



CROSS IMMEDIATE HYPERSENSITIVITY BETWEEN CIPROFLOXACIN AND LEVOFLOXACIN: A CASE REPORT AND LITERATURE REVIEW

Chotirat Nakaranurack^{1*}, Wichai Santimaleeworagun², Jantima Traipattanakul³

¹Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok 10330, Thailand

²Department of Pharmacy, Faculty of Pharmacy, Silpakorn University, Nakorn Pathom 73000, Thailand

³Division of Infectious Disease, Department of Medicine, Phramongkutklao Hospital, Bangkok 10400, Thailand

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ABSTRACT

Fluoroquinolones can reveal cross-reactivity because of the similar chemical structure. However, levofloxacin is a new fluoroquinolone and might be a safe alternative due to low cross-reactivity. This was a case report showing cross-reactivity between ciprofloxacin and levofloxacin. A 64-year-old man was diagnosed as cellulitis with *Pseudomonas* septicemia. Ciprofloxacin was given intravenously. After infusion for a few minutes, patient felt pain around the injection area, following by burning sensation along the course of his superficial vein. He also had diffuse skin flushing, dizziness, blurred vision, pruritus and urticaria on the waist. Piperacillin/tazobactam was administered instead of ciprofloxacin. Before hospital discharge, he received oral levofloxacin. Within 1 hour after starting levofloxacin oral, he had swollen upper lip and numbness on the right side of the face. In conclusion, healthcare providers have to be aware when prescribing levofloxacin to patients with hypersensitivity reaction to ciprofloxacin.

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Introduction

Fluoroquinolones are one of the most widely used antibiotics[1]. However, the increasing of resistant pathogens, especially Enterobacteriaceae, the role of fluoroquinolones have been dramatically decreased [2]. The most common adverse drug reactions of this group include gastrointestinal tract intolerance, and rare events such as arthropathy, tendinitis, cardiac arrhythmia, photosensitivity, skin reaction and immediate hypersensitivity reaction [3,4]. In fact, immediate types of reactions (Type I hypersensitivity) involve immunoglobulin E-mediated release of histamine from mast cell, are more common but there was few case reports of cross-allergy

among fluoroquinolones [5]. Another is T cell-mediated mechanism [6].

Levofloxacin might be a safe alternative choice in cases of reaction to first-, second-, or fourth-generation quinolones due to low cross-reactivity [7]. However, we reported herein the case of suspected cross sensitivity between ciprofloxacin and levofloxacin for immediate type of reaction.

Report of a case

A 64-year-old man with history of lymphoma nineteen years ago presented with fever, feeling pain, mild swelling

*Correspondence:

Chotirat Nakaranurack

Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok 10330, Thailand

Email: cnakara@gmail.com

and warmth in both legs (from thigh to ankle) for 5 days before hospitalization. Physical examination was as follows: Lymph node: cannot be palpable, Extremities: moderate swelling with redness and warmth at left leg and mild swelling with no tender at right leg. No bleb or abscess for both legs. Seventy-six percent of the total white blood cell (n= 10,600) was neutrophils. Other laboratory values were normal. Two blood cultures were positive for *Pseudomonas* spp. sensitive to multiple classes of antimicrobials such as piperacillin/tazobactam, ciprofloxacin, levofloxacin, trimethoprim/sulfamethoxazole and tigecycline) and he was diagnosed as cellulitis with *Pseudomonas* septicemia. He had no previous history of drug allergy. Ciprofloxacin 400 mg was given intravenously based on the report of antimicrobial susceptibility. After infusion for a few minutes, patient felt pain around the injection area, following by burning sensation along the course of his superficial vein. He also had diffuse skin flushing, dizziness, blurred vision, pruritus and urticaria on the waist. Patient refused of having maculopapular rash, angioedema, face edema, chest tightness, wheezing or dyspnea. His vital signs were normal and chlorpheniramine administration greatly improved these symptoms. Piperacillin/tazobactam was administered instead of ciprofloxacin. The patient symptom got better without fever, pain or swelling at both legs. According to discharge plan, the clinician needed to treat this case as out-patient with oral antibiotics. Before hospital discharge, the patient received oral levofloxacin 750 mg with close monitoring for adverse drug reaction. Within 1 hour after starting levofloxacin oral, he had swollen upper lip and numbness on the right side of the face. He received antihistamine with immediate levofloxacin cessation. Based on the Naranjo adverse drug reaction probability scale rating criteria, a probable causal association was made (7 score). Prior to this event of immediate hypersensitivity one year ago, the patient was admitted for cataract surgery and received ciprofloxacin for ten days without any adverse drug reactions.

