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Antibiotic allergy – myths and reality

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Allergic reactions (AR) range from 5 to 10 % in the structure of adverse reactions to drugs [18, 33]. They can cause death of the patient, reduce the quality of life, lead to a prolongation of treatment, the use of suboptimal doses of alternative drugs and a lot of additional investigational tests.

Antibacterial drugs are the most common cause of drug AR (Figure). They are not able to directly stimulate the release or activation of inflammatory mediators from mast cells, like histamine, prostoglandin, leukotrienes, kinins, responsible for pseudoallergic reactions as cause only true AR [46].

The presence of AR complicates choice of antibiotic, its timely and rational prescription, which increases the risk of adverse effects at the patients with bacterial infections.

Epidemiological aspects and clinical manifestations of AR to antibiotics

According to numerous epidemiological studies frequency of AR to antibiotics varies widely from < 0,01% in the use of macrolides to 10 % with natural penicillins [21].

Administering beta-lactam antibiotics often leads to AR that can have cross character to drugs of different groups. For example, if the AR to penicillins is present, similar AR to I generation cephalosporins may be 10 %, cephalosporin II–III generation – 1–3 %, imipenem – 50 %. According Kelkar P., Li J., (2001), cross reaction to cephalosporins in patients with AR to penicillin was observed from 3 % to 18 % of cases [17].

Recently collected data has shown significantly lower incidence of cross-reactions in the group of beta-lactam antibiotics [9, 30].

Review of publications for the period 1950 to 2012, covering the cross allergy between penicillins and cephalosporins, showed that the risk of allergic reactions was observed only in the application of the first generation cephalosporins (OR 4,8), while other cephalosporins generations could be safely

used in patients with allergy to penicillin. Laboratory studies confirmed if hypersensitivity was caused by the presence of R1 side chain in the beta-lactam ring, it occurred to all antibiotics, which had a similar structure. Such structural feature causes an allergic reaction cross between amoxicillin, ampicillin and cephalosporins first and second generation. Overall, the prevalence of cross-allergies has recently reduced and accounts for 1 % according to most publications [7].

The study, conducted by active questioning of patients indicated the presence of allergy to penicillin, asking describe conditions of reactions and changes that accompanied it, revealed a probable AR in 63,0 % possible – in 28,1 % and absence of AR in 8,9 %. Only 26,6 % of patients the history of allergy to penicillin were connected with the reaction to amoxicillin, amoxicillin / clavulanate and cephalexin. Other patients were tolerant to these drugs. The use of cephalosporins 3–4 generations, carbapenems and aztreonam for treatment of infections at this group of patients is not accompanied with the development of side effects, including AR. It confirmed the minimal risk of cross-allergic reactions [19].

Analysis of preoperative antibiotic prophylaxis at orthopedic clinic in 2007–2010 found that the prevalence of AR to penicillins was 9,9 %. Cross-allergic reactions to cefazoline in this group of patients were absent that was different from previous data. The authors explained these results that modern cephalosporins better cleaned from penicillin impurities compared with drugs manufactured in the last century [14].

Although according to the Iranian pharmacovigilance database for 10 years ceftriaxone was the most common cause of death due to the use of antibiotics. Serious adverse reactions amounted to 30 % of reports of adverse events in the use of the antibiotic. The most frequent they were clinical death, anaphylactic and anaphylactoid reactions, mainly developed in people who have allergic history to beta-lactam antibiotics [44].

