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High-Dose Insulin Therapy for Refractory Shock in a Polypharmacy Overdose of Calcium Channel Blocker and Oral Hypoglycemic Agent: A Case Report and Literature Review

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Abstract

We report a case of polypharmacy overdose involving a calcium (Ca) channel blocker and an oral hypoglycemic agent, where conventional therapies failed to obtain the desired clinical outcome. High-dose insulin (HDI) therapy, a promising treatment regime in this regard, was carried out for our patient, and her condition improved over the subsequent days.

Categories: Emergency Medicine
Keywords: calcium channel blocker overdose, drug overdose, high-dose insulin therapy, refractory shock, sulfonylurea overdose, toxicology and envenomation

Introduction

Toxicity due to calcium (Ca) channel blocker overdose, although an uncommon presentation in the emergency department, poses significant challenges to the treating physician [1]. This is because conventional therapies such as IV fluid boluses, vasopressors, and glucagon often fail in severely intoxicated patients [2]. High-dose insulin (HDI) therapy is a promising alternative to such refractory cases with a high risk for mortality [3]. Although high-dose insulin therapy has proven effectiveness, its use in the concomitant intake of an oral hypoglycemic agent has limited evidence. Here, we present to you a case of a 42-year-old woman in refractory shock following amlodipine and glimepiride overdose.

Case Presentation

A 42-year-old woman was brought to our emergency department after allegedly consuming 20 tablets of amlodipine (5 mg) and six tablets of glimepiride (2 mg). She was brought two hours after the incident. On arrival, she was in shock with a blood pressure of 84/60 mm Hg and a heart rate of 100 per minute. A venous blood gas revealed a pH of 7.36 with a bicarbonate value of 18 mmol/L and a partial pressure of carbon dioxide (pCO_2) of 31 mm Hg. She was initially started on a fluid bolus (0.9% normal saline) of 1 L and later started on a vasopressor (injection noradrenaline) at 4 µg per minute and up-titrated. She was also started on an injection of calcium gluconate (10 mL in 90 mL normal saline) and shifted to the emergency department ICU. Despite these measures, her condition deteriorated as she developed bradycardia (heart rate: 40 per minute) and a further drop in blood pressure (74/50 mm Hg). She was given one dose of IV atropine (1 mg), after which the heart rate improved but hypotension persisted. We started her on high-dose insulin (HDI) therapy, where insulin was administered as an infusion at a dose of 50 U per hour. Dextrose infusion was given concurrently (25% at 80 mL per hour) and titrated according to glucometer random blood sugar (maintained between 100 and 200 mg/dL). Calcium chloride was given at a dose of 20 mL (10%) eight hourly. Over the next 24 hours, her heart rate and blood pressure showed significant improvement, and the dose of insulin was titrated down. Over the next three days, the dose of insulin was gradually titrated down and stopped, alongside noradrenaline and calcium chloride. During the course of treatment, serum electrolytes (sodium {Na}, potassium {K}, Ca, and magnesium {Mg}) were continuously monitored (initially on a four-hourly basis over the first 24 hours), and corrections were given accordingly (Table *1*).

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Day	Time (24-hour format)	Blood glucose (mg/dL)	Heart rate (beats per minute)	Blood pressure (mm Hg)	Serum potassium (mEq)	Serum calcium (mEq)	Regular insulin infusion (U/hour)	25% dextrose (mL/hour)	Noradrenaline (µg/minute)
1	15:30	220	94	80/40	3.6	8.2	50	75	18.7
	17:30	236	93	81/52	3.4	9.9	40	80	17.3
	21:30	180	107	92/57	3.6	12.0	30	90	13.3
2	02:00	250	98	103/60	4.3	11.7	30	80	17.3
	08:00	210	101	107/66	4.4	10.1	30	80	16
	14:00	88	106	99/57	4.5	9.1	15	60	2.7
	22:00	111	93	105/66	3.9	11	8	60	4
3	02:00	237	116	90/55	3.2	10.2	4	100	4.7
	08:00	230	106	106/54	5.3	12.8	4	80	4.7
	14:00	103	90	127/65	4.6	12.2	4	70	4.7
	20:00	252	102	120/65	5.7	13.3	6	50	4.7
4	02:00	159	102	109/66	4.2	13	4	60	4.7
	08:00	122	95	110/71	4.5	13.5	Stopped at 03:00	50	2.7
	14:00	102	107	105/68	4.1	13.3	-	Stopped at 05:00	Stopped at 05:00
	20:00	96	70	101/60	3.9	10.3	-	-	-
5	02:00	86	68	104/60	3.9	10.2	-	-	-
	08:00	157	75	120/76	4.3	11.1	-	-	-

TABLE 1: Clinical course in terms of vitals and serum electrolyte levels, since the initiation of high-dose insulin therapy

By day 4, she was off all support and was fully conscious and oriented. On day 5, she was shifted out of the ICU and discharged from the hospital on day 8.

