Postpartum Cerebral Angiopathy
Is There a Role for Sympathomimetic Drugs?

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Background: Postpartum cerebral angiopathy is associated with the use of ergot alkaloids. The exact mechanism is unclear but may be related to their sympathomimetic properties, as evidenced in patients already on other ergot derivatives who deteriorated only after taking additional sympathomimetic drugs. We postulate that sympathomimetic agents, independent of ergot alkaloids, may produce the same complication.

Case Description: A postpartum patient, initially presenting with headaches, subsequently manifested rapid neurological deterioration after ingesting isometheptene, a sympathomimetic drug. She was not on any ergot derivative but presented similar clinical and radiological manifestations. She experienced increased headache severity, visual disturbance, and seizures associated with multiple segmental cerebral vasoconstriction on angiography and increased T2-weighted signal in the occipital areas on magnetic resonance imaging.

Conclusions: This case is additional evidence that sympathomimetic actions of some drugs, such as ergot derivatives and isometheptene, may lead to postpartum cerebral angiopathy. Documentation of medication used by postpartum women suffering similar complications is needed to verify these findings. (Stroke. 1993;24:2108-2110.)

KEY WORDS • sympathomimetics • vasoconstriction • women

Ergot alkaloids, such as ergonovine, have been implicated as possible causes of postpartum cerebral angiopathy.¹ Physicians have not clearly defined nor consistently recognized this condition, which is generally characterized by headache, seizures, and focal neurological deficits associated with cerebral vasoconstriction on angiography.² Similar clinical neurological presentation has been reported in postpartum women who do not carry clear diagnoses but who deteriorate after the ingestion of another ergot derivative, bromocriptine.³ Of the many properties of ergot derivatives, it is unclear what produces this complication, but one report suggests that mechanisms relating to the sympathomimetic properties may play a role in the pathogenesis.⁴ In the report, two postpartum women who were already taking bromocriptine had neurological symptoms after ingesting other sympathomimetic drugs, one containing isometheptene and the other containing phenylpropanolamine. We encountered a postpartum patient who was not on bromocriptine but who exhibited similar clinical manifestations associated with cerebral vasoconstriction after ingesting isometheptene, adding further support to the possible role of agents with sympathomimetic properties in the pathogenesis.

Case Report

A 32-year-old woman, gravida 3, para 3, was admitted to the hospital after complaining of increasingly severe headaches 5 days after an uncomplicated pregnancy and delivery. She had a 4-year history of poorly defined headaches characterized as diffuse and throbbing, without aura, and occasionally associated with nausea. The headaches had occurred approximately every 3 months, were of variable duration, and were relieved by acetaminophen or aspirin. Aside from the persistence and increasing severity, her present headaches exhibited the same characteristics as those occurring during the previous 4-year period.

On initial presentation, her blood pressure, physical and neurological examinations, and routine laboratory tests, including urinalysis, were normal. Contrast computed tomography scan and cerebrospinal fluid analysis also were normal. She was treated with chlorpromazine 50 mg IV, and the headaches subsided. She was discharged and instructed to take a commercial preparation containing isometheptene mucate 65 mg per tablet, dichloralphenazone 100 mg per tablet, and acetaminophen 325 mg per tablet (Midrin, Carnrick Laboratories, Inc, Cedar Knolls, NJ). She was advised to take this medication as needed for headaches but not to exceed ingesting six tablets in 24 hours and 10 tablets in 1 week. She was also prescribed amitriptyline 25 mg every night, but she denied taking them.

After discharge, she experienced the headaches again, for which she took eight tablets of isometheptene within 24 hours. Subsequently, she complained of flashing lights and photophobia, followed immediately by generalized tonic-clonic seizures. She was readmitted. Her physical examination, including blood pressure, was