Discussion

Typically, the possible mechanism for type I (IgE-molecule) of fluoroquinolones is a covalent binding between the substitute at position 7 of the quinolone ring and IgE[5]. Therefore, most fluoroquinolones could present cross-reactivity because of the similar chemical structure. Additionally, the results of previous *In vitro* study showed that ciprofloxacin and levofloxacin could stimulate histamine releasing [8]. Levofloxacin is the levogyre form of ofloxacin and could be a safe alternative in cases of reaction to first-second-, or fourth-generation fluoroquinolones. Lobera et al. study shows that patients who had allergic history to ciprofloxacin, norfloxacin and moxifloxacin were well tolerated to levofloxacin [7]. However, the cross-reactivity between fluoroquinolones has been described.

Previously, there were some case reports in 1993 that showed cross-allergy among fluoroquinolones by oral provocation [9,10]. Only one case report of cross-reactivity between ciprofloxacin and levofloxacin in 2011 was 7 year-old patient with subacute appendicitis. Five minutes after starting infusion of ciprofloxacin, the patient developed multiple erythematous papules on his arm and chest. He felt better after stopping ciprofloxacin and

received dexamethasone and chlorpheniramine injection. By switching from ciprofloxacin to levofloxacin, close monitoring adverse drug reactions showed that the patient would develop itching and rashes on the arm after starting levofloxacin within a few seconds [11]. Similarly, our case presented the type I hypersensitivity when he received the same class of antimicrobials.

Conclusions

Levofloxacin could be cross-reactive with ciprofloxacin. The present case showed that healthcare providers should be aware when prescribed levofloxacin to patient who had hypersensitivity reaction to ciprofloxacin.

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References

1. Somasundaram S, Manivanna K. An overview of fluoroquinolones. *Annu Res Rev Biol.* **2013**;3:296-313.
2. Dalhoff A. Global fluoroquinolone resistance epidemiology and implications for clinical use. *Interdiscip Perspect Infect Dis.* **2012**;2012:1-38.
3. Lipsky BA, Baker CA. Fluoroquinolone toxicity profiles: A review of on newer agents. *Clin Infect Dis.* **1999**;28:352-64.
4. Lacy CF, Armstrong LL, Goldman MP. Drug information handbook. 19th ed. United States: Lexi-Comp Inc; **2010**.
5. Scherer K, Bircher AJ. Hypersensitivity reactions to fluoroquinolones. *Curr Allergy Asthma Rep.* **2005**;5:15-21.
6. Schmid DA, Depta PH, Pichler WJ. T cell-mediated hypersensitivity to quinolones: mechanisms and cross-reactivity. *Clin Exp Allergy.* **2006**;36:59-69
7. Lobera T, Audicana MT, Alarcón E et al. Allergy to quinolones: Low cross reactivity to levofloxacin. *J Investig Allergol Clin Immunol.* **2010**;20:607-11.
8. Mori K, Maru C, Takasuna K. Characterization of histamine release induced by fluoroquinolone antibacterial agents in-vivo and in-vitro. *J Pharm Pharmacol.* **2000**;52:577-84.
9. Alonso MD, Martin JA, Quiree s et al. Fixed eruption caused by ciprofloxacin with cross-sensitivity to norfloxacin. *Allergy* **1993**;48:296-297
10. Diavila I, Diez ML, Quiree S et al. Cross-reactivity between quinolones. *Allergy.* **1993**;48:388-390
11. Anoyadiya AP, Barvaliya MJ, Patel TK et al. Cross sensitivity between ciprofloxacin and levofloxacin for an immediate hypersensitivity reaction. *J Pharmacol Pharmacother.* **2011**;2:187-8