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Should We Use Vasopressin to Treat Hypotension in Tricyclic Overdose?

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Vasopressin Treatment for Cyclic Antidepressant Overdose

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Aim of this Case Study

The objective of this article was to report the benefit of intravenous vasopressin use in the setting of severe intractable hypotension due to amitriptyline overdose.

Methods

The authors report a case of a 56-year-old man that was found unresponsive by paramedics. He was intubated and taken to the Emergency Department (ED) where his pulse was 105 beats/min and blood pressure 48/23mmHg. Urine drug screening was positive for benzodiazepines, opiates, cyclic antidepressants and tetrahydrocannabinol. In the ED, he had refractory hypotension, recurrent episodes of seizures, was unresponsive for painful stimuli, corneal reflexes were absent and electrocardiogram had a junctional rhythm. He was initially treated with several liters of normal saline, sodium bicarbonate, lorazepam and a norepinephrine infusion, which was titrated up to 20 μg /min with no improvement in patient clinical status. After five hours of aggressive resuscitation efforts a vasopressin infusion at 0.04U/min was started.

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Results

Despite of aggressive volume hydration, serum alkalinization, sodium loading and high dose norepinephrine infusion the patient's blood pressure remained low. Soon after the administration of vasopressin infusion at 0.04 U/min his blood pressure improved. Convulsion ceased 3 hours after the vasopressin was started. The norepinephrine infusion was weaned off once the vasopressin was started. All vasoactive agents were weaned off at 35 hours. The patient was stabilized and transferred out of the intensive care unit (ICU) on day 5. Surprisingly, the patient had no neurological sequelae and was discharged to the psychiatry ward on day 7.

Conclusion

The authors of this amazing case conclude that the effects of vasopressin may be beneficial in the treatment of intractable hypotension in patients with tricyclic overdose.

Commentary

Tricyclic antidepressant (TCA) overdose is a serious illness that includes critical features such as dysrhytmias, recalcitrant hypotension, depression of the central nervous system and persistent convulsions that if left unattended, could be lethal [1,2]. Hypotension in such cases has been reported with in an incidence of 34% [3]. Se-

vere hypotension is thought to be the result of the combination of decreased myocardial contraction and peripheral vasodilatation [4]. This case study's main objective was to show the therapeutic effect of vasopressin for the control of recalcitrant hypotension in the event of TCA overdose.

Most TCA act in a similar fashion. For example, amitriptyline toxicity has been associated with postural hypotension and tachycardia. The main pharmacological properties of amitriptyline to produce toxic effects are the inhibition of norepinephrine reuptake at nerve terminals, alpha adrenergic block, membrane stabilizing or quinidine like effect on the myocardium and anticholinergic action [5].

Overdose with TCAs can result in ventricular conduction abnormalities as well as severe ventricular dysrhythmias. The dysrhythmogenic effects of these compounds are partially attributed to their direct local anesthetic actions in blocking sodium channels in cardiac membranes.

The management of TCA overdose is not uniform. Guidelines for the management of these patients have been controversial [6,7]. Current therapy includes volume and vasopressors for hypotension and sodium bicarbonate for dysrhythmias. Seizures are usually self limited but if treatment is required, benzodiazepines are the drug of choice.

In this case study, the overdose with amitriptyline included ethanol and benzodiazepines. We wonder if the use of vasopressin was specific for the TCA or all the offending events. Arginine vasopressin has been shown to be a potent vasopressor agent that helps stabilize cardiocirculatory function even in patients that are catecholamine resistant [8,9]. Vasopressin is a nonapeptide that is naturally released when there is stimulation by hyperosmolality, hypotension and/or hypovolemia. Vasopressin has a constricting effect by four mechanisms: activation of V1 receptors, modulation of ATP-sensitive K^+ channels, modulation of nitric oxide and potentialitation of adrenergic and other vasoconstrictor agents [10-12].

In critically ill patients, vasopressin is reserved in some countries for those patients with severe vasodilatory shock who are already receiving norepinephrine and remain with uncontrolled hypotension [13]. Vasopressin might increase blood pressure significantly in patients with vasodilatory shock through V1 receptors and decreases the cardiac output [14].

In the case reported by Barry and associates, the usage of vasopressin seemed to be beneficial for the patient since norepinephrine infusion by itself was not able to maintain patient's blood pressure [15]. Vasopressin generally induces an endothelium-independent contraction of the vessels by acting on the smooth muscle myocytes and may have potentiated the norepinephrine effect on this patient. A combined infusion of vasopressin and norepinephrin has been proved to be an effective regimen to treat cardiocirculatory failure in patients with catecholamine-resistant vasodilatory shock.

Some may argue that the effect of vasopressin in this patient could have been a superimposed reaction of the normal cycle of life of the amitriptyline. Amitriptyline peak time is four hours and half-life elimination is 15 hours.

Conclusion:

Vasopressin can be used as an adjunct in the treatment of patients with TCA overdose. This case study by itself, however is insufficient to support the routine use of vasopressin alone in the event of a TCA overdose.

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