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GSTM1 and GSTT1 Gene Polymorphisms with Gallbladder Carcinoma

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ABSTRACT

In order to explore the relationship between GSTM1 and GSTT1 gene polymorphisms and gallbladder cancer, so as to find a better treatment and prevention of gallbladder cancer and improve the treatment effect. In this paper, 247 patients with gallbladder cancer were selected for the experiment, including 187 male patients and 60 female patients. The total number of patients was randomly divided into two groups, namely the case group and the control group. The patients in normal condition and after treatment of tumor tissue and adjacent non-tumor tissue gene detection, and then through the logistic regression model to analyze the data. After the experiment, we found that the frequency ratio of GSTM1 and GSTT1 in gallbladder cancer patients before treatment was 57.33% and 52.37%, which was very high, which was very disadvantageous in gene detection. However, after treatment, the frequency of deletion of the two genes was 45.73% and 51.02%, which was significantly reduced. The reduced gene ratio is very beneficial to the observation of gallbladder cancer. Therefore, the surgical treatment of gallbladder cancer before the first drug after gene testing, in the understanding of various principles, will have twice the result with half the effort.

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Introduction

Cancer is one of the most important causes of death in today's world. 80-95% of biliary tract malignant tumors are gallbladder cancer, which is the most invasive malignant tumor in the biliary tract diagnosis rate. The overall survival rate of gallbladder cancer is less than 5% in 5 years. The most important thing is that the symptoms of gallbladder cancer are not obvious in the early stage, so when patients are told that they have gallbladder cancer, they are often in the middle and late stage, leading to patients missing the best opportunity for treatment (1-4).

In recent years, more and more basic studies have confirmed that gallbladder cancer is the product of multiple gene mutations, and the rise of cancer gene therapy brings hope to patients. Gene therapy uses genetic or molecular biological techniques to correct abnormal genes or compensate for defective genes, which is theoretically feasible (5-7).

In order to clarify the role of GSTM1 and GSTT1 polymorphisms in the occurrence and development of lung cancer, Malik searched PubMed, NCBI, EMBASE and the web of science to explore the relationship between GSTM1 and GSTT1 and lung cancer in different populations in recent 10 years. He believed that glutathione S-transferase is an effective candidate enzyme for lung cancer susceptibility. Although different studies have reported the relationship between GSTM1 and GSTT1 deletion polymorphism and lung cancer risk, the results are inconsistent. Therefore, he selected 6491 lung cancer patients and 7807 normal controls to conduct the experiment. The relationship between GSTM1 and GSTT1 gene polymorphism and lung cancer occurrence was analyzed with 95% CI ors. Medclac and St were used to analyze the relationship between GSTM1 and GSTT1 gene polymorphism and lung cancer ATA analyzed and explained the results. In the experiment, Malik did not analyze other factors of lung cancer patients and normal controls, so the experimental results can not explain that this is the reason for gene diversity (8-11). To assess whether genetic polymorphisms of cytochrome P450 (CYP1A1), glutathione S-transferase mu1 (GSTM1), θ 1 (GSTT1) and tumor suppressor protein p53 (TP53) regulate the susceptibility of Bolivian GBC, Yan conducted an experimental case-control study involving 32 GBC patients and 86 healthy subjects, of which GBC was based on the Bolivar Japanese gastroenterology study The healthy subjects were also IGBJ staff. Yan used PCR restriction fragment length polymorphism analysis to detect the distribution of CYP1A1 rs1048943 and TP53 rs1042522 polymorphism and used multiple PCR methods to detect GSTM1 and GSTT1 deletion polymorphism. However, Yan's experiment time was too short, and the data was not stable (8, 12-14). To investigate the relationship between GSTM1, GSTT1 and GSTP1 polymorphisms and gastric cancer risk in Chinese, Sakai studied the influence of gene-environment interaction and their impact on cancer risk. Sakai believes that the polymorphism of GSTM1, GSTT1 and GSTP1 may affect the detoxification process and increase the individual's susceptibility to cancer. Therefore, from July 2013 to June 2015, he recruited 242 gastric cancer patients and 396 healthy people as controls. Moreover, he used polymerase chain reaction-restriction fragment length polymorphism analysis to describe the genetic polymorphism of GSTM1, GSTT1 and GSTP1. However, during the experiment, Sakai did not divide the disease degree of patients, and the data was not accurate

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enough (15-17). In order to investigate the relationship between homozygous deletion genotypes of glutathione transferase gene GSTT1 (glutathione transferase theta 1) and GSTM1 (glutathione S-transferase mu1) and male infertility in Russia, peddireddy analyzed the incidence of homozygous deletion genotypes of GSTM1 and GSTT1 in Russian male infertility patients. In the study group, 160 infertile men of reproductive age (mean age 30.2 + / - 3.6 years) were included in the study group, and 104 healthy Russian volunteers (mean age 31.3 ± 5.4 years) were included in the study group, and the diagnosis of infertility was verified according to WHO guidelines. Peddireddy used PCR to detect GSTM1 and GSTT1 deletion polymorphisms and extracted genomic DNA from whole blood samples. The Peddireddy experiment lacks the data of male subjects before participating in the experiment, and does not exclude the influence of other factors, so the experimental results are unreliable (18,19).

In the past, gallbladder cancer was treated by surgery or drug therapy. Firstly, the two gene deletion ratios before and after drug treatment were detected. In addition to clearly seeing the relationship between GSTM1 and GSTT1 Genes and gallbladder cancer, the internal structure and principle of GSTM1 and GSTT1 could be well understood. The aim of this experiment is the study of GSTM1 and GSTT1 gene polymorphisms with gallbladder carcinoma.

