxicol (Phila) 2021;59(5):361–375. DOI: 10.1080/15563650.2020.1861924.
26. Roberts DM, Roberts JA, Boots RJ, Mason R, Lipman J. Lessons learnt in the pharmacokinetic analysis of the effect of haemoperfusion for acute overdose with sustained-release diltiazem. Anaesthesia 2008;63(7):714–718. DOI: 10.1111/j.1365-2044.2008.05505.x.

27. Siddiqi TA, Hill J, Huckleberry Y, Parthasarathy S. Non-cardiogenic pulmonary edema and life-threatening shock due to calcium channel blocker overdose: A case report and clinical review. Respir Care 2014;59(2):e15–e21. DOI: 10.4187/respcare.02610.
28. Graudins A, Lee HM, Druda D. Calcium channel antagonist and beta-blocker overdose: Antidotes and adjunct therapies. Br J Clin Pharmacol. 2016;81(3):453–461. DOI: 10.1111/bcp.12808.
29. Rietjens SJ, de Lange DW, Donker DW, Meulenbelt J. Practical recommendations for calcium channel antagonist poisoning. Neth J Med 2016;74(2):60–67.
30. Nguyen HB, Rivers EP, Knoblich BP, Jacobsen G, Muzzin A, Ressler JA, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. Crit Care Med 2004;32(8):1637–1642. DOI: 10.1097/01.CCM.0000132904.35713.A7.
31. Bruno RR, Wernly B, Binneboessel S, Baldia P, Duse DA, Erkens R, et al. Failure of lactate clearance predicts the outcome of critically ill septic patients. Diagnostics (Basel) 2020;10(12):1105. DOI: 10.3390/diagnostics10121105.
32. Omar S, Sooka PN, Khoza S, Van Rooyen MC, Mashamba L, Madi S, et al. Hemoperfusion for clinically suspected organophosphate and carbamate poisoning in critically ill patients: A randomized trial. Blood Purif 2023;52(2):157–165. DOI: 10.1159/000526653.