氧化及抗氧化酵素基因多形性與砷誘發之高血壓的相關性研究

Oxidative and Antioxidant Enzymes Genetic Polymorphisms and Arsenic-related Hypertension

中文摘要

本研究目的爲探討氧化酵素 nicotinamide adenine dinucleotide (phosphate) oxidase [NAD(P)H Oxidase]及抗氧化酵素包括含錳超氧歧化酵素(Manganese superoxide dismutase; MnSOD)和觸酶(Catalase)等基因多形性與砷暴露誘發之高血壓盛行率的相關性。研究對象選擇先前建立於台灣西南沿海烏腳病高盛行地區好美、復興與新民三里居民 898 人之長期追蹤世代，隨機選取在民國 80 年、82 年以及 86 年進行追蹤健檢蒐集有完整血液與尿液樣本者共 292 人。依據世界衛生組織 1999 年頒布的高血壓判定標準判定之高血壓患者共有 79 人。其中利用標準化問卷收集研究對象之基本人口學資料和可能影響高血壓的重要危險因子。另外血球萃取出 DNA 後，利用聚合酵素連鎖反應(Polymerase chain reaction; PCR)以及限制酵素作限制片段長度多型性(Restriction fragment polymorphism; RFLP)進行氧化及抗氧化酵素基因多形性分析。結果發現帶有 NAD(P)H Oxidase T 對偶基因頻率爲 5%，帶有含錳超氧歧化酵素 C 對偶基因頻率爲 17%，而帶有觸酶 T 對偶基因頻率爲 4%。調整年齡和性別後，帶有 NAD(P)H Oxidase 基因型爲 CT 或 TT 者高血壓盛行率爲基因型 CC 者的 1.31 倍(95%信賴區間 0.56~3.11)，帶有含錳超氧歧化酵素基因型爲 TC 或 CC 者高血壓盛行率爲基因型 TT 者的 1.78 倍(95%信賴區間 0.99~3.18)以及帶有觸酶基因型爲 CT 者高血壓盛行率爲基因型 CC 者的 1.07 倍(95%信賴區間 0.35~3.22)。調整年齡和性別後，身體質量指數、三酸甘油脂、低密度脂蛋白等傳統危險因子和累積砷暴露與高血壓盛行率呈顯著的正相關。在調整慢性砷暴露後，抗氧化含錳超氧歧化酵素或觸酶基因型只要帶有一股以上變異者其罹患高血壓危險性約爲正常者的二倍。而調整高血壓傳統危險因子以及氧化和抗氧化酵素基因多形性後，累積砷暴露濃度越大者其高血壓盛行率顯著偏高。可見烏腳病地區居民高血壓盛行率仍與環境因子慢性砷暴露有很強的相關性存在。

英文摘要

To examine the association between the NAD(P)H Oxidase p22phox C242T and antioxidant enzymes (Manganese superoxide dismutase and Catalase) gene polymorphisms and arsenic-induced hypertension in the blackfoot disease endemic area. A total 292 people were recruited from the blackfoot disease (BFD) cohort randomly by who had blood and urine samples. Hypertension was defined as a systolic blood pressure of greater 140mmHg, or a diastolic blood pressure of greater 90mmHg, or have a history of hypertension and treated regularly with antihypertensive drugs. There were 79 persons diagnosed as hypertension. The demographic characteristics and other important risk factors of hypertension obtained through standardized interviews based on a structured questionnaire. Moreover, DNA was extracted from buffy coat to analyze the gene variants of oxidative and antioxidat enzymes utilizing polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP). The T allele frequency of NAD(P)H Oxidase and Catalase is 0.05 and 0.04, respectively. And The C allele frequency of MnSOD is 0.17. The relative risks of NAD(P)H Oxidase CT and TT versus CC genotype, MnSOD TC and CC versus TT genotype, and Catalase CT versus CC genotype were 1.31(0.56~3.11), 1.78(0.99~3.18), and 1.07(0.35~3.22) respectively after age and sex adjustment. Body mass index, fasting serum triglyceride levels, low-density lipoprotein and cumulative arsenic exposure were all significantly positive associated with hypertension prevalence after adjusting for age and sex. After adjusted for cumulative arsenic exposure, The relative risk of MnSOD TC or CC genotype and Catalase CT and TT genotype was twice increment than the MnSOD TT genotype and Catalase CC genotype respectively. The higher the cumulative arsenic exposure was the higher the prevalence of hypertension. The results of this study suggested that long-term arsenic exposure have strong association with hypertension.