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http://dx.doi.org/10.1016/j.aller.2013.07.003

The Hacettepe Method is an efficient, safe and cost effective method of drug allergy work-up☆

To the Editor,

Drug allergy can be life-threatening, as it negatively affects and delays the treatment of diseases. It also increases healthcare costs by causing a shift towards more expensive alternative drugs.

Drug allergy is one of the most common causes of admission to allergy clinics; it is the most common cause of allergological inpatient consultation in the USA, and is the third most common cause of allergology services consultations in Spain, following bronchial asthma and rhinitis.[1,2] However, the number of specialised allergy clinics that address the problem of adult drug allergy is limited in many countries, including Turkey. In addition, waiting for an allergy examination appointment and the performance of drug allergy tests are time consuming. The current gold standard for drug allergy diagnosis and work-up – the oral provocation test (OPT) – takes one day for each drug tested. Different drugs are not usually tested on consecutive days, as a waiting period is necessary (of at least one day) before testing each new drug.

In Turkey there are 70 adult allergy specialists and 22 centres that perform the OPT in adults (data obtained from the Turkish National Society of Allergy and Clinical Immunology). Adverse drug reactions affect 10–20% of hospitalised patients and ≥7% of the general population.[3] Considering that the population of Turkey in 2012 was 75,627,384 and that 75.1% of the population is aged >15 years, the number of adult allergy clinics is not sufficient to effectively treat such a common public-health problem as drug allergy.[4]

Our allergy clinic has a fixed number of two professors and 1–2 fellows who provide patient care. Table 1 shows the total number of patients who were seen at the outpatient clinic and the number of OPTs performed for the corresponding year.

For the reasons stated above the Hacettepe Method has been used at our clinic since 2002 to perform OPTs simultaneously with multiple drugs (i.e. 2–3 drugs from the same or different groups) on the same day in an effort to identify safe alternatives. Use of the Hacettepe Method has reduced the amount of time, money, and manpower used for diagnostic work-up. OPTs were performed by randomly selecting three drugs the patient was not intolerant to based on anamnesis (paracetamol, codeine, meloxicam, rofecoxib, celecoxib, benzydamine, and azapropazone), and those drugs were tested on the same day; the drugs were administered in 30-min intervals at the following doses: lactose (placebo) 50 mg; paracetamol 500 mg and 750 mg; codeine 20 mg and 30 mg; meloxicam 7.5 mg and 15 mg; rofecoxib 12.5 mg and 25 mg; celecoxib 100 mg and 150 mg; benzydamine 50 mg and 75 mg; and azapropazone 300 mg and 450 mg. Tests were completed when a reaction was observed or when the higher test dose of the third drug was reached.[5] Subsequently, the identical methodology was used for antibiotic and antibiotic-analgesic drug provocation tests.[6,7] We tested 2–3 different groups of antibiotics or antibiotics plus analgesics on the same day.

Table 1 Number of patients tested at the outpatient clinic and the number of OPTs performed for the corresponding year.

Year	Patients seen at the clinic (*n*)	OPTs performed (*n*)[a]
2006	1980	250
2007	3495	300
2008	5261	275
2009	5258	400
2010	5583	375
2011	5744	405
2012	5585	394

[a] Each test included 1–3 drugs.

☆ This research letter was not funded from any organisation.

In our first study, which was published in 2005, the effectiveness of the Hacettepe Method was demonstrated in 84 analgesic-intolerant patients by a decrease in the number of test days from 264 to 148 days.[5] Subsequently, we performed a similarly designed study using the Hacettepe Method and 53 antibiotic-allergic patients, and again test days were reduced from 136 to 65.[6] The third of our studies was published in 2012, and the Hacettepe Method saved 32 test days in 42 patients diagnosed with antibiotic and analgesic intolerance/allergy, as compared to the conventional OPT method.[7] There were no serious adverse reactions in any patients in any of the three studies. Additional research on the Hacettepe Method is ongoing at our clinic.[8,9]

Based on the findings of our three studies, it is reasonable to conclude that the Hacettepe Method is a safe, cost-effective, time-effective, and manpower-effective method of identifying safe alternative drugs in drug–allergic–allergic/intolerant patients. Considering the difficulty of finding a new approach to an old problem, the Hacettepe Method is recommended for use in all adult allergy clinics worldwide.

Ethical disclosures

Confidentiality of data. The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Protection of human subjects and animals in research. The authors declare that no experiments were performed on humans or animals for this investigation.

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http://dx.doi.org/10.1016/j.aller.2013.08.002

Pomegranate anaphylaxis due to cross-reactivity with Peach LTP (Pru p 3)

To the Editor,

The pomegranate, the fruit of *Punica granatum*, belonging to Lythraceae family and commonly cultivated in the Mediterranean area, has been involved in some immediate reactions,[1,2] including severe symptoms such as anaphylactic shock and laryngeal oedema.[3,4] Cases of hypersensitivity reactions to pomegranate have been reported and the implication of 29-kDa[1,2,4] and 9-kDa[3] protein allergens has been described. Subsequent characterisation of the 9-kDa allergen demonstrated its belonging to the lipid transfer protein (LTP) family, a family widely distributed in fruits, vegetables and nuts, which has been suggested as being responsible for immunological cross-reactivity between fruits, nuts and/or pollens. Allergy cases involving LTPs from pomegranate and peach, hazelnut and peanut have been published.[1–4] Furthermore, a study of LTPs in pomegranate identified and isolated two LTP isoforms with different IgE binding capacities [LTP1a (9-kDa) and 1b (7-kDa)].[5]

We describe the case of an 18-year-old women, without history of allergic disease, who suffered from angio-oedema, generalised urticaria, glottis oedema, vomiting, abdominal pain and malaise five to ten minutes after ingesting a pomegranate. Three years before she had two episodes of angio-oedema and urticaria after apple ingestion and one episode of urticaria, abdominal pain and angio-oedema after drinking pear juice. The patient did not develop any kind of allergic symptoms after performing a *Rosaceae* and pomegranate free diet.

The patient underwent skin prick tests with a commercial extract panel of common inhalants, fruits, vegetables and nuts allergens (Leti laboratories, Spain) and the results were positive to *Dermatophagoides pteronyssinus*, grass pollen, mugwort pollen, peach, apple, pomegranate, strawberry, cherry, almond, peanut, tomato, bell pepper, green beans, black bean and soybean seed. Prick test with profilin and