

Tolerability of moxifloxacin in patients with antibiotic hypersensitivity

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ABSTRACT

Background: Allergic reactions to antibiotics are commonly reported in the clinical practice. The treatment of antibiotic hypersensitivity (AH) consists of suggesting to avoid the offending antibiotics and to use safe alternatives after performing oral provocation tests (OPT). Moxifloxacin is a new fluoroquinolone antibacterial agent with a broad spectrum activity. Allergic reactions to moxifloxacin have rarely been described and therefore it could be tolerated by antibiotic allergic subjects.

Objectives: The aim of this survey was to investigate the tolerability of moxifloxacin in antibiotic intolerant patients.

Materials and methods: A prospective study was conducted in 20 patients diagnosed with AH at our clinic between 1 January 2003 and 31 December 2003. We performed single blind, one day OPT protocol for moxifloxacin with a total dose of 1000 mg.

Results: The mean age of the patients was 38.05 ± 14.1 and 17 (85 %) of them were females. There were only two patients with accompanying allergic diseases; one with bronchial asthma and the other with chronic urticaria. The rates of common anamnestic antibiotic hypersensitivities were 50 %

with amoxicillin, 40 % with penicillin, 20 % with sulphonamides, respectively. Urticaria (80 %) was the leading reaction appearing after antibiotic ingestion. Seventeen of 20 patients tolerated moxifloxacin at therapeutic doses without any problem. One patient experienced generalized urticaria 4 hours after ingestion of the first dose of the drug, which resolved spontaneously 5 hours after the onset. Another patient experienced tachycardia (heart rate did not exceed beyond 115 per minute) 2.5 hours after ingestion of first dose of the drug, which resolved spontaneously 2 hours after the onset. And a third one developed severe nausea lasting for two hours.

Conclusion: Given the high incidence of hypersensitivity reactions to beta-lactam antibiotics the use of new fluoroquinolone, moxifloxacin might represent a therapeutic alternative.

Key words: Antibiotic hypersensitivity. Moxifloxacin.

RESUMEN

Antecedentes: En la práctica clínica se dan habitualmente casos de reacciones alérgicas a los antibióticos. El tratamiento de la hipersensibilidad a los antibióticos (HA) consiste en evitar los antibióticos responsables y utilizar alternativas seguras tras realizar pruebas de provocación oral (PPO). La moxifloxacina es una nueva fluoroquinolona de acción antibacteriana con un amplio espectro de actividad. Raramente se han descrito reacciones alérgicas a la moxifloxacina, por lo que puede que sea tolerada por sujetos alérgicos a los antibióticos.

Objetivos: El objeto de este estudio fue investigar la tolerancia de la moxifloxacina en pacientes con alergia a antibióticos.

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Materiales y métodos: Se efectuó un estudio prospectivo sobre 20 pacientes a los que se había diagnosticado una HA en nuestra clínica entre el 1 de enero y el 31 de diciembre de 2003. Realizamos una PPO, simple ciego, de un día de duración con moxifloxacina, a una dosis total de 1.000 mg.

Resultados: La edad media de los pacientes era de $38,05 \pm 14,1$ y 17 (el 85 %) de los mismos eran mujeres. Sólo había dos pacientes con enfermedades alérgicas concurrentes; uno con asma bronquial y otro con urticaria crónica. Los porcentajes de hipersensibilidad a antibióticos fueron del 50 % a la amoxicilina, del 40 % a la penicilina y del 20 % a las sulfonamidas. La urticaria (80 %) fue la principal reacción tras la ingestión de antibióticos. 17 de los 20 pacientes toleraron la moxifloxacina a dosis terapéuticas sin ningún problema. Un paciente experimentó una urticaria generalizada 4 horas después de la ingestión de la primera dosis del fármaco, que remitió espontáneamente 5 horas después de su aparición. Otro paciente experimentó taquicardia (el ritmo cardíaco no excedió las 115 pulsaciones por minuto) 2,5 horas después de la ingestión de la primera dosis del fármaco, que remitió espontáneamente 2 horas después de su aparición. Un tercer paciente presentó unas fuertes náuseas que duraron 2 horas.

