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Wuling Capsule Can Improve Cognitive and Depression Defects of Stroke

Idress Hamad Attitalla
Department of Microbiology, Faculty of Sciences, Omar Al-Mukhtar University, Box 919, Al-Bayda, Libya

Stroke is the impairment of brain's functions due to nerve injury. Sleep apnea syndrome and the use of non-steroidal anti-inflammatory drugs, which inhibit the cyclooxygenases, increase the risk of having stroke (Al-Turki *et al*., 2010; Yaggi *et al*., 2005). Stroke lowers the albumin levels in body, known as hypoalbuminemia, which results in high mortality rate of stroke patients (Vahedi *et al*., 2011). It was found in almost 75% of non-surviving stroke patients. Stroke has high risk in developing countries, where two-third of total stroke patients lives (Durai *et al*., 2007). Although, in some developing countries e.g. Iran, Pakistan, China, India etc., it has been treated with stroke thrombolysis, the high cost of therapy limits its efficiency. Most probably, after a stroke, patient gets depression which is called Post-stroke Depression (PSD), it results in cognitive as well as physical imbalance and mortality (Narushima and Robinson, 2002). Moreover, the depression itself through unknown mechanism increases the risk of stroke. The co-occurrence of depression and stroke cause high impairment in short or long distance walking and climbing (Goodwin and Devanand, 2008). These imbalances were independent to gender, age, race, educational and economic status. According to a study, polymorphism of Brain-Derived Neurotrophic Factor (BDNF) gene *val66met* increases the association of stroke and depression (Kim *et al*., 2008). The BDNF *val66met* has inhibitory effect on BDNF neuroprotective activity; an increase in its alleles increases the cognitive disorderness and chances of PSD. Moreover, BDNF has strong association with PSD; its level in serum of PSD patients was extremely lower than non-PSD patients, which could enhance the severity of stroke (Yang *et al*., 2011). The use of antidepressants can reduce the severity of stroke and depression. BDNF help in reducing the depression, its levels in mouse and neural stem cells were enhanced by the use of antidepressants (Blondeau *et al*., 2009). These higher BDNF levels increased the neurogenesis, glutamatergic neurotransmission proteins activity and expression of other proteins involve in signaling pathway of neurons. Thus the use of antidepressant can help in inhibiting the PSD related cognitive problems and may also help in reducing mortality.

Wuling capsule is a Chinese herbal medicine derived from mycelia of *Xylaria nigripes* in China. It has some sedative effects; it is well known for its depression and anxiety reducing abilities (Wang *et al*., 2009). Recently De-Qiang *et al*. (2011) examined its effects on hippocampal-dependant cognitive functions of PSD rats. To observe its antidepressant effects, wuling capsules (100 mg kg^{-1} b.wt.) and reference drug; escitalopram (0.2 mg kg^{-1} b.wt.) treated rats were subjected to unpredictable Chronic Mild Stress (CMS). These animals were then passed from different depression test and the effect of wuling capsule in comparison to non-CMS rats was examined. CMS caused the reduction in normal cognitive behaviors of rats, these rats showed less interest towards glucose in glucose preference test. But the application of wuling capsule improved these expressions and unlike non-antidepressant treated CMS rats, the wuling capsule treated CMS rats showed high preference to sucrose. Moreover its application was found effective in Morris Water Maze (MWM) test. As CMS rats without any antidepressant treatment showed memory impairments and lower efficiencies towards learning in MWM 120 sec test. These animals took large time to escape from water table, while wuling capsule treated CMS rats took least time to escape and in every trail they rapidly identified the location of escape platform. Thus the wuling capsule administration modulated the memory and learning tendencies of CMS rats. These cognitive and anti-depression effects of wuling capsules were non-significantly different from normal and escitalopram treated rats. But its mode of action did not involve any modification in BDNF production and its gene expression. The BDNF levels were lower in CMS rat's hippocampus, which were improved by the application of escitalopram. But the administration of wuling capsules did not improve these levels nor showed increment in BDNF mRNA level. Thus it followed any other pathway for antidepressant action, which was different from escitalopram mode of action. Its amino acid contents of glutamate and Gamma-Aminobutyric Acid (GABA) might be responsible for this. As its anti-depressant activity was associated with increased neural absorption of glutamate and enhanced activity of GABA synthesizing glutamate acid decarboxylase. Hence, wuling capsules showed potency to act as antidepressant for PSD rat; it improved the cognitive activity of brain by following a non-BDNF dependant pathway.

Stroke is a serious mortality causing disease in human beings. It is usually followed by state of depression (PSD) which accelerates the stroke causing cognitive impairments in patients, it also results in mortality. The stroke resultant problems e.g., cognitive disorders etc., are not affected by the age, gender, education and economic status rather it may be influenced by BDNF inhibitory genes. BDNF play an important role in reducing the neuronal injuries by activating various proteins and its activity can be increased by the use of antidepressants. According to De-Qiang *et al*. (2011) a Chinese medicine; wuling capsules acted as an antidepressant in PSD model rats suffering from CSM. It enhanced the memory and reduced the depression in tested animals, which was comparable to normal and escitalopram treated rats. But its mode of action did not involved the increased in BDNF concentration and expression of its mRNA. Instead it might be due to its glutamate and GABA composition. Hence it can be used to treat PSD and more investigation on its mode of action will help in elucidating its therapeutic mechanism.

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