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제 목	국문	p53 Codon 72와 자궁경부 암과의 환자-대조군 연구 및 Meta-analysis			
	영문	Case control study on polymorphism in codon 72 of p53 and cervical cancer and Meta-analysis			

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1. 연구목적

Storey et al (1998) found that individuals homozygous for p53Arg are seven times more susceptible to HPV-associated cervical carcinogenesis than heterozygotes. However, since then many other researchers have failed to confirm these results in various ethnic populations. Furthermore, most previous studies have not considered the combined genetic and environmental effects on cervical cancer. The main aims of our study were to examine the independent effect of polymorphism in codon 72 of p53 on cervical carcinogenesis, to examine the effect of the genetic and environmental interactions, and to quantitatively summarize the evidence for a relationship between codon 72 of p53 and invasive cervical cancer.

2. 연구방법

Case group had been collected on 375 patients with HPV-infection associated cervical neoplasia. The control group consisted of 721 healthy patients who underwent routine physical examination at the Catholic University Medical Center. Length of education, age at first sexual intercourse, number of children, and cigarette smoking history were obtained from an interviewer-administered questionnaire. The genomic DNA was prepared from peripheral blood samples using a Puregene blood DNA kit (Gentra Inc.) following the manufacturer's protocol. The genotypes of the patient and control samples were assayed by a single base primer extension assay using a SNaPShot assay kit according to the

manufacturer's recommendation (ABI). For the meta-analysis, our data sources included a MEDLINE search of the literature published before June 2002, bibliography review, and expert consultation. Sixty-three studies (21,320 persons) met the inclusion criteria. Information on sample size, study design, Hardy-Weinberg equilibrium, method of genotype determination and diagnostic method of cervical cancer were abstracted by two reviewers using a standardized protocol. The overall odds ratio (OR) of the p53 gene on invasive cervical cancer was estimated using the Mantel-Haenzel method.

3. 연구결과

There was a strong combined effect between the less educated women and p53Arg homozygosity. Women with 6 or less years of education who possess the p53Arg homozygosity had a risk of cervical cancer 12.0 times higher than women with 13 or more years of education and p53 Pro/Pro. From the meta-analysis, the overall odds ratio (OR) [95% confidence interval (CI)] for cervical cancer among those with homozygous mutant (Arg/Arg) was 1.2 (1.1 1.3) compared to those with heterozygous (Arg/Pro). However, the significant association of the p53 gene on the cervical cancer disappeared after excluding studies from Greece and Sweden. By cellular type of cervical cancer, the overall OR among those with the homozygous mutant (Arg/Arg) was statistically significant in adenocarcinoma (1.5, 1.0 2.2), but not in squamous cell (1.1, 0.9 1.4), compared to Pro/Pro. Compared to Arg/Pro, the OR among those with the homozygous mutant (Arg/Arg) was statistically significant in both HPV type E16 and E18 and in the papers published lately.

4. 고찰

These results mean that even among those with the same genotype, the risks of cervical cancer differ according to the level of education. The trend for women of lower education to have a higher risk for developing cervical cancer may be explained by their lower use of condoms, greater risk of coming into contact with HPV, and higher rates of smoking. The present study revealed the increased risk for female smokers with p53Arg homozygosity. Smoking women with the arginine allele had a risk of cervical cancer 4.0 times higher than non-smoking women with homozygous for the proline allele. Olsen et al (1998) also reported a strong interaction between tobacco smoking and HPV-16. In conclusion, although individuals homozygous for the arginine variant of codon 72 of the p53 gene are not at an increased risk for contracting cervical cancer due to this factor alone, the effect may be significantly increased in association with certain environmental factors like lower education level or smoking in Korean women. Based on the results from the meta-analysis, overall, the p53 gene was slightly associated with increased risk for invasive cervical cancer. However, the risk varied by countries, cellular and HPV type and material source for DNA abstraction and year published.