Knowledge, attitudes, and practices survey of drug allergy among healthcare practitioners in central China: a multicenter study

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Background: Drug allergy (DA) is one of the most important contributors to iatrogenic morbidity and mortality. Currently DA remains a major challenge for healthcare practitioners (HCPs).

Objective: To assess the knowledge, attitudes and practices of DA among HCPs in Central China.

Methods: A 25-item self-administered DA questionnaire were developed and applied in our study. The questionnaire covered 3 domains: knowledge, attitudes, and practice patterns. From July 2015 to October 2015, HCPs in 7 cities of Central China anonymously participated in the cross-sectional study.

Results: A total of 350 HCPs participated the study, 91 questionnaires uncompleted and 259 were analyzed. Among the respondents, 166 (64.1%) were doctors, 55 (21.2%) were nurses and 38 (14.7%) were medical students. The mean knowledge precision was 59.8%. HCPs agreed that drug induced immediate allergic reactions were IgE mediated (83.4%) and happened within 6 hours after drug administration (89.6%), and epinephrine was the first choice for drug induced anaphylaxis (79.5%). They also agreed that penicillin skin test was valuable to predict allergic reaction (88.4%). However, high proportion of HCPs (66.0%) believed glucocorticoids had an impact on drug skin test rather than antihistamines (4.2%), 47.1% never performed positive and negative control during skin test. More than 90% of the respondents would take patients' allergic history before drug administration, 98.8% agreed that they should receive advanced training of DA knowledge and practice.

Conclusion: The HCPs demonstrated a low level of knowledge regarding DA. Advanced education is urgently needed for better understanding and filling the gaps exist in knowledge and clinical practice of DA.

Keywords: Knowledge; Attitude; Practice, Drug allergy, Healthcare practitioner

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INTRODUCTION

Drug allergy is defined as immunologically mediated drug hypersensitivity reactions (DHRs) after showing the evidence of either drug-specific antibodies or T cells [1]. Till now there are still lack of reliable biological tests to identify these antibodies and cells, DHRs is recommend as the appropriate term for drug reactions resembling allergy. These reactions are mostly unpredictable and can be life threatening, may require or prolong hospitalization and necessitate changes in subsequent therapy [2]. DHRs affect more than 7% of the general population and therefore represent an important public health problem [3]. However, currently the diagnosis of DHRs remains largely clinical, underdiagnosis (due to underreporting) and overdiagnosis (due to an overuse of the term 'allergy') are both common [4]. Accurate diagnosis and management of DHRs are still the major challenge of healthcare practitioners (HCPs) and the unmet needs of the patients. In recent years, several guidelines and/ or international consensus documents are available to support medical decision made on all aspects of DHRs, which greatly facilitate the understanding and management in clinical practice [5-8]. In China, there is no national epidemiology data of DHRs nowadays, several studies show numerous severe DHRs in hospitalized patients [9, 10]. Thus, proper management of DHRs is imperative and the HCP's knowledge is crucial for the patients. KAP (knowledge, attitude, and practice) survey is a representative study of a specific population to collect information on what is known, believed and acted on in relation to a particular topic. Protection measures against a specific disease are related to the knowledge and beliefs of people, hence KAP studies are increasingly becoming important in improving disease control activities [11]. Our intention in this study is to assess the knowledge, attitudes, and practices of DHRs among HCPs in Central China.

MATERIALS AND METHODS

Study design and study population

A cross-sectional survey was conducted from July 2015 to October 2015 in 7 cities of Central China. The study population included physicians and allied healthcare professional (nurse, medical students). The study was approved by the Independent Ethical Committee of Tongji Hospital.

Instrument

A structured Chinese questionnaire was developed for data collection. The survey comprised of 3 domains: knowledge, attitudes, and practice patterns. Demographic data were also collected. The questionnaire consisted of 25 closed ended questions that aimed to collect the following information from the respondents:

(1) Knowledge domain, including mechanism, clinical manifestations, diagnosis and management of DHRs. A binary variable scale were used to ascertain level of the knowledge (from 0 to 1: 0, wrong; 1, right). Answers formats consisted of 4-choice questions (total 14 questions).

(2) Attitudes domain, including attitude towards the needs for advanced education, current diagnostic tests, the impact of DHRs on patient's quality of life. A five point Likert-type scale were used to ascertain level of agreement or disagreement for the questions (from 1 to 5: 1, strongly disagree; 2, disagree; 3, uncertain; 4, agree; 5, strongly agree) (total 5 questions).

