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Original article

Cross sectional questionnaire-based internet study: Self-perception and clinical course of drug allergy in Greece



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ADR Adverse drug reaction

ABSTRACT

Background: Data on self perception of drug allergy in the general population are lacking. Epidemiological studies focus either on specific populations or document adverse drug reactions in general. Our objective was to document self-reported drug allergy in Greece, through a simple, informative internet-based questionnaire.

Methods: A questionnaire on drug allergy was accessible online for a 3-month period. Participants voluntarily answered 28 questions referring to: suspected drug, clinical manifestations, concomitant factors, received treatment, reaction's re-occurrence.

Results: A total of 2528 questionnaires were included in study analysis. Beta-lactams and non-steroidal anti-inflammatory drugs were the most prevalent culprit agents (53% and 27.5% respectively) while half of the participants acknowledged skin manifestations as the most common symptoms. One out of three reported subsequent exposure to the drug presumed to be responsible for the reaction and 74.5% of those stated a new reaction upon re-exposure. Only 26.7% underwent allergological evaluation. Reactions manifested with respiratory or cardiovascular symptoms, parenteral administration of the culprit drug and personal history of allergy to agents of >1 different pharmacological categories were associated with increased risk of hospitalization.

Conclusions: Allergic reactions to drugs are adverse events difficult to define and diagnose. A remarkable proportion of presumed as hypersensitivity reactions are not referred to allergists; therefore these patients may be either re-exposed to potentially noxious drugs, or needlessly avoid whole classes of drugs as b-lactams for more costly or less appropriate treatments. Internet-based questionnaires may contribute to awareness programs concerning drug allergy and help improve proper referral.

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Introduction

Adverse drug reactions (ADRs) account for 3–6% of hospital admissions while their prevalence among hospitalized patients is estimated between 10 and 15%. ADRs represent a major health problem with increased morbidity, prolonged hospitalization and risk of mortality. According to the World Health Organization, an ADR is defined as "a response to a medicine which is noxious and

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unintended, and which occurs at doses normally used in man". Furthermore ADRs are divided in Type A that are predictable and dose-dependent and Type B that are unpredictable, dose independent and comprise 15–20% of all ADRs. The latter group includes both immunologically mediated drug hypersensitivity (alternatively called drug allergy) and non-immune mediated reactions. ¹

Although drug allergy is of major importance, its true incidence and other epidemiological features are not well studied. The vast majority of epidemiologic data refers rather to ADRs than to drug allergy specifically.² Besides, a great confusion about drug allergy exists among health care providers and patients. Previous studies reported a large number of medication errors and hospital admissions due to allergic reactions attributed to drugs in outpatient

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settings.³ It is likely that only the more severe and/or complex cases are referred to specialists and therefore only in these cases the diagnosis is well documented; thus studies that use clinical questionnaires for addressing drug allergy may not present the "real life" situation.

Internet portals have created new opportunities for the assessment of numerous medical conditions. Internet-based questionnaires encourage a greater number of individuals from a broad geographic area to take part providing thus the opportunity to perform wide scale surveys by overcoming traditional problems like high financial costs. Information transmitted via secure portals could allow for the identification of chronic problems even better than visits to non-specialists in these medical entities. Based on this information, the web-users can provide important data about certain medical conditions that reflect the patients' perception about their own problem. However, a selection bias to internet-users exclusively and self-reporting are potential limitations. Our previous experience with internet surveys was very positive as we revealed interesting aspects about the patients' perspective and the way they handle disease. 4,5

We have conducted this study in order to record self perception of drug allergy among internet users in Greece. Secondary goals of the study were the assessment of management of these conditions, the compliance of patients to the advice provided by treating physicians, as well as the identification of risk factors for severe reactions.

