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The effect of substance P on the secretion of interleukin-8 and MCP (Monocyte Chemoattractant Protein)-1 from human dental pulp cells

Sang-Hyuk Park*, Gi-Woon Choi, Sang-Jin Park
Department of Conservative Dentistry, College of Dentistry, Kyung-Hee University, Seoul, Korea

I. Objectives

Neurogenic inflammation has been recognized to play an important role in initiating and sustaining of pulp inflammation. The pulpal innervation may modulate several aspects of the inflammatory response via secretion of neuropeptides. In this present study, these neuropeptides that may be questioned about roles in recruiting leukocytes by inducing the release of the chemokine IL-8 in the pulp during inflammation were tested. The response of human pulp cells in releasing IL-8 after the stimulation with SP and/or CGRP were investigated.

II. Material and Method

The purpose of the present study was to examine the coordinate activity between neuropeptide and cytokine, and their important role in sensing and eliciting rapid immune response to the external irritations to the dental pulp. For the purpose, the induction of the IL-8 and MCP-1 by the stimulation of neuropeptide in the pulp cells and endothelial cells(ECV304 cells) was done in the dose dependent manner and in the course of time. The specificity in the dental pulp cells and endothelial cells(ECV 304 cells) was measured using Spantide(SP antagonist). In addition, the secretion of the IL-8 and MCP-1 in the human dental pulp tissue was measured after the stimulation of SP and TNF-α(IL-8 agonist).

III. Results

1. When SP concentration was higher than 10^{-8} M, IL-8 secretion from human dental pulp cells was significantly increased comparing to mock stimulation($p<0.05$). And IL-8 secretion from human dental pulp cells at 10^{-4} M of SP was significantly higher than lower concentration of SP (10^{-5} to 10^{-8} M)($p<0.05$).
2. SP(10^{-5} M) stimulation of the human dental pulp cells to secrete IL-8 and MCP-1 was inhibited by Spantide(10^{-5} M).
3. When the human dental pulp cells were stimulated by CGRP(10^{-4} M) , IL-8 secretion was not increased, and synergistic induction of IL-8 with SP(10^{-5} M) plus CGRP(10^{-5} M). There was no synergistic induction of MCP-1 from human dental pulp cells with SP(10^{-5} M) plus CGRP(10^{-5} M) comparing with SP(10^{-5} M) only.
4. There was only mild induction of IL-8 and MCP-1 in the endothelial cells(ECV304 cells).
5. SP stimulation of endothelial cells(ECV304 cells) to secrete IL-8 and MCP-1 was inhibited. by Spantide.
6. Pulp cells were stimulated with SP(10^{-4} M) at every 4 hours during 24 hours in the course of time, and IL-8 secretion was measured, which increased at 4 hours and reached the maximal level at 8 hours($p<0.05$), MCP-1 secretion was maximum at 8 to 12 hours of SP stimulation(10^{-4} M).
7. 36 hours after the pulp tissues were stimulated with SP(10^{-4} M), There was minimal increase of IL-8 secretion, and no increase of MCP-1 secretion at the stimulation with SP(10^{-4} M), whereas a minimal increase of MCP-1 secretion at the stimulation with TNF-α(40 ng/ml) stimulation, there was no significant difference.

IV. Conclusions

These results suggest that SP played an important role of IL-8 and MCP-1 induction from human dental pulp cells, but CGRP did