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SHORT COMMUNICATION

Approach to Penicillin Allergy – A Survey

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ABSTRACT

Individual approaches to the diagnosis and management of penicillin allergy are practiced by clinicians. This cross-sectional survey of physicians was aimed at exploring their ways of dealing with diagnosis and management of penicillin G allergy. Of the 235 respondents, 63% believed patients' self-reported history of penicillin allergy and avoided using penicillin G; 97% do so for patients whose allergic status was confirmed with positive skin test results. Researchers insist on skin testing for patients claiming penicillin allergy and for those whose allergic status was confirmed with positive skin test results, before considering antibiotic substitution, in an attempt to minimize the development of multi drug resistant pathogens. Undue concern about penicillin allergy may negatively influence the therapeutic outcome of rheumatic fever and syphilis. Repeated skin testing is recommended before each subsequent course of penicillin G, even in patients who have tolerated it before which was practiced by an appreciable number (89%) of our respondents. Epi cutaneous followed by intra dermal routes with major and minor determinants have been recommended for penicillin G skin testing. 100% of our respondents skin tested by intra dermal route alone, using penicillin G and its repository preparations before injecting the respective full dose preparations. Legal problems arising from serious clinical outcomes of penicillin allergy may pose a threat to the physician of losing self esteem in the society forcing him to be overcautious with its use. Educating both the public and health care providers is necessary in this regard.

Keywords: *Penicillin allergy, Hypersensitivity reaction, Penicillin skin testing, Drug induced anaphylaxis, Resensitization*

Penicillin G(PnG) one of the most useful antimicrobial drugs, is relatively inexpensive and non toxic, but is the most common cause of drug induced anaphylaxis and drug induced allergic reactions, in general [1]. Penicillin can cause many different types of allergic reactions, from minor drug rashes to fatal anaphylaxis. The reported incidence of penicillin allergy ranges from 1-10%, the true incidence of life threatening anaphylactic reactions ranging between 0.004-0. 015% [2]. Skin testing with the penicillin skin test reagents has proven to be very reliable in predicting the risk of anaphylactic reactions with penicillin [1]. Patient alleged penicillin allergy may adversely impact the emergence of antibiotic resistance and the health care costs. Several researchers emphasize on skin testing before considering antibiotic substitution in such patients [1,3]. It is claimed that allergy to penicillin is not lifelong, patients with penicillin allergy tend to lose sensitivity over time and also that negative skin test does not guarantee safety to take repeated courses of penicillin [1,4]. However, definitive practice guidelines concerning PnG allergy management is still lacking and individual approaches are being practiced [5]. Hence this survey was conducted to investigate how our clinical practitioners manage with the dilemmas related to diagnosis and management of PnG allergy.

MATERIAL AND METHODS

In this cross-sectional survey, we distributed the questionnaire to the clinicians (N=250) of the town, after confirming that they use/ prescribe PnG injections. The questionnaire that was in English language carried five questions pertaining to their approach to PnG allergy, along with the response options. The questions were framed based on the available literature about penicillin allergy. Initially, the questionnaire was distributed to 10 clinicians, and based on their queries and response, questions were reframed and the final revised version was administered as the survey instrument. Percentage of respondents choosing each option was calculated.

Sample Questionnaire

1. Which of the following penicillin G preparations you use / prescribe
   A. Crystalline penicillin
   B. Procaine penicillin
   C. Benzathine penicillin
2. When your patient gives history of allergy to penicillin G
   A. Will you totally avoid penicillin G in that patient ***OR***
   B. Confirm allergic status with skin testing
3. In patients whose allergic status to penicillin G is confirmed with positive skin Test results
   A. Will you avoid future use of penicillin G ***OR***
   B. Attempt skin testing, whenever penicillin G is indicated
4. In patients who have tolerated penicillin G previously, do you repeat skin testing before each subsequent course of penicillin G injections
   A. YES B. NO
5. Tick the appropriate skin test preparation and the route you administer before injecting The three preparations of penicillin G

Test Dose preparation used	Full Dose treatment used		
	Crystalline penicillin	Procaine penicillin	Benzathine penicillin
Crystalline penicillin			
Procaine penicillin			
Benzathine penicillin			
Benzyl penicilloyl + Crystalline penicillin			
Route of test dose	Prick / Scratch Intra dermal	Prick/ Scratch Intra dermal	Prick/ Scratch Intra dermal

RESULTS AND DISCUSSION

Table 1 presents the number and percentage of respondents answering each question. Of the 235 who responded, 63% believe patients' self-reported history of penicillin allergy and deny PnG injections for them. 97% totally avoid PnG administration for patients whose allergic status confirmed previously with positive skin test reactions. Studies show that many patients claim to have penicillin allergies and only a small percentage is actually allergic when assessed by skin testing and hence clinical history is not predictive of subsequent skin test results [2,3,6-12]. Patients with history of penicillin allergy are usually prescribed more expensive alternative antibiotics. Excessive use of these antibiotics is associated with emergence of pathogens that are resistant to multiple drugs. The development of these pathogens causes infections that are associated with higher rates of morbidity and mortality [1]. Researchers insist that history of penicillin allergy should not be taken at the face value and recommend skin testing before considering antibiotic substitution [1,3].

