In vitro effect of histamine on monocyte chemotaxis

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Histamine has been reported to be a selective chemoattractant for eosinophils^{1,2)}, to modulate eosinophil migration³⁾ and to inhibit basophil chemotaxis⁴⁾ by interacting with H₁- and H₂-receptors. Furthermore, neutrophil chemotaxis is inhibited by histamine, an effect associated with elevated levels of intracellular cAMP⁵⁾. However, the effects of histamine on monocyte migration mediated by chemoattractants have not been investigated.

Therefore, the effects of histamine, diphenhydramine, the H₁-receptor antagonist, and cimetidine, the H₂-receptor antagonist, to attract human monocytes as measured by chemotaxis, were tested.

The chemotaxis of human peripheral blood monocytes was performed with the membrane filter method⁶⁾. Human peripheral blood from healthy adult donors was drawn into a heparinized syringe (final concentration 20 units/ml). The monocytes were separated by Ficoll-Paque (Pharmacia), washed with phosphate-buffered saline (pH 7.2) and the mononuclear cells containing approximately 28% monocytes were suspended at 5×10^6 cells/ml in Gey's balanced salt solution containing 2% bovine serum albumin and 20 mM HEPES (Nakarai) and added to the upper wells of the micro-chemotaxis chambers (Neuro Probe). The cells were separated from 10^{-8} M FMLP (Sigma) and the samples to be tested of the lower wells by a 5 μ m polycarbonate membrane filter (Neuro Probe). After a 90 min incubation at 37°C in a humidified incubator, the filters were removed from the chambers, stained and quantified. Chemotactic activity was ex-

pressed as the mean number of migrating cells per oil immersion field of triplicate samples ± 1 SE by counting the number of monocytes that had migrated through the filter at 20 random oil immersion fields for each sample. Histamine (Nakarai) as the varying concentrations of 10^{-7} M to 10^{-4} M resulted in a significant inhibition of monocyte chemotaxis at 10^{-5} M, and at 10^{-6} M, inhibition was frequently noted (Fig. 1).

The effect of histamine on tissues can be blocked by antagonists that are thought to bind to two classes of cell surface receptors for histamine, which are designated H₁ and H₂⁷⁾.

To determine if monocytes have a surface receptor for histamine, the effects of the H₁-receptor antagonist, diphenhydramine, and the H₂-receptor antagonist, cimetidine upon histamine-induced inhibition of monocyte chemotaxis was examined.

The depressed monocyte chemotaxis in the presence of 10^{-5} M histamine was restored by the addition of 10^{-5} M cimetidine (Smith, Kline & Fujisawa).

However, there was no effect by 10^{-5} M diphenhydramine (Iwaki) of histamine-induced inhibition of monocyte chemotaxis to FMLP (Table 1), and at 10^{-4} M of diphenhydramine tested gave the same results. In addition, diphenhydramine or cimetidine alone did not affect monocyte chemotaxis.

It was concluded that histamine-induced inhibition of monocyte chemotaxis mediated by chemoattractant depend on the H₂-receptors, since the action of histamine was reversed by H₂ but not by H₁-receptor antagonist.

Fig. 1

Table 1 Effects of Histamine, Diphenhydramine and Cimetidine on Monocyte Chemotaxis

Agent added	Monocyte Chemotaxis (cells/oil immersion field ± 1 SE)
Control	10 ± 2
FMLP	109 ± 1
FMLP + Histamine 10 ⁻⁵ M	39 ± 3
FMLP + Histamine 10 ⁻⁵ M + Diphenhydramine 10 ⁻⁵ M	42 ± 4
FMLP + Histamine 10 ⁻⁵ M + Cimetidine 10 ⁻⁵ M	101 ± 6

Thus, histamine would be involved in the modulation of monocyte chemotaxis in the inflammation such as gingivitis.

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