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Meeting abstract

The role of prostacyclin in the interaction of endothelial cells and eosinophil granulocytes

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Background

Enhanced eosinophil migration from the blood into the tissue is a hallmark of bronchial asthma and other allergic diseases. So far, very little is known how the function of vascular endothelial cells is modulated in this process. Our aim was to characterize the role of prostacyclin (PGI_2) in endothelial function and endothelium-eosinophil interaction.

Materials and methods

Cell interaction studies, like adhesion and transmigration assays, were performed with freshly isolated human blood eosinophils on confluent layers of human lung microvascular endothelial cells. The changes in endothelial monolayer integrity were detected by means of transendothelial electrical resistance and by fluorescence microscopy.

Results

Under basal conditions, the major prostaglandin released by human microvascular endothelial cells is PGI_2. Exogenous PGI_2 markedly attenuated the migration of isolated eosinophils through cell-free filters. This effect was prevented by the IP receptor antagonist Cay10441 and the adenylyl cyclase inhibitor SQ29548. Treatment of endothelial cells with diclofenac, a non-selective COX inhibitor, abolished the PGI_2 production which was accompanied by enhanced eosinophil adhesion to endothelial monolayers. Similarly, the transmigration of eosinophils through endothelial monolayers was enhanced by diclofenac. The diclofenac treatment itself decreased the electrical resistance of endothelial monolayers and compromised the intercellular cell junctions as visualized by VE-cadherin staining.

Conclusion

Based on these observations, we conclude that the basal synthesis of PGI_2 by endothelial cells can down-regulate the endothelial adhesion and transmigration of eosinophils. Furthermore, endogenous PGI_2 seems to be important for the maintenance of endothelium barrier function. These results suggest that PGI_2 may have a protective role in the case of allergic inflammation and provide a novel explanation for previous observations that IP knock-out mice show enhanced eosinophilic inflammation in response to allergen [1].

References

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