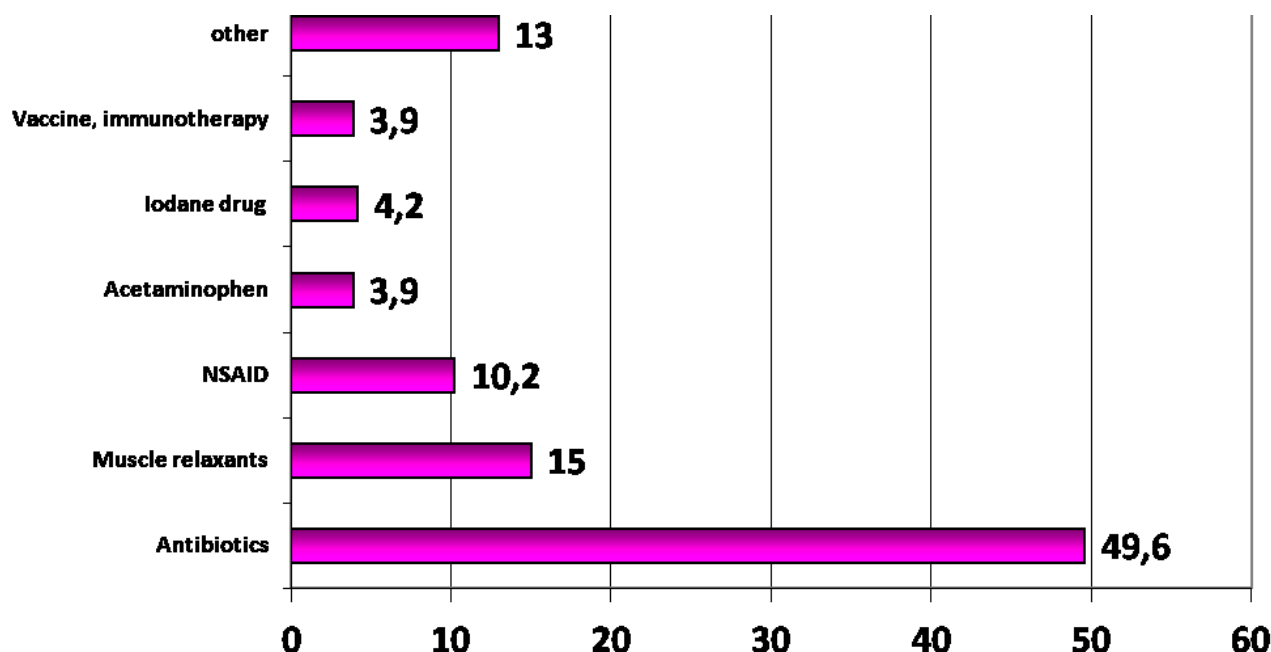


Figure. Structure of anaphylactic reactions to medicines by Renaudin JM, et al (2013) [31].

Analysis of AR developing was performed by Macy E., Ngoc J.Ho. (2011) during ($4,5 \pm 2,9$) years by observing patients who had AR due to antibiotics use, showed that average ($8,2 \pm 10,5$) courses of antibiotics was taken. Positive skin tests to penicillin were 7,0 %, for amoxicillin – 0,2 % of patients. The highest rate of new AR was observed in patients with negative skin tests to penicillin (2,9 %) and sulfonamides (2,7 %). AR was developed more often at women (3,3 %) than men (1,9 %). AR to cephalosporins was in 1,2 % uses. AR to macrolides ranged from 1,8 % at the patients with negative skin tests to penicillin and 4,2 % in the case of positive. For fluoroquinolones, its level was 1,2 % and 2,3 %, respectively. A statistically significant difference in the occurrence of AR to cephalosporins, macrolides, fluoroquinolones have been identified [26].

Interestingly, despite the risk of cross allergy to penicillins and cephalosporins, there was a high level prescriptions cephalosporin for patients with positive tests for penicillin, but a high level of AR to these drugs was not observed. AR was represented mainly with rash and urticaria. Severe AR, such as Stevens-Johnson syndrome, Lyell's syndrome, anaphylaxis is not developed [10, 26].

Drugs that are well tolerated by patients with immediate hypersensitivity to penicillins are carbapenems. Cross-reactions occurs no more than 1 % of cases. Using dose titration allows all to avoid any side effects [35, 36].

The study of cross T-cell-mediated AR to carbapenems in patients with confirmed delayed reaction to penicillins, conducted by Romano A. et al. (2013), found absent of hypersensitivity to carbapenems, accompanied with good tolerability of therapeutic doses of drugs [37]. The lack of a statistically significant risk to carbapenems AR in patients allergic to penicillin was proved Wall GC. et al (2013) in a retrospective study of 958 patients were treated with carbapenems [49].

The research of delayed type hypersensitivity to penicillins (amoxicillin, amoxicillin / clavulanate, benzylpenicillin)

in pediatric patients which was manifested with maculopapular rash, by applying repeated provocation tests with a gradual increase in dose allowed to establish the existence of a positive reaction in 71 % of patients. Some patients during repeated administration, which was carried out in 4–6 weeks showed negative results. This group of patients was younger, which allowed researchers to make assumptions about the possible latent infection with influenza viruses or Epstein-Bar interacting with penicillin could trigger a rash and false positive diagnosis of an AR to penicillin. Re-investigation after recovering from a viral infection showed negative provocative test. Indeed delayed positive reaction to penicillin confirmed only half of patients studied [4].