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normal. A neurological examination only revealed lethargy. A repeat work-up, including an echocardiogram, electroencephalogram, erythrocyte sedimentation rate, and antinuclear antibody, was normal. A toxicological screen was not performed, but there was no history of illicit drug use. Magnetic resonance imaging (MRI) within 24 hours of admission showed bilateral occipital increased signal on T2-weighted images (Figure, left panel). There was no evidence of hemorrhage. Transcranial Doppler study (TCD) performed 2 days later demonstrated mild to moderate elevated velocities diffusely, interpreted as diffuse arterial narrowing or hyperemia. In addition, the anterior cerebral artery (ACA) velocities were abnormally greater than the middle cerebral artery (MCA) velocities, and there was a sudden increase in basilar artery velocity at a depth of approximately 85 mm, suggesting a focal stenosis of the basilar artery. Four-vessel cerebral angiography, 3 days after admission, revealed widespread segmental vasospasm (Figure, right panel). After being treated with phenytoin, her seizures did not recur. In addition, her headache subsided with acetaminophen. A repeat cerebral angiography was not performed, but a repeat TCD was performed 6 days after the first study. The TCD showed persistent global elevation in velocity but normalization of the ratio of ACA to MCA velocity as well as near disappearance of the focal velocity elevation previously seen in the basilar artery. A repeat MRI 10 days later was normal.

Discussion

Our patient had a presentation similar to that of patients with toxemia and postpartum cerebral angiopathy. However, she did not have hypertension, proteinuria, or edema to satisfy the minimal clinical and laboratory criteria for toxemia and more likely had postpartum cerebral angiopathy. Her rapid deterioration occurred after the ingestion of more than the recommended amount of medication. The medication may have been excessive for anyone. Alternatively, the medication may have been contributory to a predisposed state or a progressing pathological process peculiar to the postpartum period.

Isometheptene, the major component of Midrin, is a sympathomimetic agent with direct vasoconstrictive activity on cranial and cerebral arteries and is widely used in the treatment of migraine and other vascular headaches. To our knowledge, the syndrome pre-
sent by our patient has not been reported as a specific side effect of this drug. The only other documented case involving isometheptene was with a postpartum patient who was also on bromocriptine for lactation suppression. The patient experienced progressively severe headache and cardiovascular distress 6 days postpartum after ingesting three tablets of a commercial preparation containing isometheptene. Unfortunately, no angiographic studies were performed. The authors used the case to suggest a sympathomimetic interaction with bromocriptine as the mechanism for the complication, especially since the patient also had been on bromocriptine in a previous pregnancy but did not experience any complications. They supported this hypothesis by reporting another postpartum patient who was also on bromocriptine and who deteriorated only with the ingestion of another sympathomimetic drug, phenylpropanolamine. In this case, the patient showed a presentation similar to that of our patient, experiencing headache, blindness, and two generalized tonic-clonic seizures associated with cerebral vasoconstriction on angiography.

No specific mechanism has yet been proven for postpartum cerebral angiopathy, but mechanisms relating to severe hypertension, as in toxemia, have been proposed. In toxemia, it is postulated that the neurological deterioration is a result of severe hypertension with resultant cerebral vasospasm and subsequent loss of autoregulatory control leading to ischemia, edema, infarction, or hemorrhage. In patients on bromocriptine, transient acute increases in blood pressure were recorded. In our patient, hypertension was not recorded at any time. Still, transient hypertension could have been present but merely missed. However, other mechanisms, such as reversible vasospasm secondary to increased vasomotor responsiveness or an arteriopathy relating to direct vasoconstrictive activity independent of hypertension, also could have been present. The latter mechanism already has been implicated in cerebrovascular complications arising from more potent sympathomimetic drugs, such as cocaine and amphetamine in pregnant and nonpregnant patients. The more commonly used sympathomimetic drugs also may produce vasoconstriction with or without hypertension. For example, in large doses isometheptene can produce generalized vasoconstriction and increased blood pressure. However, in low doses it only causes selective vasoconstriction in certain vascular beds before any effects on blood pressure can be seen. Phenylpropanolamine, a commonly used nasal decongestant, acts through local vasoconstriction in the nasal mucosa. However, it also has pressor effects secondary to both vasoconstriction and increased cardiac output.

Overall, our case lends support to the hypothesis that postpartum cerebral angiopathy may arise from drugs with sympathomimetic properties. It also raises the question of whether postpartum patients are truly more vulnerable to the less potent sympathomimetic drugs. Documentation of medications, particularly those with sympathomimetic properties, in women suffering similar clinical and radiological manifestations during pregnancy and immediately after delivery is needed to verify these findings.

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References

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