

SEVEN EXERCISE

FOOD AND DRUG PROVOCATION TESTS

I FOOD ALLERGEN PROVOCATION TESTS

INDICATIONS

The food allergen provocation test (FAPT) provides a goldstandard diagnostic for food-related adverse reactions leading to appropriate food avoidance. The test is also indicated for follow-up of previously diagnosed food sensitivities. There is also a positive effect of the food challenge on quality of life of patients with food allergy. Previously, to the procedure, a predictive analysis of the test result should be undertaken. A severe anaphylactic reaction to a given food with highly positive IgE tests, and a history of several reactions to the same food, will in most cases not need a FAPT.

PROCEDURE

Before the performance of an oral provocation test a diagnostic elimination diet over a limited time frame is necessary.

During the test, the patient is exposed to a given food in a safe place, under a standardized protocol. FAPT is stopped if objective reactions are observed or the last dose is consumed without symptoms. Immediate reactions usually appear within 2 h after the last food intake, while atopic eczema may worsen several hours or days following the challenge. Urticaria and angioedema are the most common objective signs, with gastrointestinal, respiratory, or cardiovascular system involvement also common. For patients with a very low risk of a systemic reaction, food allergen provocation test (FAPT) can be carried out at home, while for a very high risk of an anaphylactic reaction, an intensive care unit is recommended.

Most often, tests are undertaken in an ambulatory setting of an allergy referral centre.

Most importantly, the staff needs to be trained to recognize and treat early symptoms of allergic reactions

The gradual amounts of food and the interval between the doses are dictated by the history of the patient. For immediate type reactions, intervals of 20–30 min are sufficient. For delayed-type reactions (e.g., atopic eczema), longer intervals might be necessary to ensure an accurate assessment. Food allergen provocation test (FAPT) can be ‘open’ or ‘double-blind placebo-controlled’ The double-blind procedure allows a more objective interpretation and is used in most experimental protocols, as well as in patients with subjective symptoms, important anxiety or delayed-type symptoms. The food should be blinded for taste, smell, texture, and appearance (consistency, color, and shape), with the

placebo indistinguishable from active food. Reactions to several foods, such as eggs, fruits, or vegetables, are dependent on the degree of cooking. In addition, a matrix effect has been observed for various food allergies. For example, the allergenicity of egg in baked foods also containing wheat is diminished.

Vital signs should be closely monitored during FAPT, and equipment and appropriately trained staff should be in place to deal with allergic reactions, including anaphylaxis. The FAPT is a safe procedure following the predictive analysis, if the appropriate dosing schedule is chosen and if the challenge is performed by a well-trained staff.

II DRUG PROVOCATION TESTS

The DPT is widely considered to be the "gold standard" to establish or exclude the diagnosis of hypersensitivity to a certain substance, as it not only reproduces hypersensitivity symptoms, but also any other adverse clinical manifestation, irrespective of the mechanism.

INDICATIONS

1. To exclude hypersensitivity in non-suggestive histories of drug hypersensitivity and in patients with non-specific symptoms, such as vagal symptoms under local anesthesia.
2. To establish a firm diagnosis in suggestive histories of drug hypersensitivity with negative, non-conclusive, or non-available allergologic tests. A positive DPT result optimizes allergen avoidance, while a negative one allows a false label of drug hypersensitivity to be removed. For these reasons, DPTs are often carried out to exclude a diagnosis of hypersensitivity to beta-lactams when other allergologic tests are negative. DPTs are also performed when the sensitivity of allergologic tests for evaluating allergic reactions to certain drugs, such as non-beta-lactam antibiotics, heparins, and glucocorticoids, is limited. On the other hand, DPTs are also performed to diagnose hypersensitivity reactions to nonsteroidal anti-inflammatory drugs in subjects with the cross-reactive pattern, because both skin tests and in vitro diagnostic methods are ineffective in such patients.

The DPT can be harmful and thus should only be considered after balancing the risk-benefit ratio in the individual patient.

A drug provocation test (DPT), or drug challenge, consists in the gradual administration of a drug to a patient who reported a previous reaction to that drug or a similar one. A DPT is mainly a diagnostic tool allowing the identification of drug hypersensitivity (DHS)

A DPT should be carried out if no other safer procedures (such as skin or in vitro tests) are available or cannot support the diagnosis. DPTs are considered the gold standard for diagnosing DHS to NSAIDs, local anesthetics, non-beta-lactams antibiotics, and other drugs for which safer tests are inexistent or not standardized. DPTs are also the last diagnostic step for drugs such as beta-

lactam antibiotics if skin tests and in some cases in vitro tests yield inconclusive results. DPTs may also be important to reassure patients who fear a future reaction or suffer from anxiety due to an unconfirmed diagnosis. When the clinical history strongly supports the diagnosis of DHS (two or more reproducible previous reactions) and reactions were severe or life threatening, performing a DPT with an alternative drug is recommended. The coexistence of a severe disease or pregnancy is considered contraindication, although exceptions can apply. If the suspected drug would not be needed for future treatments or if there are known alternatives with comparable efficacy, DPT is not recommended.

PROCEDURE

Guidelines have been proposed, and protocols have been published for most common drugs such as beta-lactams, NSAIDs, and radiocontrast media.

DPT should be done only after performing skin tests, and possibly determination of specific IgE-antibodies. If either of these is positive, in combination with a compatible history, then DPT is not recommended because of the risk involved.

A DPT should be carried out ideally with the culprit drug. Theoretically, the route of administration should be the same as the one evoking the reaction, but international guidelines favor the oral route whenever possible and when there is no major chemical difference between the parenteral and the oral forms. Adjustments of the dose, dose intervals, number of doses, and total dose given are made accordingly to the drug involved, the initial reaction, patient's conditions, and future needs for drug administration. The drug is administered at increasing doses, with a minimum of 30 to 60-minute interval between each if good tolerance is established at the previous dose. Whenever possible, the DPT should be carried out with the exact formulation and commercial brand involved in the initial reaction. Multiple molecules present in the drug formulation should be tested separately. Although considered the gold standard for DHS diagnosis, DPT sensitivity is not 100% as unrecognized confounders (infections, underlying disease and its control, concomitant medications, exercise, food intake) might influence the reaction.