

Tolerance of Fondaparinux in Immediate-type Hypersensitivity to Heparins

To the Editor:

Subcutaneously administered anticoagulants—including unfractionated heparin (UFH), low-molecular-weight heparins, semisynthetic heparinoids, and the synthetic pentasaccharide fondaparinux—are used for treatment and prophylaxis of thromboembolic disorders. Delayed-type hypersensitivity reactions are common adverse events of subcutaneous heparin.¹ Conversely, immediate-type hypersensitivity reactions to heparins are rare.¹ Clinical manifestations of immediate hypersensitivity to heparins range from local wheals to anaphylaxis.^{2,3} According to single case reports, 1) switch to a chemically different anticoagulant³ or heparinoids,⁴ 2) specific immunotherapy,⁵ or 3) switch to the synthetic pentasaccharide fondaparinux² have been reported as alternatives for immediate hypersensitivity to heparins. Yet this is based on mostly single observations, and thus very little expertise (beyond acute care) for treatment of immediate hypersensitivity to heparins is available.

We report a 47-year-old female Caucasian patient who underwent endoluminal laser coagulation of the right great saphenous vein for chronic venous insufficiency. The low-molecular-weight heparin tinzaparin was prescribed to prevent deep vein thrombosis. The patient took no other concomitant drugs. Thirty minutes after the third tinzaparin injection (1 × 3500 IU/d), the patient experienced dizziness, nausea, and headaches. Tinzaparin was discontinued, and symptoms resolved. The patient was referred to our allergy department for testing. A skinprick test (SPT) with tinzaparin, danaparoid, and fondaparinux was performed. We refrained from including UFH and other LWMH, because (albeit on the basis of few reports) a high grade of cross-reactivity has been documented.²⁻⁴ Approximately 10 minutes after start of the SPT, she complained of dizziness. At this time point, reading for negative control (saline) was negative, whereas positive control (histamine) had induced a wheal and erythema.

Response to tinzaparin and danaparoid were comparable to histamine, whereas SPT with fondaparinux was negative at this and later time point(s). The patient's history and SPT results led to the diagnosis of an immediate reaction to tinzaparin and danaparoid. To confirm the negative SPT result for fondaparinux, an alternative anticoagulant that can be used for treatment of myocardial infarction and pulmonary embolism, the patient underwent a challenge test with fondaparinux, which was administered subcutaneously at increasing doses starting from 0.025 to 2.5 mg. The latter, at a cumulative dose of 3.84 mg, was well tolerated by the patient.

Collectively, we describe the second patient with immediate hypersensitivity to heparins and heparinoids who tolerated fondaparinux, which should be considered as a potential alternative for patients with immediate hypersensitivity to heparins. Compared with the other described alternative (see above), fondaparinux is an alternative that, given tolerance has been shown in prick testing, can be used readily and is licensed for emergency situations (ie, pulmonary embolism).⁶ Before use of any heparin-based alternative anticoagulant, prick testing is required. Testing should also include fondaparinux, because positive prick tests for this anticoagulant have been reported.³ Switching to intravenous heparin (UFH), which is tolerated in delayed-type hypersensitivity,¹ is not an option for immediate-type hypersensitivity.

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