Increased circulating fibrocytes in asthmatic patients with severe OSA – the role of HIF1-α and HDAC7

Department of Thoracic Medicine, Chang Gung Memorial Hospital, Taipei, Taiwan
Tsai-Yu Wang, Yu-Lun Lo, Chun-Hua Wang, Han-Pin Kuo

Background: Some asthmatic patients presents with airway remodeling, which CTGF, ET_AR plays an important role on. In addition, severe obstructive sleep apnea (OSA)-related hypoxia is reported to accelerate airway remodeling. We hypothesized that OSA-related hypoxia may result in increased expression of CTGF, ET_AR, HIF-1α on circulating fibrocytes.

Methods: To compare the proportion, proliferation, and differentiation of circulating fibrocytes from asthmatic patients with severe OSA or without severe OSA, we investigated circulating fibrocytes in 13 asthmatic patients with severe OSA and 11 asthmatic patients without severe OSA. Fibrocytes expressing ET_AR and CTGF were identified by flow-cytometry. Circulating fibrocytes were incubated with ET_AR antagonist, CTGF inhibitor, HIF-1α siRNA and HDAC7 siRNA. The expression of HIF-1α and HDAC7 were identified by confocal microscopy.

Results: A higher percentage of circulating fibrocytes was found in asthmatic patients with severe OSA. The slope of the yearly decline in FEV1 correlated with circulating fibrocytes. The ET_AR and CTGF expression of circulating fibrocytes was also elevated in asthmatic patient with severe OSA. Moreover, CTGF inhibitor inhibited fibrocytes transformation. The expression of HIF-1α significantly increased in asthmatic patients with severe OSA. In addition, the expression of HIF-1α significantly increased under hypoxic chamber and the expression can be attenuated by HIF-1α siRNA, which affected co-transportation of HIF-1α and HDAC7 in the nucleus resulting in CTGF expression.

Conclusion: Circulating fibrocytes are increased in asthmatic patients with severe OSA, which may contribute to airway remodeling.

中文題目：氣喘合併嚴重阻塞性睡眠呼吸中止症的病人血液中纖維細胞增加

作　　者：王才郁* 羅友倫 王圳華 郭漢彬

(報告者請以*表示， 如梁信杰*)

服務單位： 林口長庚醫院胸腔內科