Conclusión: Dada la elevada incidencia de las reacciones de hipersensibilidad a los antibióticos betalactámicos, el uso de una nueva fluoroquinolona como la moxifloxacina puede representar una alternativa terapéutica.

Palabras clave: Hipersensibilidad a los antibióticos. Moxifloxacina.

INTRODUCTION

Antibiotic hypersensitivity states present an often frustrating challenge for most physicians.

The knowledge of the natural history, course and pathogenesis of the reactions of these antibiotic intolerant patients remains superficial. Because of limited number of immunodiagnostic tests for these patients, many practitioners have concluded total avoidance of offending drugs and replacing with their safe alternatives¹.

Quinolones have been the centre of considerable scientific and clinical interest since their discovery in the early 1960s. This is because they potentially offer many of the attributes of an ideal antibiotic, combining high potency, a broad spectrum of activity, good

bioavailability, oral and intravenous formulations, high serum levels, a large volume of distribution indicating concentration in tissues and a potentially low incidence of side-effects. Much research has attempted to make these potential attributes real². Moxifloxacina (Avelox®), the latest fluoroquinolone, might be among safe alternative antibiotics with only few reported anaphylactoid reactions^{3,4}.

The purpose of this survey was to investigate whether moxifloxacina can be among the safe alternative antibiotics determined by OPT for antibiotic intolerant patients.

MATERIAL AND METHODS

To investigate the tolerability of moxifloxacina in antibiotic allergic/intolerant patients, 20 patients who were referred to our clinic between 1 January 2003 and 31 December 2003 and diagnosed antibiotic hypersensitivity were enrolled in this survey. The diagnosis was made by the positive history of at least one reaction with the liable antibiotic.

A standard questionnaire, including the questions about age, gender, accompanying allergic and systemic diseases, liable antibiotic, the type, the time of onset and the duration of reaction was completed by a physician for each patient.

We performed OPTs with moxifloxacina to antibiotic intolerant patients. An informed consent was obtained from each patient. Tests were performed by an allergist in the out-patient clinic where all emergency tools were available as required.

The OPT protocol was single-blind and placebo controlled. The placebo and moxifloxacina with a total dose of 1000 mg were given at thirty minutes intervals in divided dosages. During the procedure blood pressures, peak expiratory flow (PEF) values and possible allergic reactions were monitored every 15 minutes up to three hours and every one hour afterwards.

RESULTS

The mean age of the patients was 38.05 ± 14.1 and 17 (85 %) of them were females. There were only two patients with accompanying allergic diseases; one with bronchial asthma and the other with chronic urticaria (table I). The rates of common anamnestic antibiotic hypersensitivities were 50 % with amoxicillin, 40 % with penicillin, 20 % with sulphonamides, respectively (fig. 1). There were 31 reactions in 20 patients. Urticaria (80 %) was the leading reaction appearing after antibiotic ingestion (fig. 2). The mean time interval between the inges-

Table I
The demographic features of the antibiotic intolerant patients (n = 20)

Mean age \pm SD (min-max) (years)	38.05 \pm 14.1 (18-65)	
	n	%
Sex		
Female	17	85
Accompanying systemic diseases		
Gastritis	3	15
Goiter	2	10
Hypertension	2	10
Rheumatoid Arthritis	1	5
Depression	1	5
Anemia	1	5
Accompanying allergic diseases		
Bronchial asthma	1	5
Chronic urticaria	1	5
The mean time interval between the ingestion of the drug and the onset of the reactions \pm SD (minutes)	48.2 \pm 120.6	
Mean duration of reactions with antibiotics \pm SD (hours)	27.6 \pm 26.6	