(3) Practices domain, including practice pattern of taking allergy history, performing skin test and receiving advanced education of DHRs. A five point Likert-type scale were used to ascertain level of the practices (from 1 to 5: 1, never; 2, occasionally; 3, sometimes; 4, often; 5, always) (total 6 questions).

The practice patterns section was completed prior to the knowledge and attitude sections to avoid leading answers.

Data collection

Data was collected from respondents using a standardized self-administered questionnaire (Supplementary material), distributed as hard copies by trained research assistants. Research assistants explained the purpose of the study to respondents and obtained written consent for the questionnaire to be filled anonymously and returned within an hour. Each interview took approximate 15–25 min to complete. The survey questionnaire was pilot tested in June 2015 (n = 30) to ensure practicability, validity, and interpretability of answers. The questionnaire was slightly refined for wording and format before distribution to the participants based on the results of the pilot study.

Statistical analysis

Data was entered into Microsoft excel 2013, cleaned to detect any missing or invalid variable and then imported to SPSS ver. 16.0

(SPSS Inc., Chicago, IL, USA) for analysis. Descriptive parameters, such as means and standard deviations for normally distributed continuous data, frequencies and percentages for categorical data, were calculated. Multivariable linear regression was used to determine relationship between demographic characteristics and KAP scores. The comparison among groups was performed with LSD test. All tests were performed 2-tailed, and a probability value of less than 0.05 was considered statistically significant.

RESULTS

Characteristics of the study population

The study was conducted in 7 cities of Central China. The final number of respondents who completed the survey was 259, and the response rate was 74.0% (259 of 350). The study population had a median age of 35 years (range, 18–60 years). The demographic characteristics of study participants were summarized in Table 1.

Table 1. Demographic characteristics of study participants

Demographic variables	No. (%)
Gender	
Male	126 (48.6)
Female	133 (51.4)
Education	
Junior college or below	91 (35.1)
Bachelor	145 (56.0)
Master and above	23 (8.9)
Title	
Intern	88 (34.0)
Attending doctor/nurse	109 (42.1)
Chief physician/nurse	62 (23.9)
Occupation	
Doctor	166 (64.1)
Nurse	55 (21.2)
student	38 (14.7)
Level of hospital	
Tertiary hospital	125 (48.3)
District hospital	54 (20.8)
Community health center	80 (30.9)

Knowledge

The precision of the items varied from 4.2% to 89.6% and the mean precision was 59.8%. Of the respondents, 83.4% agreed drug induced anaphylaxis was mediated by IgE and occurred within 6 hours after drug administration (89.6%), 79.5% took epinephrine as the first choice for anaphylaxis, 74.5% agreed skin eruption was the most common manifestation of drug allergy, 61.8% agreed drug avoidance was the first step for DHRs management. For the drug skin test, 88.4% thought penicillin skin test was more reliable than other drugs. However, only 4.2% thought antihistamine had an impact on drug skin test, and 39.8% regarded drug provocation test (DPT) as gold standard to diagnose drug allergy (Table 2). Occupation was significant correlated with the precision of knowledge ($p < 0.05$). Doctors had a higher knowledge score (8.71 ± 2.05) compared with nurses (7.75 ± 2.18) ($p = 0.003$) and medical students (7.78 ± 2.10) ($p = 0.015$), however, there were no difference between nurses and medical students ($p = 0.931$). There were no differences between different level hospitals and education degree (Table 3)

Attitudes

Of the respondents, only one third was satisfied with their knowledge and almost all the respondents had a positive attitude to receive advanced knowledge and training of DHRs. The majority (64.9%) thought DHRs occurred frequently in their daily practice and *in vivo/in vitro* drug test was very important before drug administration (96.9%) (Table 4). Title was significantly correlated with the attitudes score ($p < 0.05$) (Table 3). Interestingly, chief physician (21.21 ± 2.27) and attending doctors (20.72 ± 2.17) had a more positive attitude than intern (19.74 ± 2.42) ($p < 0.01$), there was no difference between chief physician and attending doctors ($p > 0.05$).

