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LETTER TO THE EDITOR

Toxicology

No evidence for xylazine causing cerebral infarcts

Dear Editor,

We have read with great interest the case report by Nwodim et al.[1] However, the authors' excitement about xylazine led them to overlook the evidence and to ignore other more likely causes of the patient's multiple findings and difficult course.

The authors assert that the patient had xylazine toxicity, which was never evident in this case. While her urine drug screen was qualitatively positive for fentanyl and xylazine, detection alone does not prove toxicity as it is a clinical diagnosis. In particular, the patient had tachycardia instead of bradycardia, the latter of which may distinguish xylazine effect from opioid effect.

Although the patient had a history of bacteremia, the authors excluded infectious embolic based upon negative blood cultures and a transthoracic echocardiogram that did not demonstrate vegetations. However, the authors appear to overlook the possibility of emboli forming from insoluble excipients or adulterants in the injected material.

It also likely that the patient's injection of drugs "into a blood vessel in her neck" resulted in carotid arterial injury. The cited article described cerebral injury from intracarotid injection of 0.3 mL of a mixture of ketamine, xylazine, and butorphanol in an alpaca (*Vicugna pacos*).[2] The authors implicated the vascular injury of the inadvertent carotid puncture and not xylazine as the direct cause of resulting pathology.[2]

Furthermore, the patient's case appears similar to cerebellar, hippocampal, and basal nuclei transient edema with restricted diffusion (CHANTER) syndrome.[3] The authors offer no evidence to exclude this.

The authors suggest that the patient's cerebral injuries resulted from a transient and scattered microvascular intracerebral constriction with resultant reperfusion from subsequent vasodilation. They offer no evidence that xylazine produces scattered regions of focal arterial constriction or the rebound reperfusion.

The authors also blame xylazine for the patient's transient hearing loss. However, this is inconsistent with magnetic resonance imaging findings that did not reveal infarcts to explain deafness. There are no reports credibly attributing transient hearing loss to illicit xylazine use, but opioid-associated hearing loss is well recognized.[4] The exact mechanism remains uncertain, but most cases have partial or complete resolution, as observed in this case.

Xylazine has an inconsistent association with necrotic skin wounds that may or may not correlate with drug injection sites. A literature review by Ruiz-Colón et al. yielded only case reports and no available evidence to explain the mechanism of injury.[5] However, whether and how xylazine might be the principal cause of such wounds remain uncertain.

The patient described by Nwodim et al. had a complex presentation with the mere presence of xylazine in urine.[1] Other causes are more likely for the observed clinical findings and diagnostic findings. The current case lacks evidence to implicate xylazine as the primary cause in this patient's clinical course.

CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

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