Drug allergy testing

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ABSTRACT

Drug hypersensitivity reactions (DHRs) refers to a specific immunologically mediated drug reactions (involve antibodies and lymphocytes) and occurred on re-exposure. It is classified as immediate reactions (IRs) (1-6 hours after drug intake) presented as urticaria, angioedema and anaphylaxis and nonimmediate reactions (NIRs) (>1 hour after drug intake), induce reaction such as maculopapular exanthema (MPE) or fixed drug eruption (FDE), severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS) or drug induced liver disease (DILI). It can be classified as allergic and non-allergic reactions. Allergic reactions are mediated by a specific immune response to a drug acting as hapten that can lead to all types of Coombs and Gell-mediated immune reaction: types I (IgE mediated, produced by B cells), type II (IgG/IgM-mediated cytotoxicity), type III (immunocomplex) and IV (T cell-mediated). The most common are type I and IV, involved in IRs and NIRs, respectively. Non-allergic reactions occurred after drug interaction with mast cells, basophils, and neutrophils through mechanisms such as:1) Over-inhibition of COX-1 inhibition (pharmacological effect) in non-steroidal anti-inflammatory drugs reactions; or 2) Direct stimulation such as the Mas-related G-protein receptor (MRGPRX2) on mast cells by neuromuscular blocking agent (NMBAs). There are 3 main processes by which T cells are stimulated by drug :1) Hapten concept: Haptens are chemically reactive small compounds that bind to peptides to form hapten-carrier complexes (HPC). This HPC presented as hapten-modified peptides to react to T cells; 2) Pro-hapten concept: Pro-haptens are not chemically reactive and cannot form a covalent bond with a peptide. They need to be metabolized to convert into active hapten compound or 3) Pi Concept (pharmacology interaction): A direct pharmacology interaction with immune receptor T cell (TCR) which activate immune cells and cause inflammatory reactions. The following may be used for diagnostic tests: 1) Skin prick test and intradermal are useful for diagnosis of IgE-mediated (Type I) reaction, 2) The measurement of serum Tryptase levels proved useful in confirming acute IgE-mediated reactions in anaphylaxis, 3) Drug patch test to drugs is useful for diagnosis of delayed reaction (Type IV) cutaneous reactions especially to exanthemata but not useful for bullous eruptions (SJS/TEN), 4) Potential role of basophil activation test (BAT) in diagnosis of acute allergic reaction, 5) Potential role of lymphocyte transformation test (LTT) for delayed hypersensitivity and cutaneous drug eruption, 6) Drug provocation test (oral challenge and intradermal test) would be the gold standard and 7) Recently HLA typing has provided an important tool for testing susceptible patient population with certain drug allergy.