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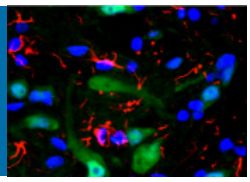

Review

Progress of IL-10 related to the cerebral ischemia stroke

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Abstract: Acute pulmonary edema and pneumonia after cerebral ischemia stroke is a major cause of mortality. However, little is known about the mechanisms leading to acute lung injury. Interleukin-10 (IL-10), known as human cytokine synthesis inhibitory factor, is an anti-inflammatory cytokine and participates in many disease processes. Here, we summarized the literatures about the IL-10 and brain ischemia and aimed for getting more information of their relationship.
Key words: Interleukin-10; Brain ischemia; Acute pulmonary edema

Introduction

Interleukin-10 (IL-10), known as human cytokine synthesis inhibitory factor (CSIF), is an anti-inflammatory cytokine. This cytokine is produced primarily by monocytes and to a lesser extent by lymphocytes. This cytokine has pleiotropic effects on immunoregulation and inflammation (Eskdale J, et al., 1997).Acute pulmonary edema and pneumonia after cerebral ischemia stroke is a major cause of mortality (Chen GF, et al., 1989). However, little is known about the mechanisms leading to acute lung injury (ALI).

Expression of IL-10 in lung

In order to demonstrate a rapid up-regulation of the immunomodulatory neuropeptide MSH in the lung within 24h after cerebral ischemia. One research divided 30 male mice into 4 groups: sham operating group, control group(treated with BSA), α-MCH group(treated with α-MCH) and agouti group(treated with agouti, antagonist of α-MSH receptor-1). Then, the mice in control group, α-MCH group, agouti group were established a stroke model (MCAO), mice was sacrificed after 24 hours, and the lung and spleen was removed. The ability of lung macrophages and spleen to secrete TNF-α, MCP-1, IL-10, IFN-γand IL-4 was evaluated by measuring concentration of cytokines in culture supernatants using the CBA Mouse Inflammation Kit and the CBA Mouse Th1/Th2 Kit. Compared with the control group, lung macrophages' secretion ability of IL-10 was up-regulated (Schulte-Herbrüggen O, et al., 2008). But the relationship of IL-10 and ALI post stroke is still a mistery.

IL-10 in Brain after BI

Previous studies showed that the increased IL-10 level in brain after acute ischemia stroke might have neuroprotective effect.

In an experiment from USA, the effects of the anti-inflammatory cytokine, IL-10, on brain injury following permanent focal ischemia were studied. Rats subjected MCAO were administered IL-10 centrally into the lateral ventricle 30 min and 3 hours post MCAO or systemically into the tail vein starting 30 min post MCAO for 3 h. Brains were removed 24 hours later and infarct size was measured. IL-10 administered centrally significantly reduced the infarct size. Systemic IL-10 administration decreased the infarct size. These studies indicated that IL-10 can provide neuroprotection in ischemic stroke (Patricia A, et al., 1998).

Another clinical research from Switzerland shown simial conclusion. Transgenic mice expressing murine IL10 (IL10T) directed by the major histocompatibility complex Ea promoter were produced and used to explore the effect of chronically increased IL10 levels on MCAO-related molecular mechanisms. IL10 was over-expressed in brain cells in IL10T compared with wild type mice. The main finding of this study was that the in vivo endogenous over-expression

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of IL10 markedly protected cortical tissue against cerebral ischemia. This neuroprotective effect was associated to the reduced activity of the pro-apoptotic protein caspase 3 (Fabienne De Bilbao, et al., 2009).

A research from Portland about the function of B-cell limiting CNS inflammation and neurologic deficits in murine experimental stroke proved that IL-10-secreted WT B-cells decreased the infarct volume, mortality rate, recruitment of inflammatory cells and neurological functional deficits at 48h after MCAO. They evaluated the contribution of B-cells to the development of MCAO by comparing infarct volumes and functional outcomes in WT versus B-cell deficient μMT-/-mice. These MCAO-induced changes were completely prevented in B-cell restored μMT-/- mice after transfer of highly purified WT GFP + B-cells which were detected in the periphery, but not the CNS. In contrast, transferring of B-cells from IL-10-/-mice into μMT-/-mice had no effect on infarct volume (Kozaburo Akiyoshi,et al.,2011).

IL-10 in serum after BI

On the contrary, the up-regulation of IL-10 in serum will activate early endogenous immunosuppressive and increase the risk of early infection.

In a clinical research, researchers try to investigate the pathophysiology of stroke-associated infection (SAI) and assess the cytokine profile and peripheral white cell response in patients with or without SAI. Patients (N=110)with ischemic stroke allocated antibiotic prophylaxis or placebo within 24h of clinical onset. Peripheral white cell counts, IL-6, TNF-alpha and IL10 were measured in plasma. Seventeen patients (15%) developed infection with a time-dependent increases of total white cell count, neutrophils, monocytes, lymphocytes, IL6 and IL10, whereas TNF-alpha and the TNF-alpha/IL10 ratio decreased. In logistic regression, IL10, monocyte count and National Institute for Health Stroke Survey score on admission were independent predictors of systemic infection, which means SAI is associated with stroke severity, excessive IL10-mediated response and an increased number of circulating monocytes (Chamorro A,et al.,2006).

