

Recent development of antihistamines

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It has been more than a century since Sir Henry Hallet Dale found the role of histamine in allergic reactions including anaphylaxis. Afterwards, numerous antihistamines have been developed. Nowadays, antihistamines become one of the most widely distributed medications in the world and nearly everyone has ever taken it in his/her life. Histamine has four receptors, designated as H1R, H2R, H3R, and H4R. H1R is mainly involved in allergic response and widely expressed in central nervous system (CNS) neurons, smooth muscle cells, endothelial cells, epithelial cells and a variety of immune cells. It is thus not surprising that the H1R antagonists, namely the H1-antihistamines, are the main treatment in allergic rhinitis, allergic conjunctivitis, acute/chronic urticaria, etc. H1-antihistamines are broadly divided into 1st and 2nd generation based on their potential to cross the blood brain barrier to produce unwanted sedative effect. The 2nd generation H1-antihistamines are associated with minimal CNS penetration and recognized as non-sedating. The GA2 LEN (Global Allergy and Asthma European Network) task force therefore prefers 2nd generation H1-histamines in the treatment of allergic diseases.

There are several newer 2nd generation H1-antihistamines in the drug market in recent decades. In addition to comparable and even superior efficacy to other 2nd generation H1-antihistamines, the requirement for newer antihistamines includes no cardiotoxicity, no interaction with cytochrome P450 (CYP) enzymes, no positron emission tomography [PET]-determined cerebral H1-receptor occupancy [H1RO] and no adverse CNS effects (no or minimal subjective sleepiness, and no impairment of objective cognitive and psychomotor functions). Exploring the development of the newer H1-antihistamines, we can better understand what is expected for an ideal H1-antihistamine.