RESEARCH ARTICLE

Glutathione S-Transferase T1 and M1 Polymorphisms and Risk of Uterine Cervical Lesions in Women from Central Serbia

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Abstract

The aim of this study was to investigate the frequencies of GSTT1 and GSTM1 deletion polymorphisms in newly-diagnosed patients with uterine cervical lesions from central Serbia. Polymorphisms of GST genes were genotyped in 97 patients with cervical lesions and 50 healthy women using a multiplex polymerase chain reaction (PCR). The GSTM1 null genotype was significantly more prominent among the patients than in controls (74.2% *vs* 56.0%), the risk associated with lesions being almost 2.3-fold increased (OR=2.26, 95%CI=1.10-4.65, p=0.03) and 3.17-fold higher in patients above >45 years old (95%CI=1.02-9.79, p=0.04). The analysis of the two genotypes demonstrated that GSTM1 null genotype significantly increased risk only for low grade squamous intraepithelial lesion-LSIL (OR=2.81, 95%CI=1.03-7.68, p=0.04). GSTT1 null genotype or different genotype combinations were not found to be risk factors, irrespective to lesion stages, age or smoking. We found that the risk of cervical lesions might be significantly related to the GSTM1 null genotype, especially in women aged above 45 years. Furthermore, the GSTM1 polymorphism might have greater role in development of early stage lesions.

Keywords: Cervical lesions - polymorphism - glutathione S - transferase T1 - glutathione S - transferase M1

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Introduction

Cervical cancer is the third most common women cancer worldwide with~530 000 new cases and 275 000 deaths in 2008 (Jemal et al., 2011). Invasive cervical cancer is developing gradually through the precancerous stages LSIL (Low squamus intraepithelial lesion) and HSIL (High squamus intraepithelial lesion).

So far, the Human Papiloma Virus (HPV) is the most well-established risk factor for cervical lesions development. Despite that the majority of diagnosed lesions are in the women with HPV (Evans et al., 2006; Zuna et al., 2007) a percent of women with cervical lesions is not HPV positive, suggesting that genetical and enviromental factors may also play a role in the cervical lesions development.

Different individual susceptibility to the cancer may be due to polymorphism in genes involved into cellular metabolism and detoxification of carcinogens products. The Glutathione S Transferases (GSTs) are a super family of polymorphic phase II enzymes involved in the metabolism of xenobiotics (Jancova et al., 2010). The deletion polymorphism of theta (GSTT1) and mu (GSTM1) gene has been described and the homozygous deletion resulting in null genotypes, leading to the absence of enzyme activity. Since these enzymes protect the cell, it is assumed that GSTT1 and GSTM1 null genotype, alone or in combination, may lead to increased susceptibility to cancer. However, in the relevant literature data there are different results on association of GSTT1 and GSTM1 polymorphism and cancer risk (Ates et al., 2005; Singh et al., 2008; Taspinar et al. 2008; Ansari et al., 2009; Kondo et al., 2009; Sivonova et al., 2009; Piao et al., 2013; Peng et al., 2014).

In the present study we have evaluated the frequencies GSTT1 and GSTM1 genotypes in the women with cervical lesions diagnoses (LSIL, HSIL and CC- cancer *in situ* or invasive cancer) and have compared them with the frequencies in the healthy women. Furthermore, we have evaluated the interaction of these genes with the risk factors (i.e. smoking, age) in modulating the susceptibility for cervical lesions development.

Materials and Methods

Patients

Our study has been approved by Ethics Committee of the Clinic of Kragujevac (No 2577) and Faculty of Medicine University of Nis (01-5518-1). The study population was composed of newly diagnosed 32 LSIL

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