Recent assessments of side effects to antibiotics indicate that AR are associated with IgE and T-cell immunological mechanisms amount small part. Most side effects of antibiotics recorded as AR have immunological mechanisms and their appearance can be predicted through skin or provocation tests. Therefore, only 5 % of patients with AR to penicillin show positive skin tests [43, 45].

Clinical manifestations of AR to antibiotics are presented in Table. The most common signs of AR are skin generalized maculopapular rash tend to spread and present during period of several days to 3 weeks after treatment. Mainly it is localized on the trunk, but can spread to the extremities. Urticaria and angio-neurotic edema may be led IgE-mediated reaction, and other mechanisms [18, 33, 42].

The most severe skin manifestations of AR are Stevens-Johnson syndrome and toxic epidermal necrolysis. Stevens-Johnson syndrome begins with macula-papular rash, which were converted to ulcerative lesions of the mucous membranes, conjunctivitis, fever, sore throat and fatigue [13]. Toxic epidermal necrolysis is a rare lesion that is similar to Stevens-Johnson syndrome, but is accompanied with a massive detachment of the epidermis from the derma and a scalded skin appearance [18].

Except skin AR accompanied with damage of other organs and systems – respiratory (rhinitis, bronchospasm), cardiovascular (anaphylactic shock), hematopoietic, liver and kidneys. Generalized polyorganic lesions include drug rash with systemic and eosinophilic syndrome, serum sickness, drug-induced systemic lupus erythematosus, vasculitis [18, 42].

One of the rare manifestations of AR to antibiotics may be Kounis syndrome or allergic coronary syndrome, which is based on acute thrombosis or spasm of the coronary arteries caused by the activation of mast cells to release biologically active substances and the development of immediate hypersensitivity reactions. Clinical syndrome manifested with typical angina or myocardial infarction symptoms, but has a time relationship with antibiotics, can occur in young people. The cases of this syndrome were described for penicillin and cephalosporin [5, 20, 22–25, 47, 48].

Thus, manifestations of AR are quite diverse and often non-specific, requiring careful differential diagnosis with many diseases.

Features diagnosis and treatment of AR on antibiotics

Diagnosis AR to antibiotics in a first includes detailed medical history to obtain the most comprehensive description of all prescription drugs that the patient is taking, with the date of admission, the form of the drug, dose and route of administration. It should collect information about clinical signs of AR, their duration and relationship with drug use immediately before the examination and that have been in the past [18, 33].

During asking patient risk factors for AR to antibiotics should be identified. There are young age (less than 50 years), female gender, genetic polymorphism of human leukocyte antigen (HLA-system), viral infections (HIV, Epstein-Bar virus), the presence of AR or atopy on any other substances in the history, frequent or prolonged use of high doses of antibiotics, parenteral (especially intravenous) or topical application of drugs. AR can be caused with high molecular weight antibiotic or its ability to bind with blood proteins, tissues and induce immune response [1; 28].

To confirm the AR to antibiotics, mainly IgE-mediated immediate reactions, one of the most common and accessible method is skin diagnostic tests: prick tests and intradermal administration of allergens. The use of diagnostic tests to penicillin allows high probability confirm lack of response, even if history of penicillin AR is present [12, 18, 28, 34, 51].

Skin patches tests that overlap the back of the patient for 48 hours and do not contain irritating concentration of potential allergens can detect cutaneous delayed-type AR [3, 11, 42].

Detection of specific IgE to antibiotics is costly, inaccessible investigation. In addition, it has a lower sensitivity and diagnostic value compared to skin tests [12, 18, 28].

Detect elevated levels of histamine and tryptase confirm severe IgE-mediated AR, such as anaphylaxis. However, a negative result does not rule out acute anaphylactic reaction [18, 50].