Practice

The majority (about 90%) of our respondents would take the history of drug allergy before the drug administration, however, 71.8% could evaluate the drug skin test result timely and accurately, more than half of the respondents never or occasionally receive medical education regarding DHRs and they never perform positive and negative control during drug skin test, which might lead to unreliable results (Table 5). Occupation and level of hospital were significant correlated with the practice score ($p < 0.05$) (Table 3). Doctors (23.24 ± 4.12) presented a better practice profile compared to nurses (21.84 ± 3.50) and medical

Table 2. Knowledge of respondents regarding drug allergy

Item	Choice A	Choice B	Choice C	Choice D
A1	168 (64.9)*	45 (17.4)	15 (5.8)	31 (12.0)
A2	122 (47.1)*	36 (13.9)	59 (22.8)	42 (16.2)
A3	143 (55.2)*	9 (3.5)	106 (40.9)	1 (0.4)
A4	232 (89.6)*	22 (8.5)	1 (0.4)	4 (1.5)
A5	216 (83.4)*	31 (12.0)	3 (1.2)	9 (3.5)
A6	63 (24.3)	193 (74.5)*	2 (0.8)	1 (0.4)
A7	10 (3.9)	29 (11.2)	117 (45.2)	103 (39.8)*
A8	77 (29.7)	29 (11.2)	142 (54.8)*	11 (4.2)
A9	106 (40.9)*	79 (30.5)	46 (17.8)	28 (10.8)
A10	29 (11.2)	70 (27.0)	125 (48.3)*	35 (13.5)
A11	11 (4.2)*	171 (66.0)	66 (25.5)	11 (4.2)
A12	229 (88.4)*	14 (5.4)	11 (4.2)	5 (1.9)
A13	22 (8.5)	21 (8.1)	56 (21.6)	160 (61.8)*
A14	0 (0)	12 (4.6)	41 (15.8)	206 (79.5)*

Values are presented as number (%).
*Correct answer.

Table 3. Multiple linear regression model of knowledge attitude and practice scores

Variable	Knowledge			Attitude			Practice		
	ßcoefficient	T	p value	ßcoefficient	T	p value	ßcoefficient	T	p value
Gender	0.155	2.308	0.022	0.019	0.277	0.078	0.098	1.455	0.147
Education	0.050	0.692	0.490	0.011	0.153	0.879	−0.080	−1.115	0.266
Title	0.088	1.241	0.216	0.194	2.745	0.006	0.090	1.275	0.203
Occupation	−0.205	−2.489	0.013	−0.078	−0.956	0.340	−0.282	−3.445	0.001
Level of hospital	−0.057	−0.701	0.484	−0.089	−1.108	0.268	0.240	2.984	0.003

Knowledge: $F = 3.909$, $p = 0.002$, $R^2 = 0.072$, adjusted $R^2 = 0.053$; Attitude: $F = 4.122$, $p = 0.001$, $R^2 = 0.075$, adjusted $R^2 = 0.057$; Practice: $F = 4.267$, $p = 0.001$, $R^2 = 0.078$, adjusted $R^2 = 0.060$.

students (19.05 ± 5.16) ($p < 0.05$). HCPs in tertiary hospitals (22.36 ± 4.79) performed better practice than in community hospitals (21.16 ± 3.11) ($p < 0.05$).

DISCUSSION

DHRs comprise about 15% of all drug adverse reactions and are of significant concern for clinicians and patients [12]. A retrospective study found drug was the major cause of anaphylaxis in hospitalized patients in China [13]. Generally multi organs or systems are involved when DHRs occur and the clinical manifestations vary from mild to severe, sometimes can be life threatening [14]. However, the diagnosis of DHRs is difficult due to the lack of reliable *in vivo* or *in vitro* drug specific test, which also had an adverse impact on the subsequent DHRs management. An international group recommends a diagnostic flow chart from clinical history to skin test or DPT when DHRs are suspected [1]. Despite evidence-based recommendations about DHRs from professional organizations, adherence to these recommendations is unknown. We conduct a cross sectional multicenter study to assess the KAP regarding DHRs in Central China.

