다발성경화증 치료제의 작용기전

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Mechanism of Drugs for Multiple Sclerosis

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The disease mechanism of multiple sclerosis (MS) involves inflammation, demyelination and neurodegeneration. Variety of cellular and humoral immunological abnormalities have been observed in MS, therefore, there are multiple therapeutic targets for MS. The five key targets of immunopathogenic process for MS treatment is; (1) T cell activation and differentiation to Th1 cell (2) Proliferation of activated Th1 cells (3) Recruitment of B cells and monocytes by activated Th1 cells (4) Activated Th1 cells trafficking across the blood-brain barrier (BBB) (5) T cell reactivation and induction of immune cell-mediated demyelination.
Interferon beta (INF β) preparations and glatiramer acetate (GA) are approved for relapsing MS firstly. INF β potentially affects processes (1) to (5), and GA affects (1) and (5). INF β reduces BBB disruption and modulates T cell, B cell, and cytokine functions, whereas GA probably stimulates regulatory T cells. These immunomodulators affect a greater number of immunopathogenic processes than monoclonal antibodies. Alemtuzumab and natalizumab are new monoclonal antibodies that act on processes (1) and (4), respectively. Mitoxantrone is an immunosuppressive drug and the only agent approved to treat secondary progressive PMS. Mitoxantrone have broad cytotoxic effects on B cells, T cells, and macrophages. This suppresses the pathogenic immune response in MS with high efficacy but is also associated with high toxicity, limiting the long-term use of these agents. Recently, three oral agents are approved for relapsing MS. Fingolimod interferes with a S1P mechanism that lymphocytes use to exit lymph nodes. Teriflunomide exerts immunological effects by inhibiting dihydroorotate dehydrogenase, an enzyme required for de novo pyrimidine synthesis in proliferating (but not resting) cells. The mechanism of dimethyl fumarate action has not been completely elucidated, but it is known to activate the nuclear-related factor 2 transcriptional pathway, which reduces oxidative cell stress, as well as to modulate nuclear factor κB, which could have anti-inflammatory effects.
In this session, we will discuss about drugs for MS with their mechanism of action according to immune pathogenesis of MS and review some interesting articles. New drugs have been developed on the basis of the knowledge of the immune pathogenesis of MS and advances in understanding of mechanism will further increase treatment options for patients and physicians.

Key Words: Multiple sclerosis, Immunopathogenesis, Treatment

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