



Letter to the Editor

Regarding the article entitled “Hypersensitivity to antibiotics in patients with cystic fibrosis”

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Dear editor,

We have been very interested with the reading of the article by Roehmel et al. “Hypersensitivity to antibiotics in patients with cystic fibrosis”, published in the Journal of Cystic Fibrosis [1]. In this study based on a review of medical records and interviews of the patients, the authors conclude that hypersensitivity (HS) reactions to antibiotics affect 60% of the patients, with a rate of 5.75% antibiotic courses, leading to changes of therapy in 65% of the cases. Most frequent reactions were reported with beta-lactams, cefepime and piperacillin/tazobactam especially (10% of treatment courses with these antibiotics), occurred within 4 days of the start of treatment, and were dependent on cumulative drug exposure.

These results are consistent with those of other studies showing that anti-infectious drug HS, to beta-lactams especially, is suspected in 29–62% (mean = 30%) of cystic fibrosis (CF) patients (*Rev. in:* [2,3]). These results strongly suggested that the high prevalence of (suspected) allergy to anti-infectious drugs in patients with CF resulted from their frequent exposition to these drugs. Indeed, it has been shown that repeated administration of antigens/allergens, especially by the IV route, was highly immunogenic/allergenic [4].

However, in these studies, diagnosis of betalactam HS was solely based on clinical history, probably leading to over-diagnosis. More recent studies based on skin and challenge tests have shown that only 0–4% of CF patients were truly allergic to beta-lactams [2,3]. In the study by Caimmi et al. [2], 23/171 (13.45%) CF patients reported a highly suggestive clinical history of betalactam

HS. Based on skin tests, challenge tests and clinical history, only 7 of these patients (30.4%), representing 4% of the CF patients, were diagnosed allergic to beta-lactams. In the recent study by Matar et al. [3], performed in a highly specialized pediatric center for CF and exploration of drug hypersensitivities, only 1.14% of the CF children reported highly suggestive reactions and needed to be explored for suspected beta-lactam HS by means of skin (pricks, ID and patch-tests) and challenge tests. In the other children, with no or less suggestive reactions such as non-immediate benign urticaria or non-urticarial rashes and isolated non-immediate fever, skin tests were not performed and diagnosis was often ruled-out directly on the tolerance of challenge tests performed with the suspected beta-lactams. Although 47.3% of the children explored by means of skin and challenge tests were diagnosed allergic to beta-lactams, all of whom reporting severe and/or immediate/very early reactions, beta-lactam HS was diagnosed in only 0.7% of the children with CF.

Thus:

- (1) although it has been claimed that frequent exposure to drugs may lead to sensitization and allergic hypersensitivity (*Rev. in:* [2,3]), repeated or chronic exposure to antigens/allergens may also lead to immunological tolerance, depending on the genetic background, the age and nutritional status of the subjects, the conditions of allergen exposure, and other environmental factors [4];
- (2) as shown in non-CF patients [5,6], most allergic-like reactions to antibiotics, beta-lactams especially, more likely result from the infectious diseases (viral infections) for which the antibiotics have been prescribed and/or from microbial death than from drug HS;

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- (3) at the risk of over-diagnosis, drug allergy/hypersensitivity diagnosis should not be based solely on a (more or less) clinical history of the patients, but on a careful analysis of their clinical history, skin tests (if feasible and validated), possibly in vitro tests, and challenge tests with the suspected and/or alternate drugs [2,3,5,6].

References

- [1] Roehmel JF, Schwarz C, Mehl A, Stock P, Staab D. Hypersensitivity to antibiotics in patients with cystic fibrosis. *J Cyst Fibros* 2013. <http://dx.doi.org/10.1016/j.jcf.2013.10.002> [Epub ahead of print].
- [2] Caimmi S, Sanfiorenzo C, Caimmi D, Bousquet PJ, Chiron R, Demoly P. Comprehensive allergy work-up is mandatory in cystic fibrosis patients who report a history suggestive of drug allergy to betalactam antibiotics. *Clin Transl Allergy* 2012;2:10 [5 pages].
- [3] Matar R, Le Bourgeois M, Scheinmann P, de Blic J, Ponvert C. Betalactam hypersensitivity in children with cystic fibrosis: a study in a specialized paediatric center for cystic fibrosis and drug allergy. *Pediatr Allergy Immunol* 2013 [doi: 10.1111/pai.12154 (Epub ahead of print)].
- [4] Husby S. Sensitization and tolerance. *Curr Opin Allergy Clin Immunol* 2001;1:237–41.
- [5] Ponvert C, Perrin Y, Le Bourgeois M, Karila C, Delacourt C, Scheinmann P, et al. Allergy to betalactams in 1865 children: results of a 20-year study based on skin and challenge tests, and clinical history. *Pediatr Allergy Immunol* 2011;22:411–8.
- [6] Rubio M, Bousquet PJ, Gomes E, Romano A, Demoly P. Results of drug hypersensitivity evaluations in a large group of children and adults. *Clin Exp Allergy* 2012;42:123–30.