

Original Article



Association between self-reported drug hypersensitivity reactions and psychological disorders

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OPEN ACCESS

Received: Sep 18, 2020

Accepted: Apr 18, 2022

Published online: Apr 21, 2022

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Conflict of Interest

The authors have no financial conflicts of interest.

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ABSTRACT

Background: Medically unexplained physical symptoms are a well-recognized problem and, in some cases, there is a well-established relationship between behavior and psychopathological disturbances. However, the association between drug hypersensitivity reactions and psychoactive disorders stills under discussion.

Objective: Our main goal was to establish if there is an association between self-reported drug hypersensitivity reaction and psychopathology with need for psychoactive drug consumption.

Methods: Retrospective study of adult patients evaluated in a first Immunoallergy appointment because of self-reported drug hypersensitivity over 1 year and register of data concerning psychoactive drugs use. Compare the study group with patients observed for allergic respiratory disease along the same year.

Results: The study group included 70 patients that referred a total of 92 self-reported drug hypersensitivity reactions. Twenty-nine (41.4%) were under treatment with psychoactive drugs: 20 (70%) were treated with anxiolytics, 13 (18.6%) with antidepressants, 15 (21.4%) with sedatives, and 1 (1.4%) with antipsychotics. The control group included 160 patients and 38 patients (23.8%) were under treatment with psychoactive drugs: 31 (19.4%) were treated with antidepressants, 29 (18.1%) with anxiolytics, and 3 (1.9%) with sedatives. The use of psychoactive drugs in the study group is higher than in the control group ($p = 0.007$), the difference is especially important for sedative drugs ($p < 0.001$). Besides a higher use of psychoactive drugs, the study group also has a higher frequency of use of several psychoactive drug ($p = 0.002$).

Conclusion: Patients with a self-report drug hypersensitivity have more tendency to be under treatment with psychoactive drugs and could have more tendency to somatization. Personality traces and psychopathology must be taken into account during an allergy workup.

Keywords: Allergy workup; Self-reported drug hypersensitivity; Psychological disorders

INTRODUCTION

Medically unexplained physical symptoms are a well-recognized problem in our society that makes people seek for medical care to treat symptoms and not mental health disturbances, in fact, after doing a comprehensive medical investigation one third of the symptoms remain

Inês Cunha, Eva Gomes. Writing - original draft: Inês Cunha, Eva Gomes. Writing - review & editing: Inês Cunha, Joana Gouveia, Eva Gomes.

medically unexplained [1, 2]. Looking for organic diseases in patients with vague complains leads to important medical resources consumption [3, 4]. In order to prevent inappropriate and unnecessary treatments and exams, we must be aware that there is a high prevalence of somatic symptoms and psychosomatic complains in correlation with mental comorbidities [5]. The reason for these association is not well known, however, there are some explanations for the association between psychological and physical disorders, including biological, behavioral, cognitive, and social pathways [6].

In the literature, there are well-established relationships between psychological disturbances and dry eye symptoms, cough, and pain perception among others [7-9].

In allergic diseases, there are some reports that concluded that anxiety, depression, and the structure of temperament are important in clinical presentation of asthma as patients with these traits have lower forced expiratory volume in the first second and have difficulty coping with asthma symptoms [10].

To our knowledge, there are few studies that enlighten us about the relationship of self-reported drug hypersensitivity and psychological disturbances. Some of these articles concluded that multiple drug intolerance syndrome was associated to anxiety and depression, however, further investigation must be done to reinforce this conclusion [11].

In our study, we aim to establish if there is an association between self-reported drug hypersensitivity and psychopathology with need for psychoactive drug consumption.

MATERIALS AND METHODS

We performed a retrospective study of adult patients (older than 18 years) evaluated in a first Immunoallergology appointment because of self-reported drug hypersensitivity over 1 year.