It is argued that natural history of allergy to penicillin is such that patients may lose sensitivity or become negative in skin testing over time because of waning of penicillin-specific IgE levels in the absence of antigenic stimulation [1,4,13,14]. Several studies have demonstrated that after an allergic reaction, the chance of having a positive response on skin testing diminishes with time [15-17]. Hence, allergy to penicillin need not be life long, with passage of time over 85% of patients lose Ig-E mediated sensitivity and can safely receive penicillin [13]. Skin testing in such patients would help to identify the presence or absence of Ig-E antibodies to penicillin, information that will help the physician to determine if penicillin or an alternative antibiotic should be given [1]. Once diagnosed PnG allergic, 97% of our respondents do not consider trying PnG later on, in such subjects, denying them the acquisition of PnG treatment throughout their lifetime. The intramuscular injection of PnG benzathine, once a month is the convenient regimen for prophylaxis of rheumatic fever. Allergy to PnG poses significant problem with treatment compliance in such patients as the alternative drugs like sulfisoxazole or sulfadiazine are to be administered every day [18]. Also there are no proven alternatives for treating tertiary syphilis, neuro syphilis and syphilis in pregnant women other than PnG [18]. In our set up, desensitization procedures are undertaken only in major hospitals and hence not affordable to all. Skin testing for such patients would play an important role to reemphasize the use of PnG.

Multiple short courses of penicillin via any route of administration increases the risk of sensitization [1]. A negative history of allergy is not always a guarantee of safety to take repeated courses of PnG, as it will not identify patients sensitized by their last exposure. Hence, repeat skin testing is recommended before each subsequent courses of penicillin even after a patient has tolerated a course of penicillin, with or without desensitization. It is best to perform skin test just before the course, or preferably within 72 hours of PnG injections.

Table 1: No. and % of Respondents answering the Questions on their approach to penicillin G allergy

Response options	No. of Respondents (N=235)	% of Respondents
Preparations of PnG used		
▪ Crystalline penicillin	141	60
▪ Procaine penicillin	115	49
▪ Benzathine penicillin	183	78
When a patient gives history of allergy to PnG		
▪ Avoid using PnG	149	63
▪ Confirm with skin testing	86	37
In patients with allergic status confirmed		
▪ Avoid future use PnG	228	97
▪ Attempt skin testing whenever PnG is indicated	07	03
In patients who have tolerated PnG previously		
▪ Skin test before each course of PnG	209	89
▪ Do not skin test before each course	26	11
For skin testing		
▪ Respective full dose preparations	235	100
▪ Direct intra dermal, no prior epicutaneous test	235	100

An interruption of three days or longer runs the risk of resensitization and reaction with subsequent course of PnG injections [1, 4]. History positive but skin test negative patients face a higher risk of sensitization [1, 4]. Chances of resensitization or occurrence of hypersensitivity reaction in previously non-allergic individuals have been debated by researchers who do not support the notion of skin testing just in advance of need for penicillin [19,20]. In a survey, program directors were more likely to repeat skin testing before future penicillin courses than were practicing allergists [5]. In our survey, majority consensus (89%) was for repeat skin testing before each subsequent course of PnG injection in patients who have tolerated it before. The concern for PnG allergy in this regard is appreciable.

All our respondents' skin test by intra dermal route alone, using respective full dose preparations of PnG i.e; crystalline penicillin and repository preparations like PnG procaine and PnG benzathine. Skin testing with major and minor determinants of benzyl penicillin is recommended standard practice for the evaluation of patients with immediate hypersensitivity reactions to beta-lactams and 99% of patients who test negative will tolerate penicillin. Using benzyl penicilloyl (major determinant) and penicillin G as a source of minor determinants (penicillin minor determinant mixture not commercially available), approximately 97% of patients who test negative will tolerate penicillin. However, a small percentage of patients at risk for anaphylactic reaction will be missed with this testing method [1]. Use of PnG alone for skin testing by our respondents, may further increase the chances of missing the anaphylactic reactions. Other beta-lactams like amoxicillin, ampicillin and cephalosporins have been suggested as skin test reagents [1], but no literature is available about use of repository preparations of PnG for skin testing. Our clinicians are using the repository preparations of PnG for skin testing, the reliability of predicting the anaphylactic reactions of which is questionable.

Epicutaneous followed by intra dermal injections for skin testing are recommended that would reduce the incidence of systemic reactions to test dose [1]. On the contrary, prick puncture is not sufficiently sensitive; hence skin testing by intra dermal route alone has been suggested by AYY Wu [4]. Our study participants appear to be in consensus with the latter concept.

CONCLUSIONS

Antimicrobials are one of the most commonly prescribed drugs in India and PnG is still the treatment of choice for many infections. Although the risk of anaphylaxis with PnG should not be under estimated, attempts should be made to enhance the use of PnG as it is relatively inexpensive and nontoxic. Despite the availability of safe skin testing procedure, the mental picture produced when one thinks of penicillin allergy is: anaphylaxis and death. Legal problems arising from such serious clinical outcomes may pose a threat to the physician of losing self esteem in the society which fact may force him to be extra cautious while managing penicillin allergy. This phobia can be overcome by educating the health care providers and general public about penicillin allergy.

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