Our study showed a low level of knowledge and a nonstandard practice profile, however, a strong positive attitude towards

Table 4. Attitudes of respondents regarding drug allergy

Item	Strongly disagree	Disagree	Uncertain	Agree	Strongly agree
B1. Do you think HCPs should receive advanced knowledge and training of DHRs?					
	0 (0)	0 (0)	3 (1.2)	70 (27)	186 (71.8)
B2. Do you think *in vivo* or *in vitro* test of drug is very important before drug administration?					
	0 (0)	0 (0)	8 (3.1)	89 (34.4)	162 (62.5)
B3. Do you satisfied with your knowledge of DHRs?					
	7 (2.7)	47 (17.1)	120 (46.3)	52 (20.1)	33 (12.7)
B4. Do you think drug allergy has an adverse impact on patient's quality of life?					
	0 (0)	13 (5)	39 (15.1)	102 (39.4)	105 (40.5)
B5. Do you think drug allergy always occurred in your daily practice?					
	4 (1.5)	25 (9.7)	62 (23.9)	88 (34)	80 (30.9)

Values are presented as number (%).
HCP, healthcare practitioner; DHR, drug hypersensitivity reaction.

Table 5. Practice of respondents regarding drug allergy

Item	Never	Occasionally	Sometimes	Often	Always
C1. Do you take the patient's history of drug allergy before the drug administration?					
	5 (1.9)	11 (4.2)	17 (6.6)	73 (28.2)	153 (59.1)
C2. Do you take the patient's allergy history before drug administration?					
	5 (1.9)	4 (1.5)	6 (2.3)	59 (22.8)	185 (71.4)
C3. Do you evaluate the drug skin test result timely and accurately?					
	20 (7.7)	16 (6.2)	37 (14.3)	102 (39.4)	84 (32.4)
C4. Do you perform positive control and negative control during drug skin test?					
	122 (47.1)	47 (18.1)	42 (16.2)	22 (8.5)	26 (10)
C5. Do you recognize and manage DHRs timely when it occurs?					
	7 (2.7)	7 (2.7)	28 (10.8)	85 (32.8)	132 (51)
C6. Do you participate continuous medical education regarding drug allergy?					
	56 (21.6)	85 (32.8)	72 (27.8)	25 (9.7)	21 (8.1)

Values are presented as number (%).
DHR, drug hypersensitivity reaction.

DHRs training among HCPs. The knowledge domain in our study covered the mechanism, clinical manifestation, diagnosis and management of DHRs. Only two-thirds of them knew the mediating molecules and cells involved in drug induced anaphylaxis. Less than 40% regarded DPT as the gold standard to diagnosis drug allergy [15], the possible explanation is that DPT might be dangerous and rarely carried out in China. Skin test has been recommended in daily practice as a simple and easily implemented approach to predict drug allergy [16], it should be noticed that only 4.2% realized antihistamine had an impact on the skin test result rather than glucocorticoids and other drugs, and less than half knew the appropriate time to preform skin test, which might cause false negative results and lead to subsequent potential risk of DHRs. Fortunately about 80% would take epinephrine as the first choice for drug induced anaphylaxis, which was a very important step emphasized in several guidelines [17, 18]. Doctors had a higher level of knowledge than nurses and medical students; however, there was no difference among HCPs in different tertiary hospitals and community hospitals, which implied HCPs in Central China generally have a low level of knowledge on DHRs. The results in the attitude domain also showed the majority were not satisfied

with their knowledge and almost all the respondents agreed to receive advanced training of DHRs. Senior HCPs had a more positive attitude than Junior HCPs, which implied they might had more experience to diagnosis and manage DHRs. However, gaps existed between the knowledge and daily practice, HCPs realized skin test was important to predict or diagnosis DHRs, while they couldn't perform skin tests correctly according to the guidelines [16, 19]. More than half of them never or occasionally received medical education regarding DHRs. In fact, few allergy centers in Central China could provide continuous medical education and training of DHRs, which might hamper the process of training program.