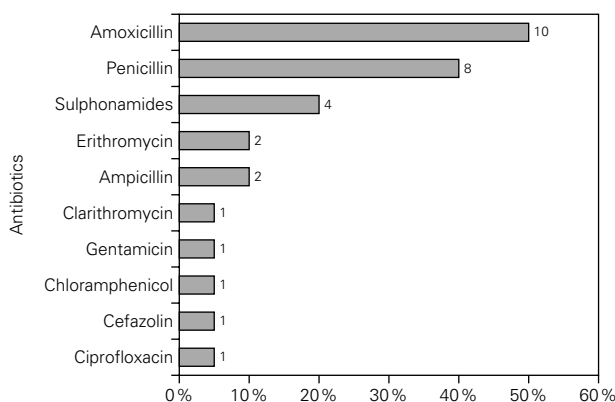


Figure 1.—The rates of common anamnestic antibiotic hypersensitivities (n = 20).

tion of the drug and the onset of the reactions was 48.2 ± 120.6 minutes and the mean duration of reactions with antibiotics was 27.6 ± 26.6 hours.

Seventeen of 20 patients tolerated moxifloxacin at therapeutic doses without any problem. One patient experienced generalized urticaria 4 hours after ingestion of the first dose of the drug, which resolved spontaneously 5 hours after the onset. Another patient experienced tachycardia (heart rate did not exceed beyond 115 per minute) 2.5 hours after ingestion of first dose of the drug, which resolved

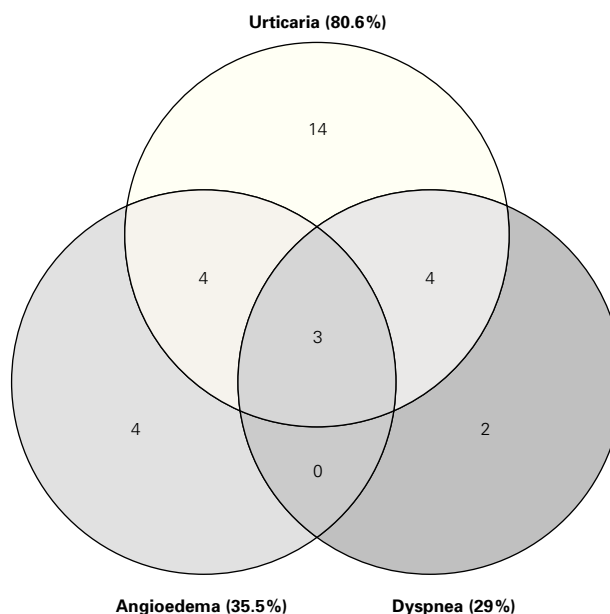


Figure 2.—The distribution of allergic reactions due to antibiotics (n = 31).

spontaneously 2 hours after the onset, and a third one developed severe nausea lasting for two hours.

DISCUSSION

In this survey, the antibiotics which most commonly caused allergy are amoxicillin, penicillin and sulphonamides, by history. Macrolides, fluoroquinolones and aminoglycosides are the antibiotics with a low risk of sensitization. The most common anamnestic allergic reaction was urticarial reaction as in a recent study⁵.

The most common drug-related adverse effects (AEs) with fluoroquinolone therapy involve the gastrointestinal tract and central nervous system and are usually transient and mild to moderate in severity⁶. In our study, only one of our patients suffered a mild nausea, and the other one suffered a mild arrhythmia without clinical significance. In the third patient, moxifloxacin induced an immediate reaction (generalized urticaria) in which an immunologic mechanism, probably directed to a specific moxifloxacin metabolite, seems to be involved. This patient had suffered an urticarial reaction with ciprofloxacin. This could be explained by the cross-reactivity with other quinolones, as reported before. The cross-reactivity between quinolones seems to be very important, and avoidance of any quinolone should be recommended to any patient who has suffered an allergic reaction to one of these drugs⁷.

In conclusion, given the high incidence of hypersensitivity reactions to beta-lactam antibiotics the

use of new fluoroquinolone, moxifloxacin might represent a safe therapeutic alternative.

Antibiotics are among the most commonly used drugs in medicine. Medical progress in understanding and managing antibiotic hypersensitivity states often requires collaborative efforts of multiple disciplines. The high morbidity and cost associated with antibiotic hypersensitivity makes this condition a high priority for future research investments¹.

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