Another clinical research aim to examine the serum levels of 13 cytokines, CRP, glucose and hemoglobin in AIS patients, and their relationship with stroke lateralization, type and infarct volume. Forty-five patients with AIS were evaluated. Blood samples were taken within 72 h, and volumetric analyses performed within 1to 7 days after AIS onset. Cytokines were measured in serum from all patients and40 control subjects using Luminex Bio-Plex XMap technology. The levels ofIL-10 ($p = 0.001$) was significantly higher in the AIS patients than in the controls. Elevated levels of the anti-inflammatory cytokines IL-10 and IL-1α demonstrated early activation of endogenous immunosuppressive mechanisms after stroke (Heidi Ormstad,et al.,2011).

A Germany clinical PANTHERIS trail, in order to test the efficacy of short-term antibacterial therapy to prevent the development of post-stroke infections, researchers assessed longitudinal changes in lymphocyte sub-populations and mitogen-induced lymphocytic interferon gamma (IFN)-γ production using flow cytometry in 80 patients with acute severe stroke at days 1, 3, 8, 90 and 180 after clinical onset. Plasma IL-6 and IL-10 concentration as well as urinary levels of norepinephrine and cortisol were assessed within the first 8 days after stroke. Patients of the placebo and verum (moxifloxacin) treatment groups who did or did not develop infections within 11 days after stroke were compared to identify immunological changes associated with the occurrence of post-stroke infections. In result, an early rise of plasma IL-10 was detected in patients who developed infections despite having been with preventive antibacterial treatment (Klehmet J,et al.,2009).

Conclusion

The effect of secretion increased IL-10 by lung macrophages remains unknown while the pleiotropic effect in immunoregulation and inflammation of IL-10 might be a double-edged sword i.e. advantageous and harmful after acute brain ischemia.

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Conflict Interests

No conflict of interest

Reference

Chamorro A, Amaro S, Vargas M, Obach V, Cervera A, F Torres, A M Planas. Interleukin 10, monocytes and increased risk of early infection in ischaemic stroke.J Neurol Neurosurg Psychiatry 2006;77:1279–1281.

Chen GF,Tang XT. Clinical analysis of the elderly with acute cerebrovascular disease complicated by pneumonia. Chinese Journal of geriatric medicine 1989;8:43 - 44.

Eskdale J, Kube D, Tesch H, Gallagher G. Mapping of the human IL10 gene and further characterization of the 5' flanking sequence. Immunogenetics 1997;46 (2): 120–8.

Fabienne De Bilbao, Denis Arsenijevic, Thomas Moll, Irene Garcia-Gabay, Philippe Vallet1, Wolfgang Langhans, Panteleimon Giannakopoulos.In vivo overexpression of interleukin-10 increases resistance to focal brain ischemia in mice.Journal of Neurochemistry 2009;110:12–22.

Heidi Ormstad, Hans Christian Dalsbotten Aass, Niels Lund-Sørensen, Karl-Friedrich Amthor, Leif Sandvik. Serum levels of cytokines and C-reactive protein in acute ischemic stroke patients, and their relationship to stroke lateralization, type, and infarct volume,J Neurol 2011;258:677–685

Klehmet J, Harms H, Richter M, Prass K, Volk HD, Dirnagl U, Meisel A, Meise A.Stroke-induced immunodepression and post-stroke infections: lessons from the preventive antibacterlal therial therapy in stroke trial…Neuroscience 2009;158:1184 -1193.

Kozaburo Akiyoshi, Xuefang Ren, Suzan Dziennis, Arthur A. Vandenbark,Paco S. Herson, Patricia D. Hurn, and Halina Offner.Regulatory B-cells limit CNS inflammation and neurologic deficits in murine experimental stroke.J Neurosci 2011;23: 8556–8563.

Patricia A, Spera, Julie A, Ellison, Giora Z. Feuerstein, Frank C. Barone.IL-10 reduces rat brain injury following focal stroke.Neuroscience Letters 1998;251:189 - 192.

Schulte-Herbrüggen O, Quarcoo D, Brzoska T, Klehmet J, Meisel A, Meisel C.Alpha-MSH promotes spontaneous post-ischemic pneumonia in mice via melanocortin-receptor-1.Experimental Neurology 2008;210:731-739.

IL-10 与脑缺血脑卒中相关的研究进展

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[摘要]：急性肺水肿和肺炎是脑缺血卒中后死亡的主要原因。然而，导致急性肺损伤的机制尚不清楚。白细胞介素 -10 (Interleukin-10, IL-10) 是一种抗炎细胞因子，参与多种疾病过程，被称为人类细胞因子合成抑制因子。本文对有关 IL-10 与脑缺血的相关文献进行综述，旨在进一步了解 IL-10 与脑缺血的关系。

[关键词]：IL-10；脑缺血；急性肺水肿

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