



REVIEW ON ALLERGY TO BETA-LACTAM ANTIBIOTICS IN CHILDRENS

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❖ ABSTRACT:-

Antibiotic is the most important prescribed drug for children and relevant number of prescriptions are associated with the emergency of adverse events .Allergic reaction are most frequently reported adverse event with an incident of up 10% of all prescriptions. The judicious use of antibiotics to compact infections in children relies upon appropriate selection of an agent dose and duration to maximum efficacy and to minimize toxicity . Critical to dose optimization is an understanding of the pharmacokinetics and pharmacodynamics of available drugs optimal dosing strategies may take advantage of pharmacokinetics / pharmacodynamics (PK/PD) principles so that antibiotics dosing can be individualized to assure effect of the bacterial killing in the patients who have altered pharmacokinetics or who have infections will less susceptible or resistant organisms.

Finally age, sex, personal history of atopy , number of reactions for beta-lactams and number of reactions to other drugs were not significant risk factors for beta-lactams allergies.

❖ INTRODUCTION :-

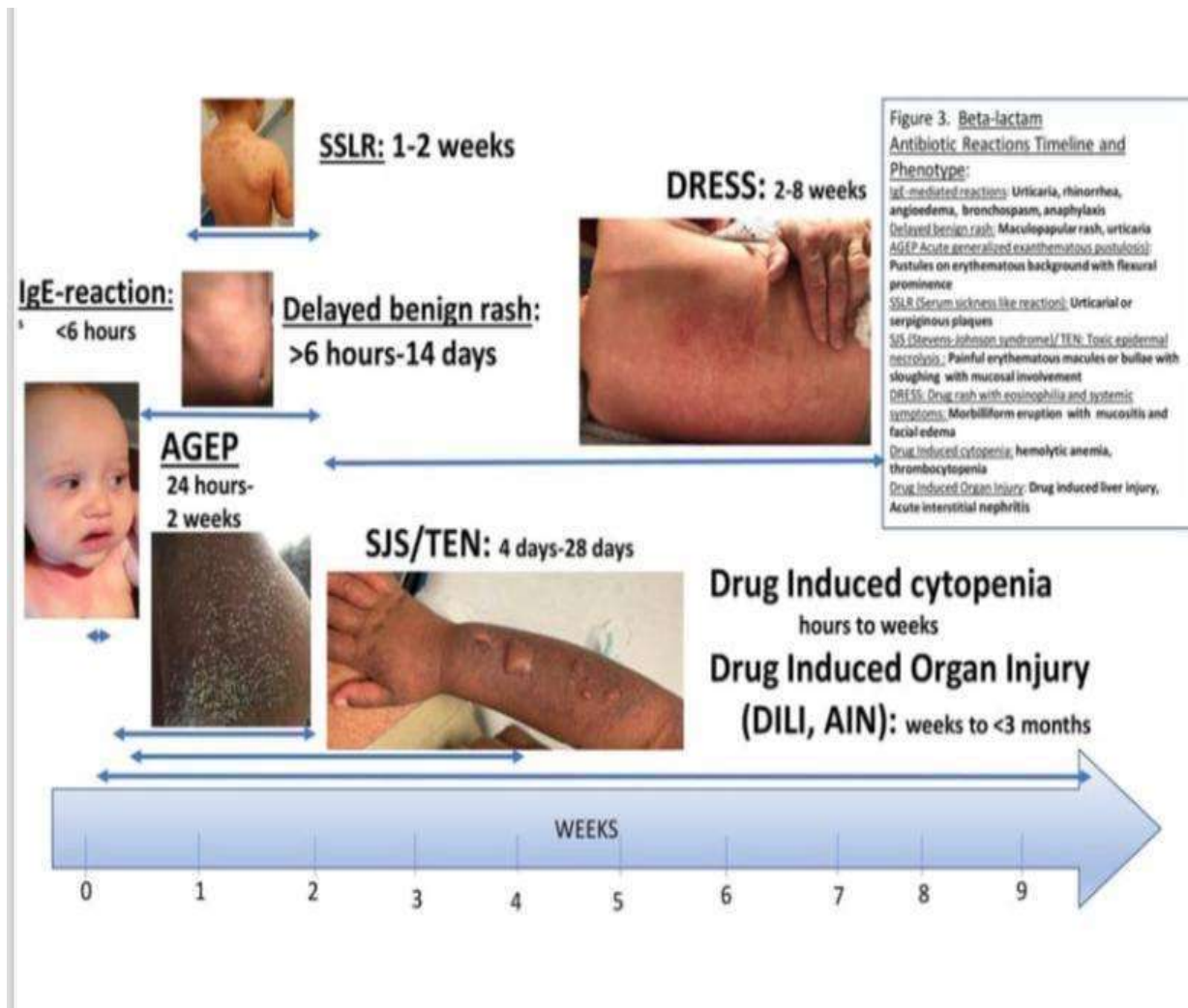
Antibiotics are compounds produced by bacteria and fungi which are capable of killing, or inhibiting, competing microbial species. This phenomenon has long been known; it may explain why the ancient Egyptians had the practice of applying a poultice of moldy bread to infected wounds. But it was not until 1928 that penicillin, the first true antibiotic, was discovered by Alexander Fleming, Professor of Bacteriology at St. Hospital in London