Complete blood count will reveal hemolytic anemia, thrombocytopenia, leukopenia, eosinophilia developing due to cytotoxic type of AR. Using direct and indirect Coombs'

Clinical manifestation of allergic reaction to antibiotics [50]

Table

Antibiotics	Clinical manifestation	Clinical features
Penicillin – 3 %, amoxicillin, ampicillin – 5 %, protected aminopenicillins – 2–3 %, carbapenems – 1–5 %, aztreonam – 2 %, cephalosporins 1–3 %, fluoroquinolones – 2–3 % sulfonamides – 1–10 %, rifampicin – 1 %, streptomycin – 4–5 %	maculopapular rash (1 % hospitalized patients)	Diffuse small spots and papules are developed in a few days after drug use
All group of antibiotics Moxifloxacin 1:50000, Sulfonamides 1–10 %.	Urticaria and angio-neurotic edema	Start in a few minutes or hours after antibiotic use, may cause anaphylactic reaction, IgE-mediated
Sulfonamides – 1–10%	Stevens-Johnson syndrome, toxic epidermal necrolysis	Fever, sore throat, fatigue, conjunctivitis, ulceration of the mucous membranes, detachment of the epidermis
Penicillin very rare, cephalosporins – 1–8 %, sulfonamides < 1 %, vancomycin, rifampicin	Hematological presentation	Hemolytic anemia, leucopenia, thrombocytopenia, eosinophilia
Sulfonamides, erythromycin 1:1000, anti-tuberculosis agents near 1 %	Liver damage	Hepatitis, cholestatic jaundice
Penicillins rare, cefoxitin – 3 %, ceftriaxon – 1 %, cefpodoxim – 4 %, claritromycin – 4 %, ciprofloxacin – 1 %, vancomycin – 5 %, sulfonamides rare	Kidney damage	Interstitial nephritis, glomerulonephritis
Penicillins 0,05 %, aminopenicillins, carbapenems, cephalosporins, fluoroquinolones, vancomycin rare	anaphylaxis	urticaria, angioedema, bronchospasm, gastrointestinal symptoms, hypotension
Cefaclor – 0,1–0,5%, sulfonamides	Serum sickness	Fever, urticaria, arthralgias
Sulfonamides	Vasculitis	Cutaneous or visceral vsculitis

reaction helps to confirm immunological changes of erythrocyte membranes due to cephalosporin use, resulting in hemolysis [18, 28].

Recent studies have focused on the diagnostic value of the basophil activation test (the quantification of basophil activation by flow cytometry). This method allows us to estimate the possible AR to beta-lactam antibiotics, but need additional studies of its effectiveness for future widespread use in clinical practice [15, 18, 40].

In cases when using the above methods could not verify AR to antibiotics provocation testing may be performed. The essence of the test is under the supervision of an allergologist, in the intensive care unit with full emergency equipment for anaphylaxis treatment, the patient gradually, starting with 1% single therapeutic dose is administered drug. Further, if there are no manifestations of AR, re-administering antibiotics in 15 minutes for parenteral or 60 minutes for oral is done. With each repeated dose administration increases in 10 times, reaching therapeutic. If during past year patient had anaphylactic reactions provocation test begins with a dose of 0,1 % of the single therapy [2].

Performing graded challenge testing is safer than entering the full dose; in addition, it may be the method of choice for the diagnosis pseudoallergic reactions. In the absence of diagnostic registered standardized allergens for skin tests with antibiotics, provocation test is one of the informative sufficient diagnostic test of AR [12].

Diagnosis of immediate hypersensitivity to beta-lactams in accordance with the recommendations of the European Network of drug allergy (European Network of Drug Allergy (ENDA)), which is performed using skin and oral provocation tests confirmed medical history in 36,2% of cases. Most patients – 72,4 %, proved positive skin tests to penicillin, 10,3 % of patients with AR confirmed using skin tests antibiotic that caused the reaction in history and in 17,2 % of cases proved positive provocation tests. Patients who showed negative results of allergic test were treated with beta-lactams safely without development of AR or they were mild, as not life threatening symptoms through a long period [8].

Evaluation of diagnostic allergy to penicillin using intradermal skin tests and skin prick test using standardized allergens showed negative results when using skin prick test and low concentrations of allergens in intradermal tests. Higher concentrations of allergen for intradermal tests and provocation test revealed immediate type allergy in 14 % and delayed type in 12 % of patients. It is interesting that in any patient diagnosed with hypersensitivity to penicillin, even with the presence of immediate systemic reactions was determined the level of specific IgE was not increased [32].

However, according to Hjortlund J et al (2012), extended examination of allergy to penicillin identification of specific IgE, conducting skin tests (prick and intradermal), provocative parenteral, oral short-term (within one day) or long-term (7 days) tests revealed that AR were confirmed only in 27,4 % of 405 patients with AR history to natural and semisynthetic penicillins. The immediate reaction was observed in 21,7 %, and by long-term oral provocation test for 7 days hypersensitivity was discovered yet in 5,7 % of patients [16].

