Increased Microvascular Permeability Induced by Eosinophil Proteins

M.		Minnicozzi ^a
G.J.		Gleich ^b
W.N.		Durán ^c
R.W.		Egan ^a

^aSchering-Plough Research Institute, Kenilworth, N.J., ^bMayo Clinic, Rochester, Minn., and ^cNew Jersey Medical School, Newark, N.J., USA

Key Words

Eosinophil
Granule proteins
Inflammatory reactions
Microvascular permeability

Correspondence to: Dr. Michael Minnicozzi, Schering-Plough Research Institute, 2015 Galloping Hill Road, Kenilworth, NY (USA)

Eosinophils can contribute to inflammatory reactions by releasing four arginine-rich granule proteins, major basic protein (MBP), eosinophil cationic protein (ECP), eosinophil peroxidase (EPO); and eosinophil-derived neurotoxin (EDN) [1]. We used intravital microscopic, fluorometric and immunologic methods to assess the effects of topical application of either MBP, ECP, EPO, or EDN on the hamster cheek pouch microcirculation [2]. The plasma clearance of FITC-dextran 150 was used to quantify changes in vascular permeability. MBP at 0.1 and 0.5 nM caused a substantial increase in the clearance of FITC-dextran 150. Furthermore, 0.5 nM MBP caused vasodilation and muscle fasciculation. ECP but not EPO at 0.5 nM was as effective as MBP at increasing microvascular permeability. However, 0.5 nMEPO supplemented with 1 nMH202 significantly increased the clearance of FITC-dextran 150. The remaining granule protein, EDN, required a 2,000-fold higher concentration (1 μ M) to effect an increase in microvascular permeability. Neither ECP, EPO, EPO + H202, nor EDN elicited vasodilation or muscle fasciculation. Quantitative analysis of the suffusate, using a competitive enzyme immunoassay, showed no detectable histamine release after treatment with any of the eosinophil proteins. Furthermore, pretreatment of the cheek pouch preparation with a nitric oxide synthase inhibitor (L-NAME) did not demonstrably effect the clearance of FITC-dextran 150 provoked by 0.5 nM MBP. Therefore, very low concentrations of eosinophil granule proteins can increase microvascular permeability, which is independent of histamine release or the generation of nitric oxide and is not strictly dependent on the cationic charge of the protein. Our results support the importance of these proteins in promoting the pathophysiology observed in eosinophil-associated diseases.

References

Hamann KJ, Barker RL, Ten RM, Gleich GJ:

The molecular biology of eosinophil granule proteins. *Int Arch Allergy Appl Immunol* 1991; 94:202–209.

Svensjö E: The hamster cheek pouch as a model in microcirculation research. *Eur Respir J* 1990; 3:595–601.