

RESEARCH ARTICLE

Systematic Analysis on the GSTM1 Null Phenotype and Prostate Cancer Risk in Chinese People

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Abstract

Objective: Glutathione S-transferase M 1 (GSTM1) is implicated as a risk factor for prostate cancer. However, this issue is not clear in Chinese population. This systemic analysis was conducted to evaluate the effect of GSTM1 null genotypes on prostate cancer risk in Chinese. **Methods:** Published studies investigating the associations between GSTM1 null genotypes and the risk of prostate cancer in China were identified by using a predefined search strategy. Main statisticals were pooled and estimated according to the primarily reported data. **Results:** The prevalence of the GSTM1 null genotype was higher in prostate cancer patients than in controls, with significance. **Conclusion:** The GSTM1 null genotypes is associated with increased risk of prostate cancer in Chinese.

Keywords: Genetic polymorphism - GSTM1 - prostate cancer - Chinese

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Introduction

Prostate cancer (PC) is reported to be the second most common cancer in man and the sixth leading cause of cancer deaths in the world (Jemal et al., 2011). In 2008, age-standardized incidence of PC by world population was 6.73/100,000, which was accounted for 3.33% of cancer incidence in Chinese man, and the average annual growth rate was estimated to be 12.07% during 1998-2008 (Han et al., 2013; Du et al., 2014). The incidence rate of PC in China is remained not high, it would be rapidly increased in recent years. Aging and environmental factors could contribute to an increased incidence of PC (Hassler et al., 2008). Also, it is reported that other well-established risk factors for PC are ethnicity, and family history of PC (Gallagher et al., 1998). And, some lifestyle factors, eg., smoking and obesity are reported to be associated with the risk of PC (Leitzmann et al., 2012; Li et al., 2014). Several studies indicated that consumption of vegetables, green tea and physical activity may be protective factors for PC (Chan et al., 2009; Parent et al., 2011; Thakur et al., 2012; Yang et al., 2013). Currently, genetic factors are also a focus of research.

GSTs are members of biotransformation enzymes, and they are phase II enzymes with both catalytic activities and noncatalytic functions (Hayes et al., 2005; Chen et al., 2013). Besides, GSTs are involved in the detoxification of electrophilic compounds by glutathione conjugation, such as carcinogens and cytotoxic drugs (Sharma et al., 2004; Hayes et al., 2005). Since the presumed function of

GSTs is to protect tissues against toxic and carcinogenic compounds, they are thought to be important determinants in the development of prostate cancer. Previous studies have shown that individuals with GSTM1 null genotype have a decreased capacity to detoxify certain carcinogens, and it is the same with individuals with GSTT1 null genotype (Hayes et al., 2000). And, the variation in the incidence of prostate cancer between different ethnic groups is well estimated, for which genetic polymorphisms could be an explanation.

Therefore, on this background, we hypothesize that genetic polymorphism of GSTs could be associated with the risk for prostate cancer for Chinese man.

Materials and Methods

Search strategy

We searched PUBMED, and focused on association studies investigating a linkage between GSTM1 and GSTT1 null genotypes with risk of prostate cancer in Chinese man. Computer searches were conducted using relevant keywords "GSTT1," "GSTM1," or "glutathione S-transferase" in combination with keywords "prostate cancer" and "prostate carcinoma". The reference lists of all relevant studies and review articles were also scanned for other eligible studies. Comparative studies that were performed to define the effect of GSTM1 and GSTT1 null genotypes on prostate cancer risk in Hongkong and Taiwan were eligible for inclusion. Family-based studies were excluded owing to different design.

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All studies evaluating the impact of Glutathione S-transferase polymorphism on the risk for prostate cancer published in English prior to December 2014 were identified. If samples of two studies overlap, only the newest one was included. We did not consider meeting abstracts or unpublished reports.

Inclusion and exclusion criteria

We reviewed abstracts of all citations and retrieved studies. The following criteria were used to include published studies: (1) studies focused on the risk of cancer for Chinese people (2) The study was performed in accordance with the Helsinki Declaration (1964, amended in 1975 and 1983) of the World Medical Association. Eligibility criteria included histologically or cytologically verified prostate cancer, and controls of the same ethnic group. Studies were excluded if one of the following existed: (a) duplicate data; (b) no sufficient data were reported.