Methods

Study design

A specific questionnaire (Supplementary Table 1) on drug allergy was generated by Drug Allergy Outpatient Clinic, Allergy Unit, Attikon General University Hospital, Athens, Greece. Subsequently, the questionnaire, consisted of 28 questions, was placed on the website of http://www.in.gr, one of the most reliable online information portals in Greece which includes a popular "health zone" through distinguished links placed on this site. All online visitors with personal history of drug allergy were invited to take part in the study through an introductory page. The questionnaire was posted by Internet portal for a 3-month period. Each participant could fill the questionnaire only once; to this end, a safety feature of the website prohibited voting from the same IP address more than once. Individuals without a history of drug allergy were excluded from the study by an introductory screening question (No 6, Supplementary Table 1). Demographic data including age, gender and address zip code of participants were also collected. Participants younger than 12 years were excluded from data analysis. Study subjects participated anonymously and the introductory page clearly stated that the obtained data would be used for epidemiological research only. After study analysis, the most important results and conclusions as well as general information and recommendations for drug allergy sufferers, were posted at the same portal.

The protocol was approved by the Ethics Committee of Attikon University Hospital.

Statistical analysis

Statistical analysis consisted of two steps. First, descriptive statistics were calculated. Continuous variables are presented as mean values \pm standard deviation (SD), whereas categorical variables are presented as absolute and relative frequencies. Secondly, potential risk factors were evaluated along three main axes: (i) hospitalization; (ii) repeated intake of the allergenic drug after the first

reaction; and (iii) reported subsequent specific allergological evaluation with skin testing. Multivariate logistic regression was performed; the factors that were significantly associated with the aforementioned items at the univariate analysis were examined as independent variables.

In the final model, after mutual adjustment, only the statistically significant variables were included (backward selection statistical procedure). Similarly to our previous work, a hierarchical approach was adopted concerning the modeling of the three axes. The underlying conceptual framework envisaged the time succession: first (serious) reaction \rightarrow hospitalization \rightarrow non-compliance with medical advice (repeated intake of the allergenic drug after the reaction) or compliance with medical advice (and allergological evaluation with skin testing). Consequently, the model for repeated intake also encompassed hospitalization as an independent variable, whereas the model concerning skin testing examined both hospitalization and subsequent intake of the culprit drug.

Symptoms were grouped according to the affected organ and system: upper (nasal congestion, runny nose, sneezing, ocular itch and or hemosis of conjunctiva) and lower respiratory system (chest tightness, wheezing, dry cough, voice hoarseness), skin (urticaria—angioedema, maculopapular exanthema, itching, generalized flushing), cardiovascular (tachycardia, dizziness, loss of consciousness), gastrointestinal (abdominal pain, diarrhea, vomiting) and

Table 1Descriptive characteristics of study participants.

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Variables	N (%)
Male sex	762 (30.3)
Education	
Primary (6 years)	67 (2.7)
Secondary (9 years)	67 (2.7)
High school (12 years)	844 (33.9)
University	1512 (60.7)
Age at first reaction (years)	` ,
0-10	299 (11.9)
11-20	446 (17.8)
21-30	818 (32.6)
31-40	444 (17.7)
41-50	220 (8.8)
51-60	124 (4.9)
>60	157 (6.3)
Administration of the culprit drug	312 (12.4)
by injection (IM or IV)	` ,
Occurrence of the reaction at home	2225 (89.4)
Time interval between drug intake	` ,
and symptoms' onset	
1–3 h	1292 (51.7)
3-72 h	799 (32.0)
>72 h after the initiation of treatment	361 (14.4)
After the completion of treatment	49 (2.0)
Hospitalization	989 (39.4)
Duration of symptoms	
<4 h	1095 (43.7)
1–7 days	1119 (44.6)
>7 days	293 (11.7)
Repeated intake of the culprit drug	737 (29.3)
Co-existing factors	1254 (49.6)
History of allergy to agents of >1 different pharmacological categories	782 (31.5)
Personal history of atopy (allergic rhinitis,	1303 (51.5)
asthma, atopic dermatitis)	1303 (31.3)
Family history of atopy (first-degree relative)	1123 (48.0)
Previous surgery	1242 (49.5)
Chronic concomitant diseases	342 (13.9)
Allergological evaluation with skin testing	666 (26.7)
Treating physician	
No evaluation at all	854 (34.3)
Allergist	574 (23.0)
Other than allergist	1065 (42.7)

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