Modulation of tryptase release from human tonsil mast cells by protease inhibitors

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Abstract:
AIM. To examine the influence of protease inhibitors on tryptase release, and as a comparison the influence of the inhibitors on histamine secretion was assessed. METHODS. Enzymatically dispersed cells from human tonsil were challenged with anti-IgE or calcium ionophore A23187 (CI) in the absence or presence of the tryptase and chymase inhibitors, and tryptase and histamine release was determined. RESULTS. IgE-dependent tryptase release from dispersed tonsil mast cells was inhibited by a maximum of approximately 35.5% and 35.7% by N-α-p-tosyl-L-lysine chloromethyl ketone (TLCK) and N-tosyl-L-phenylalanyl chloromethyl ketone (TPCK), respectively. The similar degree of inhibition of CI-induced tryptase release was observed also with these two inhibitors. Preincubation of TLCK or TPCK with cells at 37°C for 20 min before addition of the stimulus improved slightly their ability to inhibit anti-IgE and CI-induced tryptase release. Protamine showed dual action on tryptase release from tonsil mast cells. The concentration-dependent inhibition of anti-IgE and CI-induced release of histamine from tonsil mast cells was also observed with TLCK, TPCK and protamine. The maximum inhibition of anti-IgE-induced histamine release was approximately 26.6%, 30.8% and 30.1% with TLCK, TPCK and protamine, respectively. At the concentrations tested, TLCK and TPCK by themselves did not stimulate tryptase and histamine release from tonsil mast cells. CONCLUSION. It was demonstrated that protease inhibitors were able to inhibit IgE-dependent tryptase release from human tonsil mast cells, which suggests strongly that they can be developed to a novel class of anti-inflammatory drugs to treat allergic conditions in man.

Key words: tryptase, histamine, mast cell, anti-IgE, protease inhibitor