

An anaphylactic reaction caused by levodropropizine

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Levodropropizine is a commonly prescribed effective cough suppressant, that is recommended for patients with acute or chronic bronchitis (1). To date, no studies describing adverse allergic events to levodropropizine have been reported, except mild somnolence and gastrointestinal symptoms including vomiting, diarrhea, and epigastric pain (2).

This report presents an anaphylactic reaction that occurred in a 41-year-old man after taking multiple cough medications, including azelastine, methylprednisone, pronase, and levodropropizine. He had no history of allergic disease, but had taken antihypertensive medications for 3 years, including a calcium channel blocker, angiotensin receptor antagonist, and diuretics. He visited our clinic after he experienced generalized urticaria, angioedema, and dizziness within 10 min after taking medicines prescribed for cough suppression. He had the same experience 1 year earlier after taking same the medicines.

He had no peripheral eosinophilia, although the serum total IgE was elevated to 817 IU/ml. Skin prick testing (SPT) to common inhalant allergens gave

all negative responses. Open-label oral challenge tests were performed individually for azelastine, methylprednisone, pronase, and levodropropizine to identify the causative drug. After taking 60 mg of levodropropizine, he developed a systemic reaction that included periorbital angioedema, generalized urticaria, and dizziness within 30 min. His blood pressure dropped from 160/90 to 120/70 mmHg. Both *in vivo* and *in vitro* tests were performed to confirm that the systemic reaction was caused by levodropropizine. Pure levodropropizine was obtained from a local pharmaceutical company and diluted for SPT (2 mg/ml), intradermal testing, and the basophil histamine release (HR) test (0.1, 1, and 6 mg/ml).

Although SPT to levodropropizine was negative, the intradermal test gave a strong positive response to 6 mg/ml levodropropizine with a mean wheal size of 49.5 mm. The basophil HR test was performed to verify that the drug caused

the systemic reaction, according to methods described previously (3). The maximal HR from the patient's basophils occurred on incubation with 0.1 mg/ml levodropropizine (51.8%, Fig. 1). In contrast, no HR was seen with basophils from three healthy controls. Therefore, the patient was confirmed as having an anaphylactic reaction to levodropropizine based on an open-label oral challenge test, intradermal test, and HR test.

Cough suppressants mainly affect the afferent limb of the cough reflex, and are traditionally divided into the centrally acting agents, which included the opiates, morphine, and codeine, and the peripherally acting agents, including levodropropizine and moguisteine (4). Levodropropizine is an effective peripheral cough suppressant with no sedative effects (5). Although some studies have described codeine-induced allergic reactions, none has reported on allergic reactions induced by a peripherally acting cough suppressant. The mechanism of

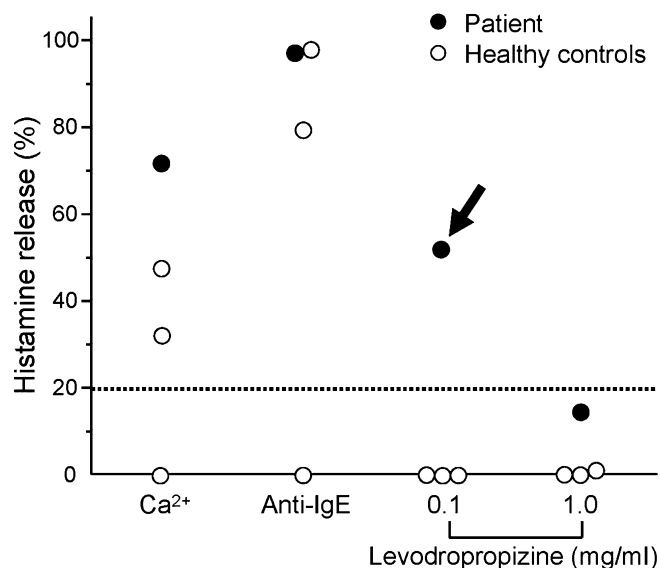


Figure 1. Comparison of histamine release (%) between our patient and three healthy controls following stimulation with the calcium ionophore A2319 (3 μ M; Sigma-Aldrich, St Louis, MO, USA), anti-human goat IgE antibodies (1 : 100 v/v; KPL, Gaithersburg, MD, USA), and levodropropizine (0.1 mg/ml).

the codeine-induced allergic reaction was explained as an immediate response of mast cells that were activated by codeine directly to release histamine (6). Based on these findings, levodropropizine induces an anaphylactic reaction via a direct HR mechanism.

In conclusion, we report a severe anaphylactic reaction caused by levodropropizine that was mediated by direct HR effects from basophils.

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