Sagar P.S. et al (2013) received confirmation of allergy only in 15,5 % of patients indicated hypersensitivity to antibiotic in history. Prick skin test in this case was ineffective; allergic reactions discovered via intra dermal administration of allergen in 3,1 %; in the other cases AR was confirmed using the technique of oral provocation test (receiving low dose ampicillin for 3 days). Most of patients had immediate type allergic reaction as urticaria. The delayed reaction was developed in 47 % of subjects with confirmed sensitization to penicillin. The authors noted clearer descriptions medical history of AR such as urticaria or anaphylaxis by patients with confirmed response that could be the basis for an appropriate management. The study showed more informative provocative test in comparison with skin and low incidence of true allergic reaction to penicillin in patients with allergic history [38].

Diagnostic value of intradermal allergy tests cephalosporins was proved controversial in the study Yoon SY. et al (2013), who found that the level of false-negative tests was 99,7 %. This resulted in urticaria and itch in patients with a negative test for cephalosporins. On the other hand, the positive response to the test is not accompanied by the development of AR [52].

As shown by Slovak researchers a comprehensive survey of patients who had a history of penicillin allergy, conformation of this reaction was only found in 13,5 % of cases. The IgE-mediated hypersensitivity was observed in 8 % of individuals. Using skin tests allergy has been confirmed at the 2,3 % of patients. Provocative tests revealed hypersensitivity at 3,5 %. The majority of patients had immediate type reactions as erythema and urticaria. Delayed type reactions were manifested delayed urticaria and maculopapular rash [22].

According to a survey of the diagnosis and treatment of drug allergy by World Allergy Organization, it was found that skin tests were used by 74,7 %, determination of specific IgE – 67,4 %, test activation of basophils – 54,4 %, lymphocyte transformation test – 36,8 %, tests with patches – 54,7 %. Provocative tests, especially to avoid an allergic reaction if patient had uncertain allergic history were applied by 68,4 %. Fast desensitization chemotherapy, antibiotic administration or biological agents was performed by 69,9 %. For the treatment of Stevens-Johnson syndrome, systemic corticosteroids were used by 72,3 % of respondents [53].

Management of AR to antibiotics is to avoid the drug that causes it, replacing antibiotic to alternative. If this is not possible, the drug is administered by desensitization as described above [18, 42, 54].

Caimmi S. et al (2011) is recommended for the prevention of anaphylactic reactions to antibiotics during surgery, to collect more carefully allergic history, to conduct skin and provocation tests for identifying true sensitization. Using *in vitro* tests, according their experience, does not have clinical significance. If the cross-reactions are possible the skin tests of alternative antibiotics and drug administration titrated with a gradual increase in dose are recommended [6].

Additional therapy of AR to antibiotics includes supportive and symptomatic drugs. For example, antihistamines and topical corticosteroids improve skin symptoms. Anaphylactic reactions require immediate administration of epinephrine intramuscularly. In case of severe systemic AR intravenous corticosteroids are used.

Identifying allergic history to penicillin requires mandatory confirmation via skin or provocation tests, because degradation AR and update tolerance of antibiotic is eventually possible.

On the other hand, doctors and patients overestimate AR, often focusing on the medical history, resulting in a violation of standards of infectious diseases treatment, particularly community-acquired pneumonia (CAP), reducing the effectiveness of therapy, lengthening hospitalization, unnecessary polypharmacy

Own data about AR to antibiotics

We conducted a study to establish the prevalence of AR to antibiotics at the in-patients treated due to CAP, to assess their impact on disease treatment.

The study included 2024 patients treated in clinical therapeutic departments of the city hospitals during 2004, 2005, 2006, 2011, and 2012, respectively. Males were in 1028 (50,79 %), female – 996 (49,21 %), the average age of patients – $52,32 \pm 18,14$ years. Most patients suffering from CAP of III group – 1880 (92,9 %), severe disease (IV group) was observed in 144 (7,1 %) patients. Concomitant diseases were 1509 patients (74,6 %). Cardiovascular (1046 (51,7 %) patients), respiratory (274 (13,5 %) patients), digestive (214 (10,5 %) patients) systems was dominated. The incidence of other chronic diseases accounted for less than 5 %.

The prevalence of AR to antibiotics was assessed by collecting history of hypersensitivity to these drugs, performing prick skin tests with antibiotics and taking into account the features of AR to a drug that has emerged during treatment for CAP.

