
**Kounis Syndrome After Intake of Levofloxacin:
Increasing Incidence of Hypersensitivity to
Fluoroquinolones**

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To the Editor:

We read with great interest the report published in the *Journal of Investigational Allergology and Clinical Immunology* [1] of a case of generalized angioedema with urticaria and immediate reaction after intake of levofloxacin by a 35-year-old man with sinusitis who had experienced an episode of type I variant of Kounis syndrome. While the results of the prick and intradermal tests were negative, the basophil activation test yielded a positive result for levofloxacin (4.5%), as did the specific IgE determination. We believe that the following comments concerning this report might be of value.

1. This patient was young and had sinusitis. Acute bacterial rhinosinusitis can be complicated by development of allergic fungal rhinosinusitis, which is the most common form of fungal sinusitis in the United States [2]. This condition is associated with a predisposed person's type I IgE-mediated allergic response to inhaled mold spores that are ubiquitous in the environment. Indeed, common allergic symptoms were found to be significantly associated with an increased risk of coronary heart disease and Kounis syndrome [3].
2. The patient developed Kounis syndrome with the first dose of levofloxacin. Clinical studies indicate that susceptible individuals simultaneously exposed to multiple allergens more frequently have symptoms than monosensitized individuals [4]. Furthermore, IgE antibodies with different specificities can have additive effects, and small, even subthreshold numbers, can join forces and trigger mast cells to release their mediators [5].
3. Given that fluoroquinolones are well-tolerated and therefore increasingly consumed, the frequency of allergic reactions has risen. Consequently,

fluoroquinolones are now the drugs most frequently involved in allergic drug reactions after β -lactams [6]. IgE-mediated anaphylaxis and urticaria are the most frequent manifestations [7]. Kounis syndrome has been induced not only by ciprofloxacin and levofloxacin, but also by the original quinolone cinoxacin [8]. More cases are expected to be reported in the future. Therefore, it seems wise to maintain a high index of suspicion.

4. We agree with the authors of the report [1] that no diagnostic and therapeutic criteria of Kounis syndrome have been established to date. However, a large group of expert immunologists, allergists, cardiologists, anesthesiologists, and surgeons has agreed to convene in order to establish these criteria. We urge any scientist with interest and experience in this syndrome to participate.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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