The possibility of a psychopathologic disease was surrogated on patient's use of psychoactive drugs (anxiolytics, hypnotics, antidepressants, and antipsychotics) once we were not allowed to access psychiatric consultations registry and because the majority of patients were evaluated and medicated in primary care and a firm diagnosis was not established. The drug registry was obtained from clinical history or electronic medical prescription (PEM) registration. PEM is an electronic platform used by Portuguese national health system to prescribe medication where data about all kind of drug prescribed and purchase are available. We considered patients treated with psychoactive drugs if there were registered prescriptions in the year prior the allergy appointment.

We compared the study group with a control group that included adult patients evaluated in a first Immunoallergology appointment in the same 1-year period because of suspected allergic respiratory disease without self report of drug hypersensitivity reactions. We also collected data for psychoactive drug use in this group.

Statistical analysis was done using IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, USA), and to compare groups we used χ^2 test with 95% significance.

RESULTS

Study group

The study group included 70 patients, 51 females (72.9%) and the median age was 44 years old (interquartile range [IQR], 34–78).

The 70 patients referred a total of 92 self-reported drug hypersensitivity reactions: 72 nonimmediate reactions (78,2%) (97.2% cutaneous, 2.8% unspecific) and 20 immediate reactions (21.8%) (80% cutaneous, 5% anaphylaxis, and 15% unspecific). The presumed hypersensitivity reactions were: 43 (46.7%) to antibiotics (17 to penicillin, 12 to amoxicillin, 4 to amoxicillin plus clavulanic acid, 3 to ciprofloxacin, 2 to azithromycin, and 1 to clarithromycin, clindamycin, minocycline, nitrofurantoin, and cefixime); 38 (41.3%) to nonsteroidal anti-inflammatory drugs (19 to ibuprofen; 5 acetaminophen; 4 to acetylsalicylic acid; 4 to diclofenac; 1 to ketorolac, celecoxib, metamizole, flurbiprofen, and thiocolchicoside; 2 [2.2%] to contrast media; 2 (2.2%) to statins [atorvastatin and pravastatin]; 2 (2,2%) to anaesthetics [lidocaine and propofol], and 1 [1.1%] to venlafaxine, pantoprazole, B12 vitamin, restikinumab, and tibolone). Analyzing according to drug class; 62 patients (88.6%) reported reactions to drugs from the same drug class, 7 patients (10%) from 2 different drug classes, and 1 (1.4%) to 3 different drug classes.

From the study group, 41 patients (58.8%) denied previous treatment with psychoactive drugs and 29 (41.4%) were under treatment. From those that were taking psychoactive drugs 20 (70%) were treated with anxiolytics, 13 (18.6%) with antidepressants, 15 (21.4%) with sedatives, and 1 (1.4%) with antipsychotics.

Analyzing the data evidencing the number of used psychoactive drugs by patients: 16 (22.9%) were treated with one psychoactive drug (7 with anxiolytics, 7 with antidepressants, and 2 with sedatives), 7 (10%) with 2 psychoactive drugs (7 with anxiolytics plus sedatives), 5 (7.1%) with 3 psychoactive drugs (5 with anxiolytics, antidepressants, and sedatives), and 1 (1.4%) with 4 psychoactive drugs (anxiolytics, antidepressants, sedatives, and antipsychotics).

Control group

The control group included 160 patients, 107 females (66.9%) and the median age was 38.5 years old (IQR, 30–84). Ninety-three patients (58.1%) were referred for rhinitis, 66 (41.3%) for rhinitis and asthma, and 1 (0.6%) only for asthma.

In the control population, 122 patients (76.3%) denied previous treatment with psychoactive drugs and 38 patients (23.8%) were under treatment.

From those that were on psychoactive drugs 31 (19.4%) were treated with antidepressants, 29 (18.1%) with anxiolytics, and 3 (1.9%) with sedatives.

