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LETTER TO THE EDITOR

Letter in response to "MDMA-induced angioedema treated with icatibant"

Sir,

We read with great interest the article by Escalante et al. regarding a patient with angioedema, presumed to be caused by 3,4-methylenedioxy-methamfetamine (MDMA) and treated with icatibant, a peptidomimetic bradykinin B_2 receptor antagonist.[1] We have concerns regarding the assumptions and conclusions the authors made about this case presentation.

Angioedema is a transient physical examination finding of swelling of subcutaneous and submucosal tissues. Multiple causes of angioedema have been described: allergic/immunologic reactions, hereditary conditions, and the use of various medications. The mediators of the swelling are predominately histamine and bradykinin. When angioedema is induced by angiotensin-converting enzyme inhibitor (ACEi), the pathophysiology is thought to be secondary to bradykinin, though additional factors are likely at play. Bradykinin is a short-acting nonapeptide that is metabolized primarily by ACE (kininase II). In patients with C1 inhibitor deficiency, the kallikrein–kinin system is not regulated, allowing increased formation of bradykinin from high-molecular-weight kininogen. Escalante and colleagues concluded that their patient's uvular swelling was the result of MDMA consumption, based solely on the contemporaneous association. They did not describe a mechanism that explains why bradykinin would have accumulated in response to MDMA use. Uvular swelling is most commonly idiopathic.[2] Furthermore, the authors relied on urine drug screening that indicated the patient's use of MDMA. It is known that such screens are not the gold standard for confirming or excluding drug use. Their sensitivity and specificity vary from institution to institution, and they do not necessarily give an accurate representation of what (or how much) a patient has consumed. We feel that to conclude that MDMA caused this patient's swelling and that the mediator was bradykinin is premature.

The authors also report that icatibant is effective in the treatment of ACEi-induced angioedema. This statement is based on a small phase 2 study in a homogeneous population.[3] That single study should not be considered conclusive evidence that icatibant is effective for this indication. The authors state that because the patient's swelling resolved after administration of icatibant, the drug must have been effective. Alternatively, the swelling might have run its natural course. Icatibant is an expensive orphan drug that costs about $6800 USD per dose [4] and recommendations for its use should be evidence-based.

We encourage the authors to present a mechanism for MDMA-induced bradykinin accumulation and to proceed with caution before suggesting that icatibant is effective for the treatment of undifferentiated angioedema.

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R. Gentry Wilkerson and Bryan D. Hayes
Department of Emergency Medicine,
University of Maryland School of Medicine, Baltimore, MD, USA
gentrywlk@gmail.com

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