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Vitamin D3 Treatment Decreases Frequencies of CD16-Positive and TNF-α-Secreting Monocytes in Asthmatic Patients

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Description

Previously, we demonstrated that glucocorticoid (GC) treatment of asthmatic patients resulted in decreasing frequencies of monocyte subsets expressing CD16 and capable of releasing TNF-α. Here, we wished to analyze whether active form of vitamin D (vitamin D_3, 1,25-$(OH)_2D_3$) can exert GC-like proapoptotic effects on CD16-positive monocytes and thus decrease proinflammatory potential of these cells. Finally, we set out to investigate whether the addition of 1,25-$(OH)_2D_3$ would facilitate use of lower GC doses without decreasing their antiinflammatory properties.

Peripheral blood mononuclear cells collected from healthy individuals and asthmatic patients were cultured with 1,25-$(OH)_2D_3$ and/or varying doses of GC in presence or absence of caspase inhibition. Cells were either directly stained for extracellular markers or prestimulated with lipopolysaccharide for assessment of intracellular cytokine production and then analyzed by flow cytometry.

We found that 1,25-$(OH)_2D_3$ alone (and in combination with GC) decreased frequency of CD14++CD16+ and CD14+CD16++ monocytes from asthmatic patients and significantly diminished TNF-α production by monocytes. With regard to the CD14+CD16++ subset, monocyte-depleting effects of 1,25-$(OH)_2D_3$ were abrogated in the presence of pan-caspase inhibitor, suggesting proapoptotic mechanism of 1,25-$(OH)_2D_3$ action. Interestingly, we found that combined treatment of 1,25-$(OH)_2D_3$ and GC allowed for 5-fold reduction of the GC dose while maintaining their anti-inflammatory effects.

This study has revealed novel immunomodulatory properties of 1,25-$(OH)_2D_3$ directed against monocyte subsets capable of TNF-α production. In addition, our data suggest that introduction of 1,25-$(OH)_2D_3$ to antiinflammatory therapy would possibly allow for use of lower GC doses.