Peculiarities of CAP in patients with AR to antibiotics were determined by comparing the clinical symptoms, laboratory and instrumental examination data, course of the disease under the treatment and outcome.

Accordance prescribed antibiotic therapy to national guidelines for CAP treatment and its effectiveness.

AR to antibiotics was found in 16 individuals, representing 0,79 % of the total number of patients. AR occurred more frequently in women – 15 (93,8 %) than in men – 1 (6,2 %) ($p = 0,024$).

In most of patients there were medical history of hypersensitivity to antibiotics – 15 (93,8 %) patients were confirmed by skin tests. In one patient AR to ceftriaxone was identified only by the skin test. The vast majority of AR was determined to use penicillin – 14 (87,5 %) patients. Polyvalent AR, which included intolerance cephalosporins, tetracycline, co-trimoxazole, was observed in one patient.

Clinically AR manifested with urticaria 8 people (50 %), maculopapular rash was in 4 patients (25 %). Bronchial obstructive syndrome occurred in 4 (25 %) patients.

Symptoms of CAP in patients with AR to antibiotics did not have clinical features compared with other patients. However, if they had AR duration of ambulatory treatment before hospitalization was shorter.

Calculating risk of negative outcome of CAP according to PSI scale found that most patients with AR (11 (68,8 %)) belonged to class 2, and severity of CAP allowed them to be treated as outpatients. Hospitalization in this group of patients can be considered justified as having a risk of immediate-type

AR to antibiotic patient requires careful supervision of medical personnel and create conditions for emergency assistance in the life-threatening AR.

The average length of inpatient treatment in the event of AR was higher than in their absence – $15,50 \pm 1,19$ days against $11,86 \pm 0,18$ days ($p < 0,001$).

The choice of antibacterial therapy in most cases accorded to recommendations of clinical guidelines for the treatment of CAP. Third generation Cephalosporins received 12 (75,0%) patients, macrolides – 5 (31,2 %) patients, levofloxacin – 3 (18,8 %) patients. The guidelines recommended combination antibiotics were prescribed the half of patients. Inadequate treatment: a combination of third generation cephalosporin with amikacin received 2 (12,5 %); gatifloxacin and metronidazole – 1 (6,3 %) patient. Other patients received only one antibiotic, and in one case, despite the presence of allergy to penicillin in history, appeared safe and effective use of amoxicillin / clavulanate.

Initial antibiotic therapy proved ineffective in 7 (43,75 %) patients. They needed a change of antibiotics. Drugs of second line were fluoroquinolones, the third and fourth cephalosporins generation, amikacin.

We did not observe any negative reactions to cephalosporins in patients with confirmed AR by skin tests to penicillin, despite the fact that their use in these patients is three times higher risk of adverse side effects to antibiotics [29, 39].

In our investigation the duration of hospitalization of the patients with AR to antibiotics was longer, due to inefficacy of the initial therapy in 43,8 % and patients need repeated courses of alternative antibiotics, mainly fluoroquinolones.

Similar results were received by Macy E et al (2013) who compared antibiotic treatment of persons with allergy to penicillin or without it using case-control method. In case of allergy patients were often treated with fluoroquinolones, clindamycin, vancomycin, length of hospitalization was longer by 9,9 %. Using alternative antibiotics often associated with *C. difficile* infection in 23,4 %, methicillin resistant *S.aureus* 14,1 %, vancomycin-resistant Enterococci 30,1% [27].

Analysis of compliance with recommendations for diagnostics and management of patients with allergy to antibiotics, conducted by British researchers Satta G. et al, showed that all patients were questioned about the presence of allergy. However, signs of an allergic reaction and its severity were described in 52% of cases. Only one patient with history of penicillin hypersensitivity was performed diagnostic skin tests. If patients had penicillin allergy and required antibiotic therapy alternative antibiotics were prescribed. It caused almost doubled increase of treatment cost compared with patient without allergy [41].

Conclusion

Despite the fact that the prevalence of AR to antibiotics remains at 0,1 % to 10 %, there is a tendency to reduce the frequency of cross-reactions in the group of beta-lactam antibiotics, especially the last generations. It has been found that eventually AR to antibiotics may be negated, allowing safe use of these drugs in patients with the AR in the past, after a specific allergy tests.

The most informative diagnostic methods for AR to antibiotics are skin and provocation tests. The use of provocative tests, can not only detect the AR, but it is one of the methods to overcome them.

