Comparative analysis of the prevalence of the glutathione S-transferase (GST) system in malignant and benign thyroid tumor cells

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ABSTRACT

CONTEXT AND OBJECTIVE: When null, the \( \mu \) and \( \theta \) genes of the glutathione S-transferase system (GSTM1 and GSTT1, respectively) are related to malignant tumors affecting the lungs, colon, prostate, bladder and head and neck. In the thyroid, the appearance of cancer has been correlated with deletion of these genes. The aim of this study was to compare the frequencies of these genes in patients with benign and malignant thyroid tumors.

DESIGN AND SETTINGS: This was a cross-sectional clinical trial carried out in the Head and Neck Surgery Division, Faculdade de Medicina da Santa Casa de São Paulo.

METHODS: Samples of thyroid tissue were collected from 32 patients and divided into two groups: benign tumor (A) and malignant tumor (B). After DNA extraction, the genes were amplified using PCR.

RESULTS: The B group presented four cases of positive genotyping for both genes, seven positive for GSTT1 and negative for GSTM1, two negative for GSTT1 and positive for GSTM1, and only one case of double negative. The A group showed 11 cases with positive genotyping for both genes and none with the double negative genotype.

CONCLUSION: In this study, there was no relationship between the presence of the GSTT1 and GSTM1 genes and the benign and malignant thyroid tumors.

was sent for anatomopathological study, in 10% formol. To extract the thyroid DNA, the Qiagen DNeasy® kit was used. The GSTM1 and GSTT1 genes were amplified using the polymerase chain reaction (PCR), including amplification of the β-globin gene as a positive control for the DNA sample, and then the genotype was identified by viewing under ultraviolet light.

**Statistical analysis**

The statistical method used was Fisher’s exact test, with a confidence interval of 95% (p < 0.05).

### RESULTS

After DNA extraction, we observed the PCR pattern that is shown in Table 2. In group A, there were no cases of double negative genotype, while 61.1% were double positive and 38.9% were positive for one of the genes. In group B, one of the cases presented double negative genotype, while the others were distributed between double positive (28.6%), positive genotyping only for GSTT1 (50%) and positive only for GSTM1 (14.3%).

### DISCUSSION

The data collected for analyzing the benign tumor group showed high frequency of the double positive genotype (61.1%) and no double negative genotype. In group B there was a more homogeneous distribution. Cases with positive GSTT1 genotype and negative GSTM1 (T + M -; 50%) predominated, while the double negative genotype was observed in only one case (7.1%). The double positive genotype occurred in 28.6%.

Analysis of the GSTM1 gene alone showed that there was a relatively high frequency of the negative GSTM1 genotype in group B, i.e. 8 out of the 14 cases (57.1%), in comparison with group A, in which the frequency was 27.8%. However, statistical analysis showed that this was not significant (p = 0.09). Analysis of the GSTT1 gene alone showed that it was present in 88.9% of the cases in group A and 78.6% of the cases in group B, and also was not statistically significant (p = 0.3).

In the literature, separate analyses of the genes GSTT1 and GSTM1 are inconclusive regarding the risk of developing thyroid cancer. Our results from separate analyses of these genes are in accordance with the literature, although we observed the presence of GSTM1 in 72.2% (13/18) and GSTT1 in 88.9% (16/18) of the benign tumor cases. These frequencies are quite high and, although non-significant, cannot be ignored.

### CONCLUSION

Analysis of the data obtained, under the conditions of the present study, allows the conclusion that there is no relationship between the presence of the GSTT1 and GSTM1 genes and the benign and malignant thyroid tumors. However, the relatively small number of cases makes it impossible to reach more substantial conclusions. In order to achieve this, a larger sample would be needed.

### Table 2. Results from DNA analysis of thyroid tumors patients

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Adenoma</th>
<th>Carcinoma</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>T + M +</td>
<td>11</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>T + M -</td>
<td>5</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>T - M +</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>T - M -</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>14</td>
<td>32</td>
</tr>
</tbody>
</table>

T = genotype of GSTT1 gene; M = genotype of GSTM1 gene; + = present; - = absent.

### REFERENCES

Análise comparativa da prevalência do sistema glutatonia S-transferase (GST) em células tumorais malignas e benignas da tireóide

CONTEXTO E OBJETIVO: Os genes do sistema glutatonia S-transferase mu e theta (GSTM1 e GSTT1, respectivamente), quando nulos, apresentam relação com tumores malignos de pulmão, cólon, próstata, bexiga e cabeça e pescoço, podendo nesses casos ser utilizados como marcadores tumorais. Na tireóide, o surgimento do câncer tem sido relacionado à deleção desses genes. Assim, o objetivo deste estudo foi comparar a frequência dos genes GSTM1 e GSTT1 em pacientes com tumores benignos e malignos da glândula tireóide.


MÉTODOS: Amostras de tecido tireoidiano foram coletadas de 32 pacientes e divididas em dois: tumor benigno (A) e carcinoma (B). Após extração do DNA os genes foram amplificados em reação de polimerase em cadeia.

RESULTADOS: O grupo B apresentou 4 casos de genótipo positivo para ambos os genes, 7 positivos para GSTT1 e negativos para GSTM1, 2 negativos para GSTT1 e positivos para GSTM1, e apenas 1 caso duplo negativo. Já o grupo A mostrou 11 casos com genótipo positivo para ambos os genes e nenhum com o genótipo duplo negativo.

CONCLUSÃO: Não há relação entre a presença dos genes GSTT1 e GSTM1 com o carcinoma bem diferenciado e os tumores benignos da tireóide em nossos casos.