Special Lecture

Diagnosis and Management of Beta Lactam Allergy: An Overview for the Allergist

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Betalactams (BL) are the most widely used drugs against infections and the primary cause of antibiotic hypersensitivity reactions. Allergy to BL is an increasing worldwide problem, with an estimated prevalence of up to 10% of the population. Reaction patterns for different BL have changed in accordance with consumption trends being amoxicillin, alone or combined with clavulanic acid, the most prescribed one in Europe and the responsible of most hypersensitivity reactions to antibiotics. The diagnosis procedure includes a detailed clinical history, which is not always reliable. This is usually followed by in vivo tests: skin tests and drug provocation tests. However, most patients with suspected BL allergy cannot be confirmed with this diagnostic work-up. This implies the prescription of inappropriate medication with the use of second line alternatives which are more expensive antibiotics with greater adverse effects, potentially leading to bacterial resistance and longer hospital stays.

In vivo methods can have major drawbacks depending on the drug and the type of reaction, either immediate/IgE-mediated or non-immediate/T-cell-mediated. Moreover, they have generally only been updated in terms of the inclusion of new drugs and determinants. For immediate reactions, prick and immediate reading intradermal testing are recommended using benzylpenicilloyl, minor determinants, benzylpenicillin and the suspected drug, aminopenicillins and cephalosporins. When BL are used in combination with a β-lactamase inhibitor as clavulanic acid, it is recommended to include the individual components of the antibiotic combination. For non-immediate reactions, patch testing and delayed-reading intradermal test are recommended. In general, in vivo tests are not risk-free, they require experienced personnel, and are both time consuming and expensive for health care systems. While there is a general consensus on the importance of skin testing for evaluating BL allergy there is a need to improve in vivo testing by standardizing protocols, and performing large, multi-site studies in well-characterized patients to confirm sensitivity, specificity and predictive values.

Regarding drug provocation tests, although considered as the gold standard for the identification of a culprit

drug and safe alternatives in patients with a suspected BL allergy, they cannot be performed in patients with severe hypersensitivity.

Great efforts are currently being made to develop predictive models using data from the clinical history, although further studies are needed to implement it in the clinical practice.

The inclusion of *in vitro* tests in diagnostic algorithms could be the most rational way to improve the diagnosis. There are several approaches for the evaluation of BL hypersensitivity depending on the type of reaction: immunoassays and basophil activation test for immediate reactions and lymphocyte transformation test for non-immediate reactions. In general, these tests show a good specificity but a moderate sensitivity. The development of *in vitro* methods is driven by the need to improve sensitivity, and the hope to avoid *in vivo* assays in many situations, especially for severe and life-threatening reactions. To advance in this field, it will be necessary to obtain more insight into the chemical structure of the antigenic determinants, the nature of the carrier protein and their binding mechanisms.