S-N-6

EFFECTS OF ESTROGEN ON CATECHOL-O-METHYLTRANSFERASE (COMT)

Jiang Hong†, Feng Zhe-hui†, David Ramsden‡, Ho Shu-Leong† Division of Neurology, University Dept of Medicine, Queen Mary Hospital, The University of Hong Kong, and Dept of Medicine, University of Birnimgham‡, UK

COMT is a crucial enzyme in dopamine and levodopa metabolism. COMT inhibitors are effective adjunct therapy to Ldopa in Parkinson's Disease (PD). We have previously shown that 17β-estradiol can downregulate human COMT gene transcription via its promoter regions using CAT reporter activity assays. Purified antiserum containing human COMT antibodies developed using specifically designed oligopeptides injected into sheep, was used to carry out Western Blots. We showed that COMT protein expression was decreased in a dose-dependent manner in MCF-7 cells after exposure to physiologic concentrations of 17β-estradiol for 72 hours. A specific estrogen receptor antagonist (ICI 182780) blocked this estrogenic effect. Using a radioenzymatic assay, we further showed that COMT activity was similarly affected. We investigated the underlying mechanism of these estrogenic effects by characterizing the function of estrogen response elements (EREs) in the proximal promoter region by exploring their DNA-protein binding activities. Our gelshift assays showed that nuclear proteins from MCF-7 cells could specifically bind to our ERE1 or ERE2 probe. Preincubation of the nuclear protein with excess non-labeled probes or estrogen receptor (α and β) antibodies competitively inhibited this binding. Using semiquantitative gelshifts, we also showed that 17β-estradiol can increase estrogen receptor (ER)-ERE binding activity in a dose-dependent manner. We conclude that 17β-estradiol can decrease COMT protein expression and activity in a dose-dependent manner through estrogen receptors. These estrogenic effects were associated with a dose-dependent increase in ER-ERE binding. Our results can explain the worsening of motor control during menstruation in premenopausal PD patients, and after withdrawal of hormone replacement therapy in postmenopausal PD patients. It also suggests that estrogen can be a useful adjunct therapy for PD in postmenopausal women.

S-RC-1

NITRIC OXIDE (NO) LEVELS IN EXHALED AIR, SPUTUM, SERUM, SALIVA AND URINE OF BRONCHIECTASIS SUBJECTS: A COMPARISON STUDY

KWT Tsang, S Chan, P Fung, L Zheng, IHY Shum, R Leung, JCM Ho, S Ip, J Wang, WK Lam. *University Dept of Medicine, The University of Hong Kong, Hong Kong SAR.*

Endogenous NO has received tremendous attention in the last few years and promises to be a final common path for the pathogenesis of many respiratory, renal, neurological and liver diseases. Exhaled NO is increased in asthma but decreased in cystic fibrosis, cigarette smoking and HIV infection. However, the levels of NO in other body fluids including saliva, urine and serum have not been evaluated and compared with exhaled NO. We have, therefore, determined their correlation in a cohort of xx patients with stable bronchiectasis (xxF; mean age± SD 58.2± 14.1yrs; FEV_1 72.5± 28.9% pred; and FVC 81.5± 23.3% pred). Exhaled NO was measured by using a Sievers NO Analyser280 at a steady exhaled pressure of 20 torr with chemiluminescence. Body fluids NO contents were analyzed by measuring the total nitrate products, after de-proteinisation, using the same package. There were significant differences ($p<0.05$) between the exhaled NO (25.5± 21.8 units) levels compared with the simultaneous levels in serum (127.4± 94.3), sputum sol (1167.6± 1400), urine (2559.6± 4083.4), and saliva (3085.9± 3839.7). There no correlation between exhaled NO levels with those in the aforementioned bodily fluids. However, there was a positive correlation between the levels of NO between serum and sputum (r=0.51, p=0.0001), urine (0.56, 0.0001), and saliva (0.48, 0.0001). There was also a weaker correlation between the level of NO in sputum and urine (0.35, 0.003). Our results show, for the first time, the relationship between simultaneous levels of NO in exhaled air and other bodily fluids and should help researchers in future studies. (Supported by a CRCG Grant of the University of Hong Kong)