Analyzing the data on the number of used psychoactive drugs by patient: 15 patients (9.4%) were treated with 1 psychoactive drug (8 with antidepressants, 6 with anxiolytics, and 1 with sedatives), 21 (13.1%) with 2 psychoactive drugs (21 with antidepressants plus anxiolytics) and 2 (1.3%) with 3 psychoactive drugs (antidepressants, anxiolytics, and sedatives).

The overall analysis from the groups is registered in **Table 1**.

Table 1. General characteristics plus data regarding psychoactive drugs in the study group and control group

Characteristic	Study group (N = 70)	Control group (N = 160)	p value
Sex			0.368
Female	51 (72.9)	107 (66.9)	
Male	19 (27.1)	53 (33.1)	
Age (yr), median (interquartile range)	44 (34–78)	38.5 (30–84)	0.037
Use of psychoactive drugs			0.007
Yes	29 (41.4)	38 (23.8)	
No	41 (58.8)	122 (76.3)	
Psychoactive drugs			
Anxiolytics	20 (28.6)	29 (18.1)	0.075
Sedatives	15 (21.4)	3 (1.9)	<0.001
Antidepressants	13 (19.6)	31 (19.4)	1.000
Antipsychotics	1 (1.4)	0 (0)	0.304
Quantity of psychoactive drugs/patient			0.002
1	16 (22.9)	15 (9.4)	
2	13 (18.5)	23 (14.4)	

Values are presented as number (%).

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The use of psychoactive drugs in the study group is higher than in the control group ($p = 0.007$), the difference is especially important for sedative drugs ($p < 0.001$). Although the patients from the study group use more anxiolytics and antipsychotics, there is no significant statistical difference between groups ($p = 0.075$ and $p = 0.304$). The use of antidepressants is very similar in the 2 groups ($p = 1.000$).

The study group besides using more frequently psychoactive drugs, also has a higher frequency of use of several psychoactive drug ($p = 0.002$).

DISCUSSION

In the study population of patients with self-reported drug allergy, there was a female predominance and the main culprit drugs were antibiotics and nonsteroidal anti-inflammatory drugs in agreement with other studies [12, 13].

It is considered in our study that the use of psychoactive drugs implicates a psychiatric disorder diagnosed by a doctor, once the treatment could only be available under prescription.

We found that 41.4% of the patients with self-reported drug hypersensitivity were under treatment with psychoactive drugs a higher proportion than in the control population (23.8%) and also according to data for the Portuguese population, that describes a 22.9% of patients with anxiety, impulse control, substances abuse, and humour disturbances [14]. It is important to notice that Portugal is one of the European countries with highest consumption of psychoactive drugs and with an important prevalence of mental disorders especially anxiety and mood disorders [14-16].

The present data lead us to speculate that patients with psychiatric disorders and psychoactive drugs use are more prone to self-report drug hypersensitivity reactions. Mood changes and the need for attention could lead patients to overreact on symptoms perception blaming, in certain occasions, a drug intake. Like our population with suspect drug hypersensitivity reactions other

authors that evaluated patients for the same motif also reported higher proportion of patients with psychiatric symptoms/disorders than general population [17]. Although, the relationship is not well defined, some reports could associate anxiety and depression with increased odds of multiple drug intolerance syndrome [11, 18]. Besides doctor evaluation, it is necessary to understand how patients manage and cope with a suspected drug hypersensitivity reaction, in fact, in a recent report which evaluated patients concerns about drug allergy, Blumenthal et al. [19] concluded that patients with poorer general health and mental health had more frequent concerns, with significantly higher odds of allergic reaction and severe allergic reaction concerns.

In our study population, the use of psychoactive drugs, especially sedatives is significantly higher than in the control group and in the Portuguese population. Patients with a self-report drug hypersensitivity have more tendency to be under treatment with psychoactive drugs and could have more tendency to somatization. Personality traces and psychopathology must be taken into account during an allergy workup and in such patients, a referral to psychiatry after excluding drug hypersensitivity may be helpful and advised.

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