Discussion

The cardiovascular effects of calcium channel blocker overdose are primarily due to their inhibitory action on L-type calcium channels. This causes vasodilation, the inhibition of sinoatrial automaticity, atrioventricular conduction delay, and myocardial depression [1]. In addition, calcium channel blockers in supratherapeutic doses decrease insulin secretion by preventing calcium influx into pancreatic beta cells. This creates a diabetogenic effect of hyperglycemia and metabolic acidosis [4-6].

Although insulin is not a vasopressor, the mechanisms by which high-dose insulin proves effective in calcium channel blocker poisoning include increased inotropy, increased intracellular glucose transport, and vasodilatation [1]. The preferred energy substrate of a stressed myocardium is glucose, rather than fatty acids. Insulin in higher doses promotes intracellular glucose transport, facilitating an increase in inotropy [3]. In addition, it directly affects certain intracellular mechanisms that contribute to increased inotropy, especially those involving calcium handling and the P13K pathway [7,8]. By enhancing endothelial nitric oxide synthase activity and its effect on an insulin intracellular signalling pathway (P13K), vasodilation, primarily on the systemic, pulmonary, and coronary vasculature, occurs. This causes a reduction in vascular resistance caused by microvascular dysfunction (caused by cardiogenic shock) and ultimately results in enhanced cardiac output [9].

Despite the challenge of hypoglycemia and concurrent intake of an oral hypoglycemic agent, the titration of dextrose infusion in accordance with timely general random blood sugar (GRBS) monitoring ensured optimal blood glucose range over the course of treatment. While case trials comparing the efficacy to other treatments are lacking in current literature, multiple case reports and case series demonstrate the efficacy of HDI therapy with minimal clinically significant adverse effects [10-12]. Experimental studies have proven

increased survival while using HDI in verapamil poisoning in dogs [13]. In a case report by Greene et al., only one person out of seven developed hypoglycemia, which was immediately rectified and clinically insignificant [14]. Although there was one case report by Corcoran et al., where the patient required prolonged HDI therapy (37 hours) at 10 U/kg/hour, serum insulin levels remained supraphysiologic beyond 24 hours after the termination of therapy [15]. In our case, although the dose of HDI was lower, the duration was longer. Although dextrose infusion rates remained slightly higher when insulin infusion rates were lowered, further dextrose infusion was not required two hours beyond the stoppage of insulin infusion. In our situation, since the patient was refractory to conventional therapy, we had to resort to this alternative treatment, which improved the patient's condition dramatically. With this case, we hope to create a positive impact in the current practice of managing patients with severe calcium channel blocker toxicity in polypharmacy overdose.

Conclusions

High-dose insulin therapy can be an effective treatment for calcium channel blocker toxicity, even when there is a concomitant intake of an oral hypoglycemic agent. This case report highlights the potential benefits of this therapy and supports its consideration in patients who are refractory to conventional treatment. Further research is needed to compare the efficacy of high-dose insulin therapy to other treatments for calcium channel blocker toxicity.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Vinayak S R, Chandni Radhakrishnan, Bipenthung N. Jami, Austin J. Mangaly, Gladson Vineeth

Acquisition, analysis, or interpretation of data: Vinayak S R, Krishnakumar R S

Drafting of the manuscript: Vinayak S R, Bipenthung N. Jami, Gladson Vineeth

Critical review of the manuscript for important intellectual content: Vinayak S R, Chandni Radhakrishnan, Krishnakumar R S, Austin J. Mangaly, Gladson Vineeth