❖ KEYWORDS:-

Beta lactams, Types of beta lactam, allergies of beta lactam, skin test, material and method.

ALLERGY OF BETA LACTUM:-

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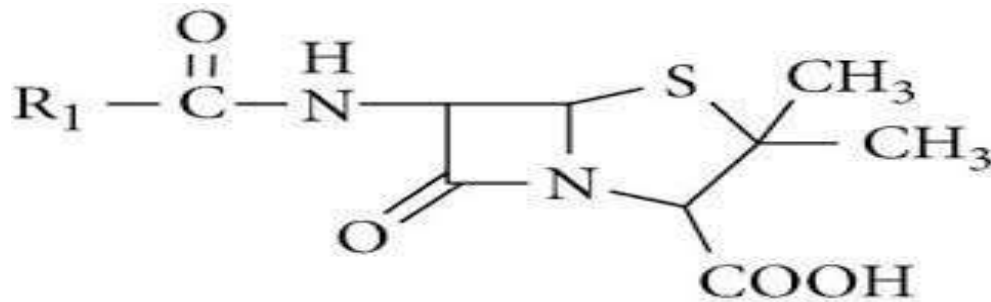


- Penicillin allergy- patients with positive DAP test penicillin G skin test and/or penicillin v provocation test, were accepted as penicillin allergy.
- Cephalosporin allergy- patient whose sensitivity was shown with cephalosporin with a skin test or provocation tests and whose penicillin skin and provocation test were found to be negative with all reagents were accepted as cephalosporin allergy.
- Beta-Lactam antibiotics are bactericidal agents that interrupt bacterial cell-wall formation as a result of covalent binding to essential penicillin-binding proteins (PBPs), enzymes that are involved in the terminal steps of peptidoglycan cross-linking in both Gram-negative and Gram-positive bacteria. Every bacterial species has it

■ TYPES OF B LACTUM ANTIBIOTICS :-

Beta-lactam antibiotics are classified into five major classes based on their chemical structure:

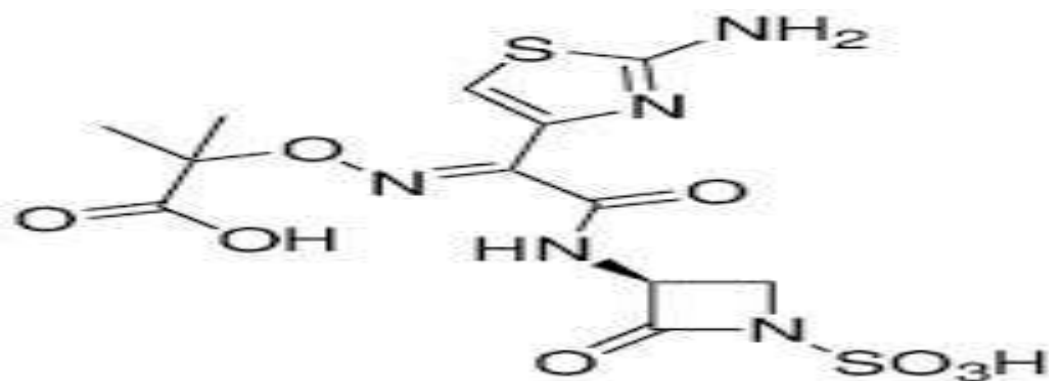
1. Penicillins: A naturally occurring compound derived from the Penicillium fungus