Our study showed HCPs in Central China had a very poor adherence to the guidelines. Firstly, when DHRs were suspected, a careful evaluation of clinical history was mandatory, 94.2% of our respondents would take the allergy history before drug administration, and 74.5% agreed skin eruption was the most common manifestation of DHRs, which implied they were very vigilant of DHRs and they performed well in clinical history taken. Two-thirds admitted DHRs were common in their daily practice. Secondly, when one specific drug was suspected, a validated skin test was recommended, and skin prick test was performed prior to intradermal test for immediate DHRs [1]. However, only few drugs skin tests such as penicillin and platin salts were validated, and the standardized procedures of them had been well stated in several guidelines [1, 20]. While in China, intradermal skin test had been applied widely regardless of whether the drug skin test been validated or not [21], only 40% of our respondents knew to take skin prick test for initial screening. Moreover, the majority had a low level knowledge and a nonstandard practice on skin test, which would lead to unreliable results. Thirdly, the guidelines recommended if validated skin test was no available, DPT would be carried out. In China, very few HCPs knew how to and were willing to perform DPT since it might be dangerous. Finally, when drug induced anaphylaxis occurred, 80% of our respondents took epinephrine as first choice, which was lower than the HCPs in the United States (94%) [22]. Thus, skin test procedure and DHRs management training should be the priority in further education courses of DHRs.

In conclusion, we firstly assessed the knowledge, attitudes and practices regarding DHRs among HCPs in Central China and found a low level of knowledge and a poor practice profile adhere to the guidelines. Advanced education became imperative to eliminate the gaps of knowledge and practices.

Future studies involving a larger sample size may lead to information sharing and collaborative care of DHRs among HCPs in China.

SUPPLEMENTARY MATERIAL

Supplementary questionnaire can be found via http://www.apallergy.org/src/sm/apallergy-6-105-s001.pdf.

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SUPPLEMENTARY MATERIAL

Supplementary questionnaires

KNOWLEDGE: Below are a series of questions aimed at assessing your knowledge surrounding drug allergy.

A1. Drug-induced anaphylaxis belongs to:
- A. Type I hypersensitivity
- B. Type II hypersensitivity
- C. Type III hypersensitivity
- D. Type IV hypersensitivity

A2. All of the following factors are related with drug allergy, EXCEPT:
- A. Drug dosage
- B. Drug exposure
- C. Administration route
- D. Heredity

A3. Which is the effector cell in drug-induced anaphylaxis?
- A Mast cells
- B. Lymphocyte
- C. Eosinophils
- D. Monocytes

A4. When will immediate drug hypersensitivity reactions occur after drug administration?
- A. <6 hr
- B. 6–8 hr
- C. 8–12 hr
- D. 12–24 hr

A5. Which antibody mediates immediate drug hypersensitivity reactions?
- A. IgE
- B. IgG
- C. IgM
- D. IgA

A6. What is the most common clinical manifestation of drug allergy?
- A. Anaphylaxis
- B. Cutaneous symptoms
- C. Serum sickness
- D. Hepatic and renal injury

A7. What is regarded as the gold standard to diagnosis drug allergy?
- A. Clinical history
- B. Skin tests
- C. Drug-specific IgE
- D. Provocation tests

A8. What is the indication of drug provocation test?
- A. Suspected drug allergy
- B. Suspected drug allergy associated with systemic disease
- C. The suspected drug is imperative or cannot be replaced for the concurrent illness
- D. Suspected drug allergy with serious cutaneous symptoms

A9. Which test is recommended as the first screening step when immediate drug hypersensitivity reactions were suspected?
- A. Skin prick test
- B. Intradermal test
- C. Skin patch test
- D. Provocation test

A10. Which is the appropriate time to perform skin test when drug allergy is suspected?
- A. Anytime
- B. Right after the symptom disappeared
- C. At least one month after the symptom disappeared
- D. Never

A11. A 24-year-old male had cough and purulent mucus for 3 days, he had an asthma history. His doctor decided to use penicillin to control the airway infection. In which situation bellowing is not appropriate for the penicillin skin test?
- A. He has been treated with Tylenol (cold medication, including chlorpheniramine, pseudoephedrine, acetaminophen and dextromethorphan) in recent 3 days.
- B. He has been treated with dexamethasone 5 mg by intravenous yesterday.
- C. He has had leukotriene modifier 10 mg/day by PO in recent 3 days.
- D. He has been treated with aminophylline in recent 3 days.

A12. Which of the following drug is recommended to perform intradermal test before administration?

    A. Penicillin

    B. Aztreonam

    C. Ofloxacin

    D. Azithromycin

A13. What is the pivotol management for drug allergy?

    A. Drug therapy

    B. Specific immunotherapy

    C. Symptomatic therapy

    D. Avoiding sensitization drugs

A14. Which medication is the first choice when an anaphylactic shock occurred?

    A. Dopamine

    B. Antihistamine

    C. Glucocorticoid

    D. Epinephrine