

Usefulness of the basophil activation test (BAT) in the diagnosis of life-threatening drug anaphylaxis

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Allergy work-up in patients suffering life-threatening drug anaphylaxis is usually impaired in clinical practice owing to the low sensitivity of the laboratory tests and the risk associated with *in vivo* tests. Even careful, properly performed skin tests can trigger an anaphylactic reaction in patients with high sensitivity to a particular drug (1), and the gold standard of diagnosis, a controlled challenge with the suspected drug, is frequently rejected on ethical grounds. The difficulty in diagnosis increases in patients receiving more than one drug at the same time or within a short period of time and/or in patients with poor medical status (advanced age, ischemic heart disease, chronic obstructive pulmonary disease, immunosuppression, etc.) in whom the consequences of an allergic reaction during skin testing or drug challenge may be potentially fatal (2).

We assessed the usefulness of the basophil activation test (BAT) in the

diagnosis of drug allergy in patients with severe anaphylaxis in whom *in vivo* tests were considered highly risky.

Consecutive patients from a general hospital referred for diagnosis after life-threatening drug anaphylaxis (sudden allergic reaction involving two or more territories, with respiratory arrest, shock, loss of consciousness, laryngeal edema, dyspnea, or fainting) occurring < 1 h after a single drug administration were recruited. After detailed anamnesis, patients with other possible causes (food or latex allergy, doubtful administration of another drug or invasive procedures in the hour prior to onset of anaphylaxis, or any other concomitant confounding conditions) were ruled out by clinical history and/or skin tests. BAT (Basotest, Orpogen, Germany) and specific IgE (amoxicillin: ImmunoCAP; Phadia, Uppsala, Sweden; metamizol, 3 patients: HY-Tec 288; Hycor, Agilent Technologies, Santa Clara, CA, USA) were performed between 2–6 months after the reaction. A positive cut-off of 0.35 kU/l was chosen for all IgE determinations. Skin tests were offered only to patients with less severe reactions who accepted the risk and gave their written informed consent. BAT was considered positive when the basophil stimulation index (drug/control) was ≥ 2 , provided more than 5% drug-activated basophils were detected. Concentrations of the more commonly implicated drugs, amoxicillin and metamizol, were 0.31 and 1.25 mg/ml for amoxicillin and 1 and 5 mg/ml for metamizol.

Thirty-two patients were recruited. After anamnesis, 8 were ruled out (2 owing to doubts concerning administration of another concomitant drug, 1 for surgery the hour before, 1 for nut-positive skin test, and 4 who declined to participate in the study). Twenty-four

patients, 21 men and 11 women, age range 29–61 years, entered the study. Severity of the anaphylactic reaction ranked from respiratory arrest (3 cases), shock (10 cases), laryngeal edema (2 cases), or loss of consciousness (4 cases) to dyspnea (4 cases) or fainting (1 case). The drugs involved were amoxicillin in 14 patients, metamizol in 5, ibuprofen in 2, and cloxacillin, pipemidic acid, and diclofenac in one patient each. BAT was positive in 10 patients (42%), negative in 12 (50%), and nonevaluable in 2 (8%), the latter corresponding to one patient with nonresponsive basophils and the other with < 5% basophils activated with the drug. BAT identified metamizol allergy in 5/5 patients (all with stimulation index ≥ 4) but only 4/14 patients with amoxicillin-related anaphylaxis. On the other hand, specific IgE was positive in only 3/17 patients (18%), two of whom where BAT nonevaluable patients. Skin tests were positive in 6 of 11 patients (54%).

BAT has recently become a useful tool in the evaluation of drug allergy (3, 4). Skin tests still remain the most reliable tools to identify severe drug allergy. However, when these tests cannot be performed for ethical reasons or are refused by the patients, the combination of BAT and specific IgE can identify the culprit drug in more than 50% of patients with life-threatening anaphylaxis.

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