Myasthenic crisis in patients with generalised myasthenia gravis

JCY Lee, SYY Pang, DCL Lam ACT Tse, KK Lau, SK Chang, SL Ho, RTF Cheung, WWW Mak, SFK Hon, CKL Chang, KC Teo, KH Chan
Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Introduction: Myasthenia gravis (MG) is an important autoimmune disease causing generalised weakness and even mortality, which is amenable to immunotherapies. Myasthenic crisis (MC) is the most serious presentation of MG typically requiring ventilator support under the care of intensive care unit. We studied factors which predict development of MC in generalised MG (gMG) patients and patients' serum cytokine levels as potential biomarkers for MG exacerbation and crisis.

Methods: Records of gMG patients being cared in Queen Mary Hospital and followed up in the neurology clinic from 1976 to 2013 were revealed. Sera / plasma taken during gMG exacerbation or crises and during follow-up from stable patients were assayed for inflammatory and anti-inflammatory cytokines levels by commercially available ELISA kit. Clinical outcome was classified according to the Myasthenia Gravis Foundation of America post-intervention status on latest follow-up.

Results: A total of 116 gMG (71.6% female) with a mean onset age of 44.8 (range, 7-83) years and mean disease duration of 7.8 (range, 1-36 years) were studied. 86.7% patients were acetylcholine receptor (AChR) autoantibodies positive, 39.3% patients had thymoma and 60.9% had thymectomy. 75% patients received immunosuppressants (corticosteroid and / or azathioprine, MMF, cyclosporin A) and 96.6% patients had satisfactory or good clinical outcome. MC occurred in 34 patients (29.3%) with a mean number of 1.9. Univariate analysis revealed that patients with MC had worse clinical severity on initial presentation (P = 0.000), increased frequencies of receiving thymectomy (76.5% vs 54.3%; P = 0.026), requiring immunosuppression (91.2% vs 68.3%; P = 0.010) than patients without MC, but are indifferent in sex, onset age, frequencies of having thymoma, positivity for Tensilon test, repetitive nerve stimulation, and AChR autoantibodies. There was no difference in long-term clinical outcome between patients with and without MC. Serum / plasma levels of interleukin-17A (IL-17A) [2.46 ± 1.19 pg/mL vs 0.063 ± 0.010; P = 0.033] and interferon-γ (IFN-γ) [8.88 ± 2.08 vs 4.35 ± 0.31; P = 0.023] were higher in patients in MG exacerbation or crisis than patients with stable disease.

Conclusion: Severe clinical weakness at disease onset may predict development of MC, and high serum / plasma levels of IL-17A and IFN-γ are biomarkers for disease exacerbation or MC in gMG.

Lipocalin 14 — a novel adipokine potentially protects mice from diet-induced diabetes

JTH Lee, Z Huang, CM Wong, KSL Lam, A Xu
Department of Medicine, The University of Hong Kong, Hong Kong

Introduction: Obesity is one of the leading causes of worldwide chronic non-communicable diseases. There is an urgent need to develop more effective therapies to combat the global pandemic of this costly disease. Previous studies in 2011 demonstrated that a newly identified lipocalin named as LCN13 have anti-diabetic activity by enhancing insulin sensitivity of liver and adipose tissues. In mouse, a putative lipocalin LCN14 are found to share high degree of homology with LCN13 (53% identity and 67% similarity). The role of LCN14 in metabolism remains to be explored.

Methods: Male wildtype C57BL/6N mice were fed with either high-fat diet or standard chow. After 16 weeks of diet treatment, the mice were sacrificed for sampling. LCN14 gene expression was detected by quantitative polymerase chain reaction analysis and protein expression of LCN14 in tissues and serum was detected by Western blotting and by enzyme-linked immunosorbent assay analysis with in-house–developed anti-LCN14 antibody.

Results: The putative lipocalin LCN14 had been experimentally proved as an adipokine. The expression of LCN14 was found to be regulated by feeding-fasting cycles in mouse. Circulating and expression level of LCN14 was found significantly repressed in the diet-induced obese and genetically diabetic-obese (db/db) mice.

Conclusion: LCN14 potentially protects mice from diet-induced diabetes by cooperating with LCN13. Both LCN13 and LCN14 are novel candidates for developing and screening of antidiabetic drugs.