

Trend of endovascular angioplasty and stenting in treating extracranial cerebrovascular steno-occlusive disease

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Introduction: Endovascular angioplasty and stenting for extracranial cerebrovascular disease is gaining popularity in recent years.

Methods: We retrospectively reviewed all extracranial cerebrovascular angioplasty procedures performed by the neurovascular team in our centre.

Results: From year 2005 to 2013, there were 71 extracranial cerebrovascular procedures performed in 63 patients (16 female; mean age, 67.5 years; range, 39-89 years), with 81 vessels treated. The number of procedure performed increased readily in recent years, with only 23 procedures done between 2005 and 2009, increased to 15 in 2010-11, and to 33 in 2012-13. The most common procedure performed was carotid artery stenting (CAS), with a total of 61 vessels stented. There was 15 vertebral artery stenting and 5 subclavian artery stenting. In nine procedures, multiple vessels stenting were performed in same session. All procedures were performed successfully, except in one case the procedure was terminated when the distal internal cerebral artery was found to be total occluded intra-operatively. There was no peri-operative transient ischaemic attack, stroke, myocardial infarction, or death. There were only one major peri-operative complication encountered. It was a transient period of profound bradycardia with hypotension shortly after bilateral CAS. There was one case of delayed hyper-perfusion syndrome. Both cases recovered completely without deficit. There were four cases of in-stent restenosis. All but one restenosis were asymptomatic.

Conclusion: Endovascular intervention had gained popularity for treatment of extracranial cerebrovascular stenotic disease. The procedure was of low risk (2.8%) with a high success rate. The restenosis rate was low (6.3%).

Adipocyte fatty acid-binding protein potentiates toxic lipids-induced endoplasmic reticulum stress via suppression of JAK2-dependent autophagy

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Introduction: Chronic inflammation is the key link between obesity and its related metabolic complications. Endoplasmic reticulum (ER) stress is the potent trigger of inflammation in obese adipose tissue but how ER stress in immune cells relates to inflammation is unclear. Adipocyte fatty acid-binding protein (A-FABP) regulates endotoxin-induced inflammation in macrophages by forming a positive feedback loop with c-Jun-N terminal kinase (JNK) which is the downstream regulator of ER stress. Defective autophagy is shown in obese liver which leads to insulin resistance and elevated ER stress. Here we investigate the role of A-FABP in association with autophagy in potentiating toxic lipids-induced ER stress in macrophages.

Methods: RAW264.7 macrophages infected with adenovirus-overexpressing A-FABP or luciferase or pre-treated with or without A-FABP inhibitor BMS3009403, and primary macrophages derived from A-FABP knockout mice or their wild-type littermates were treated with palmitic acid (PA) or vehicle. RAW264.7 macrophages were transfected with siRNA of autophagic protein Atg7 or scramble RNA followed by the stimulation of PA. Macrophages were treated with PA in the presence or absence of JAK2 inhibitor AG490. The autophagic flux, mRNA and protein expression of ER stress markers, autophagic proteins and inflammatory markers were determined by real-time quantitative polymerase chain reaction and western blot analysis.

Results: Over-expression of A-FABP potentiates PA-induced ER stress and inflammatory cytokine expression while BMS3009403 pre-treatment reverses the condition. PA-induced ER stress was alleviated in RAW 264.7 macrophages treated with BMS3009403 and A-FABP deficient macrophages and was accompanied by enhanced autophagic flux comparing to their relative controls. Suppression of autophagy in macrophages by knocking down the autophagic protein Atg7 enhanced PA-induced ER stress and inflammatory cytokine in macrophages. Treatment of AG490 reduced the autophagic protein expression while further enhanced the ER stress in response to PA stimulation. PA-induced activation of JAK2 was attenuated in the presence of A-FABP.

Conclusion: A-FABP potentiates toxic lipids-induced ER stress through inhibition of JNK-dependent autophagy in macrophages.

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