2. Cephalosporins: A class of cephem-based antibiotics originally derived from the Cephalosporium fungus

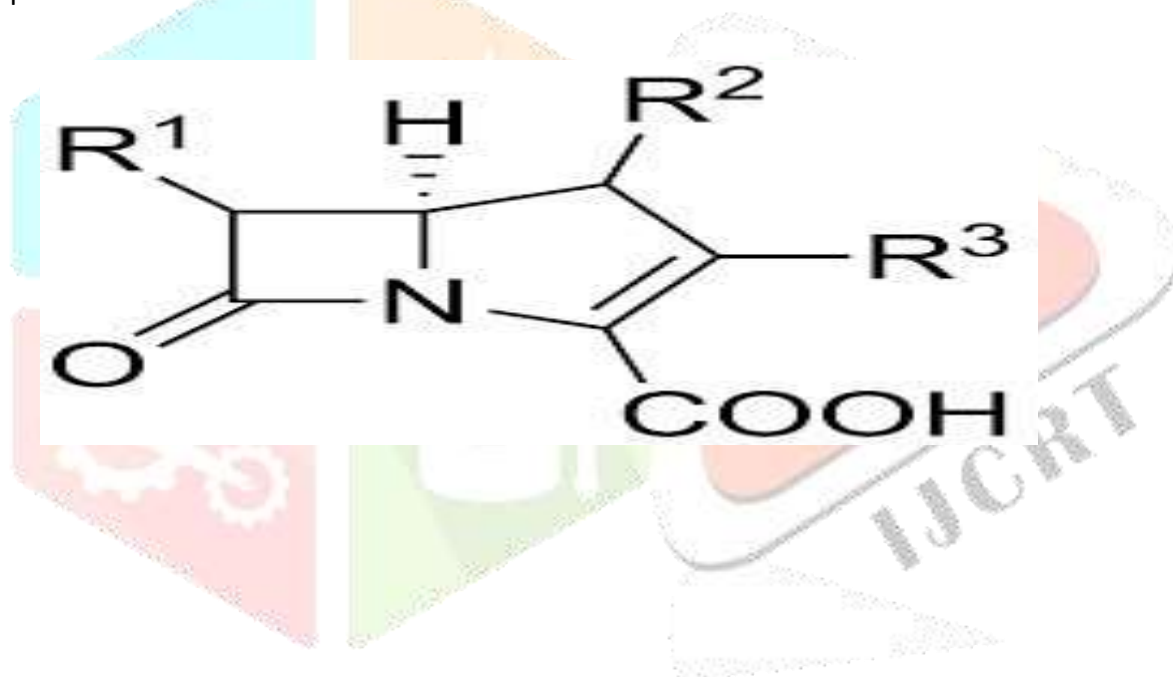


3. Monobactams: Contain no second ring system besides the beta-lactam ring

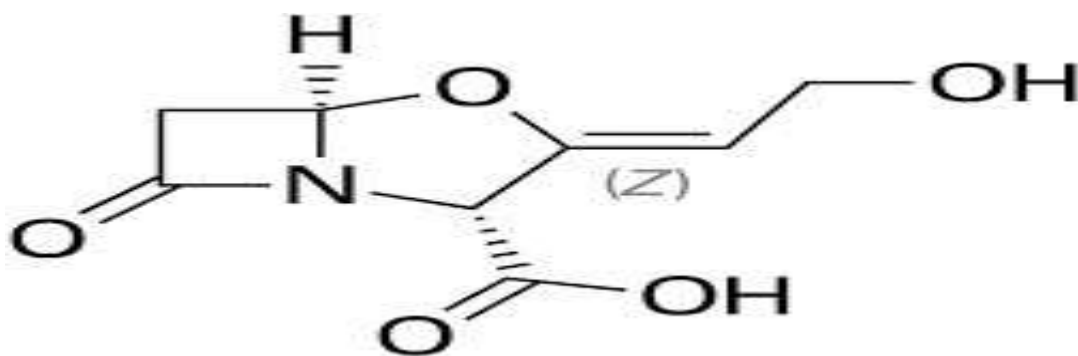


11, Aztreonam

4. Carbapenems: A class of beta-lactam antibiotics



