砷甲基化能力、胰島素受器基質-1 及磷脂醯肌醇-3 激酶;基因多形性與新陳代謝症候群

Arsenic Methylation Capability, Gene Polymorphisms of Insulin receptor substrate-1 and Phosphatidylinositol 3-kinase, and Metabolic Syndrome

中文摘要

本研究為瞭解砷甲基化能力、胰島素受器基質-1（Insulin receptor substrate-1, IRS-1）codon 972 和磷脂醯肌醇-3 激酶(Phosphatidylinositol 3-kinase, PI3-K)codon 326 基因多形性、抽菸及嚼食檳榔與新陳代謝症候群之相關性。進行一斷代研究係選擇參與嘉義縣巡迴複合式健檢的居民作為本研究之研究對象共 900 人，從中隨機選取 560 人進行基因多形性分析。經研究對象瞭解本研究目的並簽署同意書後，受過標準化問卷訓練的訪員以結構式問卷訪視研究對象，收集基本人口學、環境暴露、疾病史及生活型態等資料外，亦收集血液和尿液檢體。利用高效能液相層析儀接連氫化式原子吸收光譜儀依序分離與定量尿液中三價無機砷、雙甲基砷酸、單甲基砷酸及五價無機砷濃度。萃取血液中 DNA，利用聚合酶連鎖反應增幅特定序列及使用限制片段長度多形性方法分析 IRS-1 codon 972 和 PI3-K codon 326 之基因型。結果發現新陳代謝症候群盛行率為 28.89%，調整潛在干擾因子後，累積嚼食檳榔量>7.49 × 104 年顆數者比累積嚼食檳榔量 0 年顆數者新陳代謝症候群的危險性顯著增加，危險對比值為 1.97（95%信賴區間 1.05 - 3.70）。曾經有抽菸、有飲酒與有嚼食檳榔三項者比沒有抽菸、未飲酒和無嚼食檳榔者新陳代謝症候群的危險性邊緣顯著增加，危險對比值為 1.86（95%信賴區間 0.99 - 3.51）。總砷濃度、單甲基砷酸百分比、雙甲基砷酸百分比和二級甲基化指標依對照組三分位分層後，第二三分位者與第一三分位者相比，顯著增加新陳代謝症候群的危險性。IRS-1 codon 972 和 PI3-K codon 326 基因型與新陳代謝症候群的危險性無顯著相關。以未暴露任何一個危險因子為基準，有抽菸、有飲酒、有嚼食檳榔、砷甲基化能力差（單甲基砷酸百分比高、雙甲基砷酸百分比低和二級甲基化指標低）且攜帶 PI3-K codon 326 Met/Ile 或 Ile/Ile 基因型者新陳代謝症候群之危險性最高。

英文摘要

The cross-sectional study was conducted to explore the relationships among arsenic methylation capability, genetic polymorphisms of insulin receptor substrate-1 (IRS-1) codon 972 and phosphatidylinositol 3-kinase (PI3-K) codon 326, cigarette smoking, betel nut chewing and metabolic syndrome. The study subjects were recruited from commuity health examination of Puzih, Taibao and Budai Township of Chayi County in southwestern Taiwan. A standardized personal interview based on structural questionnaire was carried out by well-trained interviewers. Information obtained from interview included demographic characteristics, environmental exposure, personal and familial disease history and lifestyle. There were 900 study subjects who gave their consent were recruited for questionnaire interview and collectd their blood and urine samples. Random selected 560 subjects to carry out the gene polymorphism experiment. DNA was extracted from buffy coat to analyze the gene polymorphism of the IRS-1 codon 972 and PI3-K codon 326 utilizing the polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) assay. Urine samples of these subjects were examined by high performance liquid chromatography (HPLC) to separate arsenite (AsIII), dimethyarsinic acid (DMAV) monomethylarsonic acid (MMAV) and arsenate (AsV), and then quantified by hydride generator combined with atomic absorption spectrometry (HG-AAS). It was found that metabolic syndrome prevalence was 28.89%. After adjusted potential confounders, subjects had cumulative betel nut exposure >7.49 × 104 year-quids compared to those who had cumulative betel nut exposure 0 year-quids, the metabolic syndrome risk was significantly increased, the odds ratio was 1.97, 95% confidence interval was 1.05 - 3.70. Subjects had cigarette smoking, alcohol drinking and betel nut chewing compared to non smoker, non drinking and non chewer, the metabolic syndrome risk was borderline significantly increased, the odds ratio was 1.86, and 95% confidence interval was 0.99 - 3.51. Total arsenic concentration, MMA%, DMA% and SMI were divided into three groups using their tertile of controls, respectively. The odds ratio of metabolic syndrome was significantly increased for those second tertile versus first tertile group. There were no associations among IRS-1 codon 972 or PI3-K codon 326 polymorphisms and the metabolic syndrome risk. The metabolic syndrome risk was significantly higher in the study subjects had cigarette smoking, alcohol drinking, betel nut chewing, worse arsenic methylation capability, and PI3-K codon 326 Met/Ile or Ile/Ile genotype than those with non smoker, non drinker, non betel nut chewer, better arsenic methylation capability, and PI3-K codon 326 Met/Met genotype.