According to our study the presence of AR to antibiotics, mainly to penicillins, confirmed by skin tests, leads to inappropriate antibiotic use with lower efficiency of initial therapy and prolongation of hospitalization.

Monitoring AR to antibiotics, standardized approaches to their detection using skin and provocation tests will effectively diagnose and control these dangerous conditions.

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АЛЛЕРГИЯ НА АНТИБИОТИКИ: МИФЫ И РЕАЛИИ

А. В. Демчук

Резюме

Аллергические реакции (АР) на антибиотики являются одной из наиболее частых причин сенсибилизации к лекарственным средствам. Они редко встречаются при использовании макролидов, фторхинолонов, цефалоспоринов 2–4-й генерации. Применение природных пенициллинов приводит к реакциям гиперчувствительности как немедленного, так и замедленного типов в 10 % назначений. По данным последних исследований уменьшается количество перекрестных реакций в группе β -лактамов антибиотиков, что подтверждается аллергологическими тестами и позволяет их безопасно использовать даже у пациентов с аллергией в анамнезе.

С целью установить распространенность АР на антибактериальные препараты у пациентов, лечившихся по поводу негоспитальной пневмонии (НП) в условиях стационара, оценки их влияния на течение заболевания проанализировано лечение 2024 больных (мужчин 1028 (50,79 %), средний возраст — $(52,32 \pm 18,14)$ года).

АР на антибактериальные препараты были выявлены у 16 (0,79 %), преимущественно у женщин — 15 (93,8 %). Анамнестические данные о гиперчувствительности к антибиотикам у 15 (93,8 %) подтвердились кожными тестами, АР на пенициллины наблюдались у 87,5 %. Поливалентная АР с непереносимостью цефалоспоринов, тетрациклина, ко-тримоксазола наблюдалась у одной пациентки. Симптоматика НП у лиц с АР

на антибиотики не имела никаких клинических особенностей в сравнении с другими пациентами. Средняя продолжительность стационарного лечения при АР была дольше, чем при их отсутствии — $(15,50 \pm 1,19)$ против $(11,86 \pm 0,18)$ дня ($p < 0,001$), что обусловлено неэффективностью первичной антибиотикотерапии у 43,75 %. Перекрестных АР на цефалоспорины и защищенные пенициллины у тех, кто имел сенсибилизацию к пенициллинам, не наблюдали.

Мониторинг АР на антибиотики, стандартизированные подходы к их выявлению с использованием современных тестов позволяют эффективно диагностировать и контролировать эти опасные состояния.

Ключевые слова: аллергические реакции, антибиотики, гиперчувствительность, аллергологические тесты.

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ANTIBIOTIC ALLERGY: MYTHS AND REALITY

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Summary

Allergic reaction (AR) to antibiotics is one of the most frequent causes of sensitization to drugs. They are rarely seen during macrolides, fluoroquinolones, cephalosporins generation 2–4 using. But prescription of natural penicillin causes hypersensitivity reactions immediate or delayed type in 10 %. According to recent studies the number of cross-reactions in the group of beta-lactam antibiotics are reduced that is confirmed with allergy tests and allows safely use them at the patients with allergic history.

With purpose to establish the prevalence of AR to antibiotics at the in-patients treated due to community-acquired pneumonia (CAP), to assess their impact on disease treatment 2024 patients (1028 males (50,79 %), mean age — $(52,32 \pm 18,14)$ years) were analyzed.

AR to antibiotics were detected in 16 (0,79 %), mainly women — 15 (93,8 %). Anamnestic data about hypersensitivity to antibiotics was at 15 (93,8 %) and confirmed by skin tests, mostly to penicillins (87,5 %). Polyvalent AR with intolerance of cephalosporins, tetracycline, co-trimoxazole, was observed at one patient. Symptoms of CAP at the patients with AR to antibiotics did not have any clinically significant features compared with other patients. The average length of hospital staying in case of AR was higher than of their absence — $(15,50 \pm 1,19)$ days against $(11,86 \pm 0,18)$ days ($p < 0,001$), due to the ineffectiveness of initial antibiotic therapy at 43,75 %. Cross-AR to cephalosporins and penicillins by the persons who had sensitization to penicillin was absent.

Monitoring AR to antibiotics, standardized approaches to their detection using modern test will effectively diagnose and control these dangerous conditions.

Key words: allergies, antibiotics, hypersensitivity, allergological tests.

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