5. Clavams: A class of beta-lactam antibiotics

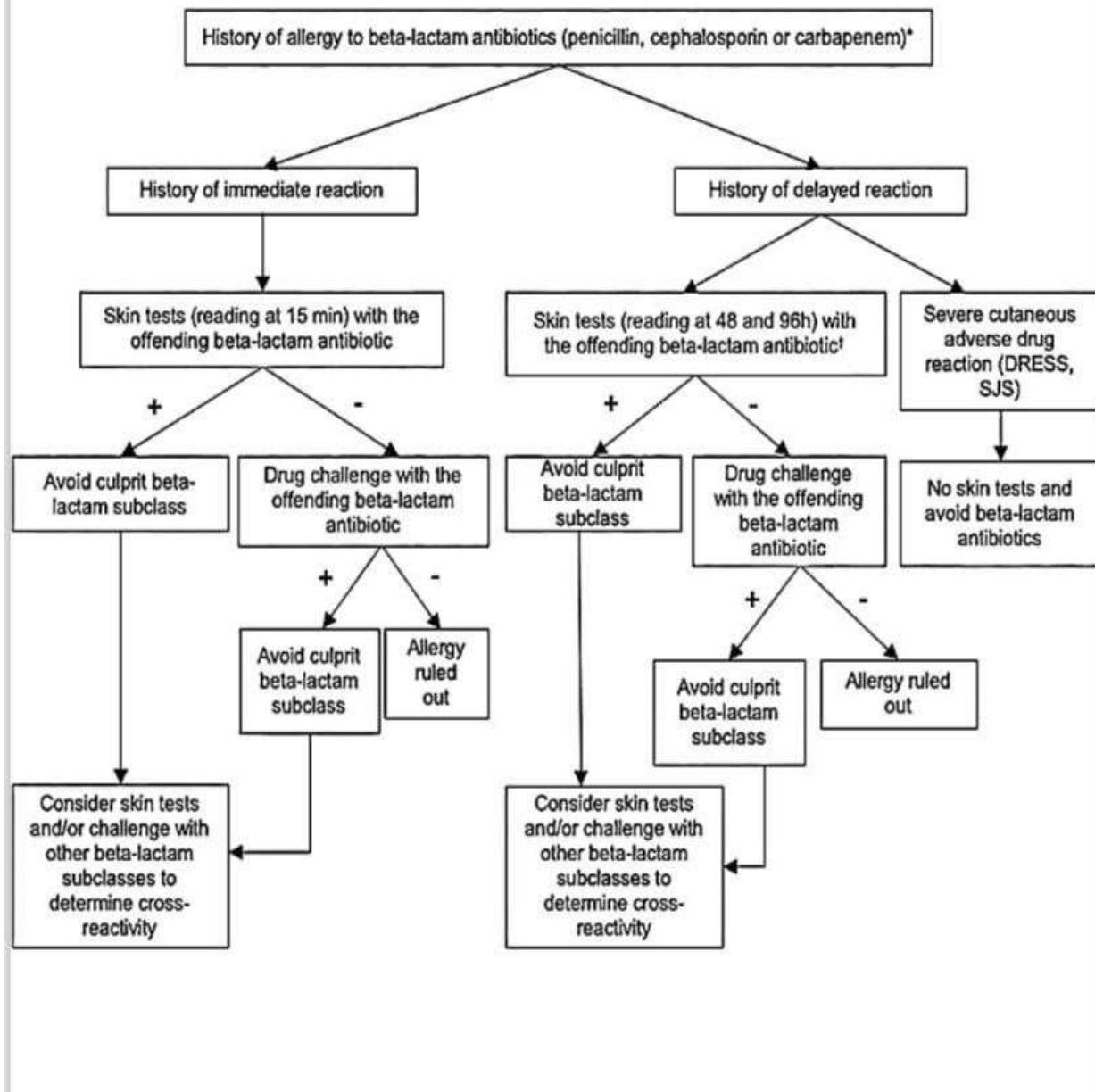


Fleming noticed that mold growing on a Petri dish of Staphylococcus bacteria prevented the bacteria from growing. He identified the mold as belonging to the Penicillium genus, and named the substance penicillin.

