Letter to the Editor

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Leg Ulceration during Amezinium Methyl Sulfate Therapy for Hypotension in a Hemodialyzed Patient with Generalized Vascular Calcification

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Dear Sir,

Hypotension is a common problem in patients with end-stage renal disease undergoing hemodialysis. In addition to hypo-volemia and acetate toxicity, abnormalities in the systemic nervous system may contribute to the pathogenesis of hemodialysis-induced hypotension. Amezinium methyl sulfate, an indirectly acting sympathomimetic drug [1], is often used to treat the hypotension of hemodialyzed patients [2]. It can stimulate the α-receptors of vessels and cardiac β-receptors and elevates the blood pressure. Therefore, patients treated with amezinium methyl sulfate may complain of palpitation and headache.

We describe a hemodialyzed man in whom amezinium methyl sulfate seemed to contribute to chronic leg ulceration. Since this association has, to our knowledge, not been reported before, we would like to introduce this case.

A 52-year-old man was admitted to our hospital having chronic painful leg ulcers which developed 7 months ago. He had been receiving hemodialysis for 22 years. His renal disease was thought to be chronic glomerulonephritis, and he was not diabetic. He had several complications, such as secondary hyperparathyroidism, severe atherosclerosis, constrictive pericarditis, congestive heart failure, carpal tunnel syndrome, and chronic hepatitis, most of which were likely due to the long-term hemodialysis treatment. A serial X-ray film revealed generalized vascular calcification. He denied experiencing claudication, but the pulses of both the bilateral posterior tibial artery and the dorsalis pedis artery could not be detected on palpation.

More than 20 months prior to this admission he had experienced hypotension, especially during the hemodialysis sessions, and amezinium methyl sulfate treatment (Ri-sumic, Dainippon Pharmaceutical Co., Ltd.) (20 mg/day) was initiated. After admission, local ulcer treatment was performed and prostaglandin administered for several weeks, but this was unsuccessful. However, after administration of amezinium methyl sulfate was stopped, the ulcers gradually decreased in size and number and healed completely during the next few weeks. Thermographic studies revealed improvement of the local temperature of the lower extremities.
These findings suggest that the amezinium methyl sulfate might have been a possible cause of the leg ulceration of the patient. Amezinium methyl sulfate (4-amino-6-meth-oxy-1-phenylpyridazinum methylsulfate) was recently developed as an antihypotensive drug [3]. This agent is unique in that it acts on the nerve endings of postganglionic sympathetic neurons through the release and reuptake inhibition of endogenous noradrenaline and through monoamine oxidase inhibition. Therefore, it is an indirectly acting sympathomimetic agent [1]. Vasoconstriction induced by the drug might have decreased the blood supply to the lower extremities, provoking the chronic ulcers. In addition to congestive heart failure, the vessels of the patient had severe atherosclerosis, so that his skin, especially in the lower extremities, seemed vulnerable to a decrease in blood supply. The patient had received 20 mg/day of amezinium methyl sulfate for a long time. Since most metabolites of this drug are excreted by the kidney [4], Japanese drug guidelines recommend physicians to prescribe 5-10 mg of the drug every hemodialysis session for end-stage renal disease patients. Therefore, an overdose of the drug might have worsened the leg ulcers of our patient.

In conclusion, we believe that when administering vasoconstricting agents, such as amezinium methyl sulfate, doctors should be more aware of their adverse effects, especially in elderly patients or long-term hemodialyzed patients.

References