Methylene blue reverses recalcitrant shock in β-blocker and calcium channel blocker overdose

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SUMMARY

β-blocker and calcium channel blocker toxicity generally present with bradycardia and hypotension. A 69-year-old woman presented after a suicide attempt with a β-blocker and calcium channel blocker overdose. Her blood pressure was 69/35 mm Hg and her HR was in the 40s. She was treated with calcium chloride, glucagon, a dextrose–insulin infusion and three vasopressors, but remained hypotensive. She suffered two cardiac arrests and required a transvenous pacemaker. When all interventions failed, she was started on a methylene blue infusion for refractory vasodilatory shock which resulted in a dramatic improvement in her blood pressure. The patient was successfully weaned off all vasopressors and from mechanical ventilation without any end-organ damage.

BACKGROUND

This case demonstrates the effectiveness of methylene blue as a treatment for shock due to severe vasodilation resulting from a calcium channel blocker and a β-blocker overdose. The incidence of polysubstance abuse and multiple drug toxicity is on the rise and often physicians face challenges in treating such patients. These patients may not respond to standard therapy due to the severity of the overdose and resultant high level of toxicity. We report a case in which methylene blue was successfully utilised as a treatment for refractory vasodilatory shock unresponsive to multiple vasopressors.

CASE PRESENTATION

A 69-year-old woman with a history of hypertension, hypothyroidism and depression presented to our hospital after a suicide attempt. She ingested multiple pills of atenolol and amlodipine approximately 5 hs before arrival. On arrival to the emergency department, she was somnolent, vomiting and barely responsive with a heart rate of 49 bpm and a blood pressure (BP) of 69/35 mm Hg. She was intubated for airway protection. Resuscitation with intravenous fluids, glucagon and calcium chloride, did not improve her BP. Infusions of norepinephrine at 1mcg/ kg/ min and dopamine at 20 mcg/ kg/ min minimally improved BP. Vasopressin was added at 0.8 U/ min with a slight improvement in BP to 93/40 mm Hg. The patient was started on a dextrose-insulin drip without any significant improvement in BP. The drip was discontinued after 4 h owing to severe hypokalaemia with a $K^+$of 2.8, which was quickly corrected. Ten hours after admission her mean arterial pressure decreased further to the low 40s. She developed two episodes of ventricular fibrillation which responded to defibrillation. An hour later her pulse went to the low 30s and a transvenous pacemaker was placed with good capture at 60 bpm. She remained hypotensive despite all resuscitative measures. We administered methylene blue at 1 mg/kg over a 10 min period. Twenty minutes later, her BP improved to 110/60 mm Hg and an intravenous infusion of methylene blue was started at 1mg/kg/h and was continued for 10 h. Her BP stabilised and 8 h after starting the methylene blue drip, we discontinued dopamine. Four hours after that, we stopped vasopressin and titrated down the norepinephrine drip over a 72 h period. She was extubated successfully and discharged from the hospital on day 4.

TREATMENT

A pacemaker was placed for the bradycardia. Three vasopressors were infused to overcome her hypotension. A methylene blue infusion finally reversed her hypotension.

OUTCOME AND FOLLOW-UP

She continued to remain normotensive and in sinus rhythm. She was advised to refrain from using β-blockers and calcium channel blockers.

DISCUSSION

Shock caused by calcium channel blockers is due to a decrease in peripheral vascular resistance and direct vasodilatation of the peripheral arteries. Apart from blocking the transmembrane influx of calcium ions into the vascular smooth muscle, amlodipine also increases endothelial nitric oxide (NO).[1 2] Nitric oxide binds with guanylate cyclase to form NO-activated guanylate cyclase (NO-GC). NO-GC increases conversion of guanosine triphosphate to cyclic guaonosine monophosphate (cGMP) leading to smooth muscle relaxation in the arterioles.[3] Even a selective β-blocker at a high dose may cause vasodilatation.[4] Thus, extreme smooth muscle relaxation in amlodipine and β-blocker toxicity may not respond to conventional vasoconstrictors utilised in shock.

Methylene blue acts by inhibiting guanylate cyclase, thus decreasing cGMP and vascular smooth muscle relaxation. It also has the ability to scavenge NO and to inhibit NO synthesis.[5 6] These actions counteract the effect that calcium channel blockers, like amlodipine, have on smooth muscle.

The effects of methylene blue on human haemodynamics have been studied,[7] but its clinical use has been primarily limited to shock after cardiac surgery.[8–10] Our case supports the hypothesis that methylene blue may have a role in the treatment of vasoplegic shock caused by calcium channel blockers and β-blockers. Despite therapy with multiple vasoconstrictors and a transvenous pacemaker, the

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patient continued to exhibit recalcitrant hypotension owing to the vasodilatory effects of calcium channel blocker and β-blocker. A methylene blue infusion dramatically increased BP within a few minutes of administration. The only side effect noticed in our patient was bluish discolouration of the urine, tears, saliva and skin that was transient, lasting only 24 h.

Learning points

- Methylene blue has a role in refractory vasodilatory/vasoplegic shock.
- Methylene blue is a possible treatment option in calcium channel blocker and β-blocker toxicity unresponsive to standard therapy.
- In patients with β-blocker and calcium channel blocker toxicity, a pacemaker reverses bradycardia, but there may be no improvement in their hypotension. Vasoconstrictors are required to reverse the hypotension.

Competing interests None.

Patient consent Obtained.

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