P7-1

Selective brain perfusion does not affect cerebral F2-isoprostane generation during hypothermic circulatory arrest, but it increases systemic F2-isoprostane levels

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Purpose: This study assessed the hypothesis that selective antegrade brain perfusion during hypothermic circulatory arrest would decrease oxidative stress during circulatory arrest.

Material and methods: Pigs (n=14) were divided in three groups: extracorporeal circulation (ECC) with circulatory arrest at 20 °C (Group 1); ECC with circulatory arrest and selective brain perfusion at 20 °C (Group 2); ECC with circulatory arrest and selective brain perfusion at 28 °C (Group 3). Samples were taken in femoral artery and jugular bulb at ten time points. Oxidative stress was determined with 8-iso-$PGF_{2\alpha}$ measurements.

Results: 8-iso-$PGF_{2\alpha}$ increased during initial ECC (1.2-3fold); peaked during circulatory arrest with/without cerebral perfusion (2.5-5.4fold); decreased during reperfusion; and further decreased to the baseline after ECC. The rank order for 8-iso-$PGF_{2\alpha}$ levels in jugular bulb was: Group 1 > Group 2 > Group 3 (249±276 vs. 206±106 vs. 125±62 pg/ml). The rank order for 8-iso-$PGF_{2\alpha}$ concentrations in femoral artery was: Group 2 > Group 1 > Group 3 (208±12 vs. 140±133 vs. 105±87 pg/ml).

Conclusion: Oxidative stress occurred predominantly during ischemia, and not during ECC or reperfusion. Selective brain perfusion during circulatory arrest at 20 °C did not provide any benefit to the brain compared to circulatory arrest without brain perfusion, but it increased systemic oxidative stress.

P7-2

Elevated acute phase response proteins and oxidative stress in epilepsy

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Purpose: The purpose of this study was to investigate the interactions between oxidative status, inflammation and Haptoglobin (Hp) phenotypes in patients with epilepsy.

Material and methods: Subjects were epileptic patients and controls with no history of epilepsy, liver, or hemolytic disorders. Oxidative stress was assessed by measuring TBARS (colorimetric assay), 8-isoprostanes (immunoassay), Total Antioxidant Capacity (colorimetric assay) and b-Carotene (HPLC). Inflammation was assessed by measuring CRP and Ferritin (immunoassay). Hp phenotype was done by gel electrophoresis.

Results: Our results show that Hp2-2 phenotype was over-expressed in patients compared to that in control subjects. Plasma 8-isoprostane and TBARS were significantly higher in patients compared to controls ($p<0.001$) and ($p<0.05$), respectively. However, serum Total Antioxidant Capacity was lower in patients compared to controls ($p<0.001$). B-Carotene levels were not only lower in patients ($p<0.05$), but also there were significant differences among patients with different phenotypes; the highest levels in patients with Hp1-1 and the lowest in Hp2-2 group ($p<0.05$). Also, plasma CRP and ferritin were higher in patients compared to that in controls ($p<0.001$).

Conclusion: In conclusion, Hp2-2 may have a role in the etiology of seizures in epileptic patients by enhancing the oxidative stress and inflammation in the body.

P7-3

Thioredoxin protects neuronal cells from 6-hydroxydopamine-induced apoptosis via supressing JNK/p38 MAPK signaling and enhancing Akt activation

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Purpose: To explore if thioredoxin (Trx) could play any role in decelerating development of Parkinson's disease (PD) via reducing ROS generation and suppressing activation of ASK1-p38/JNK signaling.

Material and methods: Over-express and knockdown Trx in neuroblastoma SH-SY5Y cells by transfection with plasmid pcDNA3.0-thioredoxin-1 and the antisense oligonucleotides corresponding to Trx mRNA sequence respectively. Activity of JNK, p38, Akt and apoptosis were detected in those cells by immunoblotting, flow cytometry under various conditions.

Results: Overexpression of Trx effectively protects the cells from apoptosis through suppressing 6-hydroxydopamine-induced ROS generation and activation JNK/p38 MAPK signaling. Knockdown of Trx enhanced the apoptosis and activation JNK/p38 signaling. It was also found that overexpression of Trx attenuated, while knockdown of Trx enhanced the 6-OHDA-induced activation of Akt/PKB signaling, the major cell survival pathway. The selective Akt inhibitor, wortmannin or LY294002, enhanced the induced apoptosis more obviously in wild-type cells, but less significantly in the cells over expressing Trx. Antioxidant N-acetyl-cysteine was found to inhibit Akt activation in the 6-OHDA-stimulated cells.

Conclusion: The protective role of thioredoxin may largely due to inhibition of JNK/p38 apoptotic signaling. Inhibition of 6-hydroxydopamine-induced Akt activation may partly account for the protective effect of thioredoxin.

P7-4

Oxidative stress in stroke disease

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Purpose: It has been hypothesized that oxidative stress is a risk factor of diverse neurodegenerative diseases, which include stroke, Parkinson's disease, and Huntington's disease. Accumulation of reactive oxygen species and oxidative damage may lead to neuronal cell death and onset of these diseases. The definite evidence for such hypothesis is still lacking.

Material and methods: In the present study, we employed the biochemical analyses to determine the oxidative damage and antioxidant profiles in patients with ischemic stroke or intracranial hemorrhage. 8-Hydroxy-2'-deoxyguanosine (8-OHdG) and malondialdehyde (MDA) were measured by sensitive HPLC methods and used as oxidative damage markers. The antioxidants such as vitamin E and glutathione peroxidase also were evaluated in this study.

Results: It was found that the ischemic stroke or intracranial hemorrhage patients had significantly higher levels of 8-hydroxy-2-deoxyguanosine (8-OHdG) and malondialdehyde (MDA) than the control cohort. Interestingly, the plasma vitamin E concentrations in these patients were inversely correlated with their 8-OHdG levels.

Conclusion: These findings suggest that the ischemic stroke or intracranial hemorrhage patients suffer from increased oxidative stress.