Cephalosporins are a type of beta-lactam antibiotic, which means they have a beta-lactam ring in their chemical structure.

They are structurally similar to penicillins, and some people who are allergic to penicillins may also be allergic to certain cephalosporins.

- Monobactams are a type of β -lactam antibiotic that are produced by bacteria, such as Pseudomonas and Bacillus. They have a monocyclic beta-lactam structure, which means the β -lactam ring is not fused to another ring.
- Carbapenems are effective against many types of bacteria, including streptococci, enterococci, staphylococci, Listeria, Enterobacteriaceae, and many Pseudomonas, Bacteroides, and Acinetobacter species.



■ MATERIALS AND METHODS:-

The authors conducted a six-year study on children under 18 years old who were referred to CUF Descobertas Hospital's Drug Allergy Center in Lisbon, Portugal, with probable hypersensitivity to BL. Patients were evaluated by an allergist in our outpatient clinic and referred to the Drug Allergy Center if they had a clinical history indicating allergy to BL. reactions. The diagnostic procedures followed the ENDA/EAACI (European Network of Drug Allergy/European Academy of Allergy and Clinical Immunology) recommendations

Clinical files contained clinical data that included a thorough explanation of the symptoms and reaction situations. Certain IgE assays, skin prick tests, and intradermal testing were conducted in consideration of the children's ages and the given clinical history. An oral drug challenge was conducted if everything came out negative or if there was little reason to suspect anything. In accordance with the Helsinki Declaration,

all legal guardians signed an informed consent form after being fully told about the procedures, including the risks and potential negative reactions. The diagnostic procedures followed the ENDA/EAACI (European Network of Drug Allergy/European Academy of Allergy and Clinical Immunology) recommendations

- In vitro tests:- were conducted using serum-specific IgE antibodies for ampicillin, amoxicillin, and penicillin G/V (ImmunoCAP®, Thermo Fisher Scientific, Waltham, MA,USA).

A cut-off value of ≥ 0.35 kU/L was taken into consideration for positive, and assays were conducted at least four weeks following the clinical reaction.

- In-vivo test:- The in vivo investigation began with skin prick tests (SPT), followed by intradermal testing (IDT) based on the children's age. Skin tests were performed using daily prepared solutions of benzylpenicilloyl octa-l- lysine (PPL) (5×10^{-5} mM) and sodium benzylpenilloate minor determinant (MD) (2×10^{-5} mM) (DAP® Penicillin, Diater, Madrid, Spain), penicillin G (25,000 IU/mL), amoxicillin (25 mg/mL), clavulanic acid (CLV) (2.5 mg/mL), and cefuroxime (2.5 mg/mL). Other medicines, including penicillin derivatives and cephalosporins, were tested based on the suspicion.

IDT was performed on patients exhibiting symptoms consistent with severe responses, starting with ten times more diluted solutions and progressively increasing them until a positive skin response appeared or until the maximal concentration mentioned above was reached. For SPT, a positive control of histamine (10 mg/mL) and a negative control of 0.9% saline solution were employed. At least four weeks following the clinical reaction, skin tests were conducted.

For SPT and IDT, the initial measurements were obtained after 15 and 20 minutes, respectively. The volar forearm was used for both examinations. A positive SPT result was defined as a mean wheal more than 3 mm, accompanied by erythema, and a

negative reaction to negative control. IDT was carried out by injecting 0.02–0.05 mL of the hapten solution, which raised a tiny, initially marked wheal. An increase in the initial wheal area's mean diameter of more than 3 mm was deemed beneficial in IDT. Every patient was made aware of the potential for a delayed reaction within a 24- to 48-hour period, and a delayed reading was collected, especially in cases where there was a high suspicion of non mediated reaction

- Drug provocation tests (DPTs) :-Following skin tests, patients were given oral challenges with the suspected medication, regardless of previous negative SPT and IDT results. For children under six years old with low clinical suspicion and negative specific Ig E tests and SPT, an oral challenge with the culprit medicine was used instead of IDT .n-immediate reactions.