Data collection and analysis

Selection of trials and data extraction: The titles and abstracts of publications identified according to the above search strategy were assessed independently for inclusion by two authors, the full text was selected for further assessment if the abstract suggests relevance. Disagreement was resolved by discussion. Data was extracted by independent authors. The following recorded data were extracted: author, publication data, country of the first or corresponding author, the number of patients. Outcome presented in at least 3 studies were extracted for combined analysis.

Results

There were 95 papers relevant to the search words by the end of December 2014. Via steps of screening the title and reading the abstract, 4 studies focused on Chinese man were identified (Guan et al., 2005; Wang et al., 2005; Yang et al., 2006; Li, et al., 2008). All these studies had been carried out in China, and all the study population were Chinese. outcomes were presented in at least all studies and extracted for combined analysis: GSTM1 [null] genotype in PC patients compared to healthy controls were systemically estimated. Characteristics of studies included in this analysis are presented as percentage of GSTM1 [null] genotype. Totally, 291 patients and 345 controls were tested for GSTM1 genotype, and 169 patients with PC were GSTM1 [null] genotype and 144 controls were GSTM1 [null] genotype. Thus, the pooled percentage of GSTM1 [null] genotype in patients with PC was 169/291 (58.1%) and in controls was 144/345 (41.7%) ($p < 0.05$).

Discussion

Etiology of prostate cancer is still not well defined. It was suggested that both environmental and genetic factors are considered to be the risk of prostate cancer, and individual difference in the susceptibility could play an important role in the carcinogenesis of prostate cancer. However, most meta-analysis in this field are conducted

with a mixed genetic background. The patients and controls come from a combination of different ethnic groups. Thus, confounding factors could not be well controlled. Because biochemical basis for the individual difference in the susceptibility to carcinogens may be attributed to the genetic polymorphisms of genes implicated in the metabolic detoxification of environmental carcinogens. Previous studies suggested that people with null genotypes of GSTM1 may be difficult to eliminate electrophilic carcinogens efficiently and suffer from high risk of cancer, and it was proposed that GSTM1 polymorphisms are risk factors for prostate cancer [Kumar et al., 2011; Choubey et al., 2013]. However, the results from Chinese population are not systemically analyzed.

In a case-control study, 208 prostate cancer patients and 230 age matched controls were analyzed (Li et al., 2008). The DNA samples from peripheral blood lymphocytes were genotyped for common genetic polymorphisms of GSTM1 genes using the oligonucleotide microarray (DNA chip) technique and the polymorphism results confirmed by sequencing (Li et al., 2008). The results of this study suggested that the prevalence of GSTM1 (null) genotype was significantly higher in prostate cancer patients (58.2%) than in controls (41.7%, $P < 0.05$) (Li et al., 2008). This is in line with an earlier study of Asians (Hu et al., 2013)..

In another report, genetic polymorphism of GSTM1 and GSTT1 genes, living habits, and risk of PC was studied in 163 patients with prostate carcinoma of Han nationality in Southern China and 202 age-matched controls (Yang et al., 2006). The genotypic polymorphism of GSTM1 and GSTT1 genes was analyzed by PCR-RFLP assay using genomic DNA isolated from peripheral blood lymphocytes. Individuals with GSTT1 null genotype (OR=2.23, 95%CI: 1.09-4.57) showed a significantly increased risk. Any other significant results with GSTM1 gene was not observed in this research (Yang et al., 2006).

Our systemic analysis screened 95 papers relevant to the search words and concentrated on Chinese man. Via steps of screening the title and reading the abstract, 4 studies focused on Chinese man were identified (Li, et al., 2008; Guan et al., 2005; Yang et al., 2006; Wang et al., 2005). All these studies had been carried out in China, and all the study population were Chinese. Totally, 291 patients and 345 controls were tested for GSTM1 genotype, and 169 patients with PC were GSTM1 [null] genotype and 144 controls were GSTM1 [null] genotype. Thus, the pooled percentage of GSTM1 [null] genotype in patients with PC was 169/291 (58.1%) and in controls was 144/345 (41.7%) ($p < 0.05$). In conclusion, we concluded that GSTM1 null genotypes are associated with an increased risk of prostate cancer in Chinese man, and GSTM1 null genotypes are risk factors for the development of prostate cancer in Chinese people.

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