RESEARCH COMMUNICATION

MTHFR Gene Polymorphisms in Bladder Cancer in the Turkish Population

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Abstract

Bladder cancer is the 9th most common cancer and is responsible for malignancy related death all over the world. Folate and folate related enzyme polymorphisms related to the cancer risk. The methylene tetrathydrofolate reductase (MTHFR) enzyme is folate related and association of bladder cancer and MTHFR gene. Our purpose was to assess the prevalence of MTHFR gene 677 CT and 1298 AC polymorphisms and Bladder cancer in Turkey. We intended that bladder cancer patients and controls and we used the Polymerase Chain Reaction (PCR) and Restriction Fragment Length Polymorphism (RFLP) methods. The MTHFR gene C677T and A1298C polymorphisms were associated with an increased risk of bladder cancer in our population (For the MTHFR gene C677T polymorphism and A1298C polymorphism; \( p=0.036<0.05; p=0.278>0.05 \) respectively). Consequently, the MTHFR gene C677T polymorphism augments the risk of bladder cancer in Turkey.

Keywords: Bladder cancer - MTHFR gene - polymorphism

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Introduction

Bladder cancer is cause of cancer death globally and is the 9th most common malignancy. Parkin et al. reveal that bladder cancer appears 357,000 new cases and causes 145,000 death worldwide (Shelley et al. 2002).

Folate plays the key role of supplying methyl groups for deoxynucleoside synthesis in humans (Blount et al. 1997). Duthie et al. has been shown low folate levels association between uracil disincorporation, chromosomal DNA damage, DNA strand breaks, impaired DNA repair and DNA hypomethylation (Duthie et al., 1999). A lot results have been revealed suggesting the role of folate and folate related enzyme polymorphisms in the etiology of cancer (Potter et al., 1993; Steinmetz et al., 1996). Folate related enzymes consist of lots of enzymes which one of them is the methylene tethra hydrofolate reductase (MTHFR) (Friedman et al., 1999; Parle-McDermott et al., 2006). The gene of this enzyme is called MTHFR gene and located on chromosome 1p36.3. Two common polymorphisms in the MTHFR gene are C677T and A1298C. First polymorphism C677T positioned in exon 4 (Goyette et al., 1994) leading to an alanine to valine conversion (Frosst et al., 1995). The other polymorphism A1298C is located in exon 7 and glutamic acid to change alanine.

Previous studies have been shown that folate related to DNA damage causing cancer. Folate metabolism including MTHFR gene and having polymorphisms are affected ethnic backgrounds. Therefore, we designed this study about association of MTHFR gene and Turkish population.

Materials and Methods

Study Population

This study was designed on cases were diagnosed with bladder cancer in urology institute on Cukurova University Medical Faculty Hospitals. 54 cases of having bladder cancer disease (59.85±14.089; 49 male, 6 female) and 50 controls (57.00±10.105; 34 male, 16 female) were recorded into the present study. Control group was composed of not having bladder cancer themselves and relatives. Whole came from the Cukurova region of southern Turkey, whose clinical data were on record at Cukurova University, Faculty of Medicine Hospitals, Adana, Turkey. The obtained bladder tissues were collected (fixed) into % 10 formolin solution and stored at -20°C. The research protocol was approved by the Ethical Committee of Cukurova University, Medical Faculty.

Genotype Assessment

The DNA isolation of the bladder tissues from bladder cancer patients groups the DNA isolation of the tissue samples collected from cases was performed by a
precipitation method in which a saturated saline solution was used (Miller et al. 1988).

PCR amplification used primers and conditions as described in for the C677T polymorphism. The 198-bp PCR product was digested 3 hours with Hind I at 37°C. For the A1298C polymorphism, PCR amplification used primers and conditions as described in (Izmirli et al. 2009). PCR product was 138-bp, being digested with Hind I at 37°C at 3 hours. Finally, genotypes were assessed on a 10% polyacrylamide gel (Figure 1). According to this; C677T polymorphism CC, CT and TT genotypes were 198-bp, 175/23-bp and 23-bp respectively. The other polymorphism was A1298C; AA, AC and CC genotypes were 138-bp, 119/19-bp and 19-bp respectively.

**Statistics**

The statistical analysis of data was performed by a SPSS (11.5 version) program. Outcomes were assessed with Pearson Chi-Square test which was utilized to compare ratios and p<0.05 was accepted as statistically meaningful.

**Results**

The genotype frequencies of CC, CT and TT in the bladder cancer patients were 51.9% and 40.7% and 7.4% respectively and for the control group were 72%, 28% and 0% respectively (Table 1). The adjusted p value between the patients and controls for the C677T polymorphism was significant. This shows that there was a meager relation in risk of prostate cancer between cases and controls for the C677T polymorphism (p=0.036).

AA, AC and CC genotypes frequencies for the A1298C polymorphisms in the MTHFR gene were 40.4%, 53.2% and 6.4% respectively in bladder cancer patients and those of genotypes in the controls were 28%, 58% and 14% respectively. We show that no difference between the patients and controls for A1298C polymorphism (p=0.278).

**Discussion**

We studied the influence of common MTHFR C677T and A1298C polymorphisms on the risk of bladder cancer in Turkish population. We propose that significant differences between the bladder cancer patients and controls for C677T polymorphism in the MTHFR gene. For the other polymorphism, no association is found with risk of prostate cancer between cases and controls for C677T polymorphism in the MTHFR gene. According to our sample size, MTHFR gene C677T polymorphism correlates with the healthy person have bladder cancer is important for susceptible populations, the ailment diagnosed before the healthy person have bladder cancer is important for preventive medicine.

**References**


<table>
<thead>
<tr>
<th>Genotype</th>
<th>Bladder Cancer n(%)</th>
<th>Control n(%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GC677T Polymorphism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CC</td>
<td>28 (51.9)</td>
<td>36 (72.0)</td>
<td>0.036</td>
</tr>
<tr>
<td>CT</td>
<td>22 (40.7)</td>
<td>14 (28.0)</td>
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</tr>
<tr>
<td>TT</td>
<td>4 (7.4)</td>
<td>0 (0.0)</td>
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<tr>
<td>A1298C Polymorphism</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>AA</td>
<td>19 (40.4)</td>
<td>14 (28.0)</td>
<td>0.278</td>
</tr>
<tr>
<td>AC</td>
<td>25 (53.2)</td>
<td>29 (58.0)</td>
<td></td>
</tr>
<tr>
<td>CC</td>
<td>3 (6.4)</td>
<td>7 (14.0)</td>
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</table>

**Figure 1. Polyacrylamide Gel Photograph of the MTHFR gene C677T and A1298C Polymorphisms**
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