❖ CONCLUSION:-

Finally, prolonged challenge test (full therapeutic dose · several days) may be performed at home in the children reporting mild to moderately severe non-immediate reactions to beta lactams, provided that the children have been prescribed an emergency treatment (oral anti histamine and/ or Corticosteroid)

Skin tests and DPT appear to be useful procedure in the diagnosis, and determination of an alternative

safe antibiotic in patients with beta lactam allergy. Most the patient tolerate the drug. A majority of the patients with confirmed allergy should all beta lactam antibiotic due to probability of cross reactivity.

REFERENCES:-

1. Abe Y, Wakabayashi H, Ogawa Y, Machida A, Endo M, Tamai T, Sakurai S, Hibino S, Mikawa T, Watanabe Y, et al. 2016. Validation of cefazolin as initial antibiotic for first upper urinary tract infection in children. *Global Ped Health* 3: 1–7. [DOI] [PMC free article] [PubMed] [Google Scholar]
2. Abraham EP. 1987. Cephalosporins 1945–1986. *Drugs* 34: 1–14. [DOI][PubMed] [Google Scholar]
3. Torres MJ, Blanca M, Fernández J, Romano A, Weck A, Aberer W, et al. ENDA and the EAACI interest group on drug hypersensitivity. Diagnosis of immediate allergic reactions to beta-lactam antibiotics. *Allergy*. 2003;58:961---72.
4. Romano A, Torres MJ, Castells M, Sanz ML, Blanca M. Diagnosis and management of drug hypersensitivity reactions. *J Allergy Clin Immunol*. 2011;127 3 Suppl.:S67---73
5. Thakuria B, Lahon K. The Beta Lactam Antibiotics as an Empirical Therapy in a Developing Country: An Update on Their Current Status and Recommendations to Counter the Resistance against Them. *J Clin Diagn Res*. 2013 Jun;7(6):1207-14. [PMC free article] [PubMed]
6. Ibrahim ME, Abbas M, Al-Shahrai AM, Elamin BK. Phenotypic Characterization and Antibiotic Resistance Patterns of Extended- Spectrum β -Lactamase- and AmpC β -Lactamase-Producing Gram- Negative Bacteria in a Referral Hospital, Saudi Arabia. *Can J Infect Dis Med Microbiol*. 2019;2019:6054694. [PMC free article] [PubMed]
7. Probst-Kepper M, Geginat G. [New Antibiotics for Treatment of Highly Resistant Gram-negative Bacteria]. *Anesthesiol Intensivmed Notfallmed*
8. Misirlioglu ED, Guvenir H, Toyran M, Vezir E, Capanoglu M, Civelek E, et al. Frequency of selective immediate responder to aminopencillins and cephalosporins in Turkish children. *Allergy Asthma Proc*. 2017;38:376– 82. doi: 10.2500/aap.2017.38.4065. [DOI] [PubMed] [Google Scholar]
9. Schmerzther. 2018 Jul;53(7-08):529-542. [PubMed].
- 2023). "Structural Insights for β -Lactam Antibiotics". *Biomol Ther (Seoul)*. 31 (2): 141–147. doi:10.4062/biomolther.2023.008. PMC 9970833. PMID 36788654.
9. Kim D, Kim S, Kwon Y, Kim Y, Park H, Kwak K, Lee H, Lee JH, Jang KM, Kim D, Lee SH, Kang LW (March Zambonino MA, Corzo JL, Munoz ~ C, Requena G, Ariza A, May-orga C, et al. Diagnostic evaluation of hypersensitivity reactions to beta-lactam antibiotics in a large population of children. *Pediatr Allergy Immunol*. 2014;25:80---7.
10. Manuyakorn W, Singvijarn P, Benjaponpitak S, Kamchaisatian W, Rerkpattanapit T, Sasisakulporn C, Jotikasthira W. Skin testing With lactam antibiotics for diagnosis of-lactam hypersensitivity in children. *Asian Pac J Allergy Immunol*. 2016;34:242---7.
11. Ponvert C, Perrin Y, Bados-Albiero A, Le Bourgeois M, Karila C, Delacourt C, et al. Allergy to beta lactam antibiotics in children :results of a 20-year study based on clinical history, skin challenge tests. *Pediatrics Allergy Immunol*. 2011;22:411---8.