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Disclosures

Human subjects: Consent for treatment and open access publication was obtained or waived by all participants in this study. The Institutional Ethics Committee of Government Medical College, Kozhikode, India, issued approval GMCKKD/RP2024/IEC/263. The Institutional Ethics Committee of Government Medical College, Kozhikode, India, has evaluated the protocol of the study entitled "High Dose Insulin Therapy for Refractory Shock in a Polypharmacy Overdose of Calcium Channel Blocker and Oral Hypoglycaemic Agent: A Case Report and Literature Review" submitted by Dr. Vinayak S R, Senior Resident, Department of Emergency Medicine, Government Medical College, Kozhikode, and the committee has provisionally approved the same (dated 06/09/2024). **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. DeWitt CR, Waksman JC: Pharmacology, pathophysiology and management of calcium channel blocker and beta-blocker toxicity. Toxicol Rev. 2004, 23:223-38. 10.2165/00139709-200423040-00003
2. Shepherd G, Klein-Schwartz W: High-dose insulin therapy for calcium-channel blocker overdose . Ann Pharmacother. 2005, 39:923-30. 10.1345/aph.1E436
3. Lheureux PE, Zahir S, Gris M, Derrey AS, Penaloza A: Bench-to-bedside review: hyperinsulinaemia/euglycaemia therapy in the management of overdose of calcium-channel blockers. Crit Care. 2006, 10:212. 10.1186/cc4938
4. Kline JA, Leonova E, Raymond RM: Beneficial myocardial metabolic effects of insulin during verapamil toxicity in the anesthetized canine. Crit Care Med. 1995, 23:1251-63. 10.1097/00003246-199507000-00016
5. Kline JA, Leonova E, Williams TC, Schroeder JD, Watts JA: Myocardial metabolism during graded intraportal verapamil infusion in awake dogs. J Cardiovasc Pharmacol. 1996, 27:719-26. 10.1097/00005344-199605000-00015

6. Kline JA, Raymond RM, Schroeder JD, Watts JA: The diabetogenic effects of acute verapamil poisoning . Toxicol Appl Pharmacol. 1997, 145:357-62. 10.1006/taap.1997.8195
7. Bechtel LK, Haverstick DM, Holstege CP: Verapamil toxicity dysregulates the phosphatidylinositol 3-kinase pathway. Acad Emerg Med. 2008, 15:368-74. 10.1111/j.1553-2712.2008.00088.x
8. von Lewinski D, Bruns S, Walther S, Kögler H, Pieske B: Insulin causes [Ca2+]i-dependent and [Ca2+]i-independent positive inotropic effects in failing human myocardium. Circulation. 2005, 111:2588-95. 10.1161/CIRCULATIONAHA.104.497461
9. Holger JS, Dries DJ, Barringer KW, Peake BJ, Flottemesch TJ, Marini JJ: Cardiovascular and metabolic effects of high-dose insulin in a porcine septic shock model. Acad Emerg Med. 2010, 17:429-35. 10.1111/j.1553-2712.2010.00695.x
10. Ortiz-Muñoz L, Rodriguez-Ospina LF, Figueroa-Gonzalez M: Hyperinsulinemic-euglycemic therapy for intoxication with calcium channel blockers. Bol Asoc Med P R. 2005, 97:182-9.
11. Yuan TH, Kerns WP 2nd, Tomaszewski CA, Ford MD, Kline JA: Insulin-glucose as adjunctive therapy for severe calcium channel antagonist poisoning. J Toxicol Clin Toxicol. 1999, 37:463-74. 10.1081/clt-100102437
12. Marques M, Gomes E, de Oliveira J: Treatment of calcium channel blocker intoxication with insulin infusion: case report and literature review. Resuscitation. 2003, 57:211-3. 10.1016/s0300-9572(03)00026-1
13. Engebretsen KM, Kaczmarek KM, Morgan J, Holger JS: High-dose insulin therapy in beta-blocker and calcium channel-blocker poisoning. Clin Toxicol (Phila). 2011, 49:277-83. 10.3109/15563650.2011.582471
14. Greene SL, Gawarammana I, Wood DM, Jones AL, Dargan PI: Relative safety of hyperinsulinaemia/euglycaemia therapy in the management of calcium channel blocker overdose: a prospective observational study. Intensive Care Med. 2007, 33:2019-24. 10.1007/s00134-007-0768-y
15. Corcoran JN, Jacoby KJ, Olives TD, Bangh SA, Cole JB: Persistent hyperinsulinemia following high-dose insulin therapy: a case report. J Med Toxicol. 2020, 16:465-9. 10.1007/s13181-020-00796-2