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Therapeutic Usefulness of Mast Cell-Stabilizers in Chronic Kidney Disease

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Summary

Mast cells, which are also of hematopoietic origin, produce pro-inflammatory cytokines in addition to their exocytotic release of chemokines. Recent studies also revealed that mast cells produce fibroblast growth factors in certain pathological conditions, such as chronic inflammation, and thus facilitate the progression of organ fibrosis. Using rat models with chronic renal failure (CRF), we have recently demonstrated that mast cells do not increase, nor are they activated in the fibrotic kidneys of CRF. However, in the fibrotic peritoneum of CRF rats, they proliferated *in situ* and increased their activity to produce fibroblast-activating factors. Since treatment with tranilast, one of the potent mast cell-stabilizers, actually ameliorated the progression of peritoneal fibrosis, mast cells were thought to be responsible for the progression of peritoneal fibrosis in CRF.

According to previous patch-clamp studies, including ours, the exocytotic process in mast cells was continuously detected electrophysiologically by the changes in the membrane capacitance (Cm). In our recent patch-clamp study using rat peritoneal mast cells, anti-allergic drugs, such as olopatadine and loratadine, significantly suppressed the increase in the Cm and directly inhibited the process of exocytosis, indicating their high potency as “mast cell-stabilizers.” Morphologically, these drugs actually induced inward membrane bending of mast cells and counteracted the cellular surface deformation induced by exocytosis. Together with our *in vivo* evidence, the studies strongly suggested the therapeutic usefulness of targeting mast cells in the treatment of organ fibrosis with chronic diseases, in addition to the treatment for allergic disorders.