Materials and Methods

Subjects

Methods: 247 patients with gallbladder cancer were tested. The tumor tissue and other tissues adjacent to the tumor were detected by gene detection. The experiment was divided into two groups, 187 male and 60 female, aged 43-67 years, with an average age of 54.5 years. The inclusion criteria of this experiment include: Patients with gallbladder cancer confirmed by pathological diagnosis and in line with the relevant standards in the diagnosis and treatment guidelines; one is that they have not received chemotherapy, radiotherapy and other medical means; the second is that the family members know and agree; the third is that they need to be approved by the ethics committee of the hospital. The exclusion criteria included patients with other malignant tumors, surgical contraindications, severe heart, liver, lung and other system dysfunction. Finally, the patients could not be followed up after surgery or there were other hidden dangers.

Experimental Steps

Part of the tumor tissue and other adjacent tissues were taken from gallbladder carcinoma. After adding liquid nitrogen, it was ground. Then promethazine reagent was used to extract the tissue. The concentration and purity of the extracted tissue were detected by T-6 ultraviolet spectrophotometer. The results showed that the concentration of the extracted tissue was 800 ~ 1500 μ g / ml, and the ratio of a260 / A280 was between 1.8 ~ 2.1. Then, the extracted tissue was synthesized into cDNA by Takara reverse transcription kit, and the concentration of cDNA was diluted to the same level as the template for RT-PCR detection. The relative expression of mir-155-5p and Elk3 mRNA was calculated with β-actin as the internal parameter. The total survival time (from the date of diagnosis to the death or end of the patient) was used as the prognostic index. Finally, the gene in gallbladder carcinoma was detected to judge the relationship between GSTM1 and GSTT1 and gallbladder cancer.

Experimental Methods

The database is mainly established by epidata3.0. After obtaining the data, it is processed by spss20.0 software, and then the comparison data results are statistically described. The relationship between GSTM1, GSTT1 gene and gallbladder cancer was analyzed by the unconditional logistic regression model. The test method in the experiment was a bilateral test, and the level was $\alpha = 0.05$. Estimating odds ratio (or odds ratio) is one of the important applications of the logistic regression model in life. That is, in the experimental control study, it is used to show an index between exposure factors and diseases, which is the ratio between the probability of illness and non-disease when a certain factor f takes a certain value x, and the ratio of the probability of both diseases when the reference value a is obtained, The value is in the range of 0 to $+\infty$. When the value is more than 1, the disease risk of X is higher than that of a, which is a positive correlation. When or < 1, on the contrary, the risk is reduced, which is a negative correlation; when or = 1, the table shows that f is not related to disease. On the other hand, 95% of the interval is helpful to detect the judgment significance of or value.

Results and Discussion

Frequency of Gene Deletion

In the experiment of the control group and case group, the frequency of GSTM1 gene deletion was 57.33% and 52.37% in two different states, and the difference was statistically insignificant (P = 0.678), while the frequency of GSTT1 was 45.73% and 51.02%, respectively, the difference was also insignificant (P = 0.664). By detecting the deletion frequency of these two groups of genes, we can get the proportion distribution of the two groups of genes in different states, and the results are shown in Table 1.

It can be seen from Table 1 that when the number of groups is similar, the internal frequency of GSTM1 gene and GSTT1 gene does not change much in the experimental group and the control group, while the frequency of the experimental group is lower than that of the control group, and the data of the two groups are statistically meaningless. Lin et al. (2018) studied on the correlation of GSTM1 gene deletion in joint synovial fluid with the reco-

Table 1. Relationship between GSTM1 and GSTT1 genotypes [n(%)].

	GSTM1		GSTT1	
Group	+	-	+	-
Case Group (n = 24)	10(41.67%)	14(57.33%)	13(54.17%)	11(45.73%)
Control Group(n= 223)	106(47.53 %)	117(52.37%)	109(48.88%)	114(51.02%)

very of patients undergoing artificial hip replacement (20).

In addition, in the drug treatment experiment for gallbladder cancer, the gene frequency before and after the use of drugs was measured to detect the frequency ratio in vivo. It can be seen that the normal gene deletion

It can be seen from Figure 1 that there was no significant difference in gender, BMI, disease type of gallbladder cancer and treatment scheme (drug treatment or no drug treatment) between the two groups ($P > 0.05$). Wensheng et al. (2019) confired that MBD1 promotes the malignant behavior of gallbladder cancer cells and induces chemotherapeutic resistance to gemcitabine (21).

The values of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in the gallbladder were kept within the normal range before medication, and the difference between the two groups was not statistically significant ($P > 0.05$). After treatment, the difference in serum ALT and AST between the two groups was statistically significant due to the change in values ($P < 0.05$). The values of both before and after treatment are shown in Table 2.

It can be seen from Table 2 that the contents of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in the body were relatively low before medication, and after the use of drugs, their contents increased significantly, and the difference between the two groups was not statistically significant.

Zhang et al (2015) determined the upper cut-off values of serum alanine aminotransferase and aspartate aminotransferase (22).

There are many different enzyme interactions in gallbladder carcinoma. The typical three enzymes are alt, AST and TBIL(23,24). Therefore, in the experimental drug before the detection of gallbladder cancer enzymes, the obtained value can be compared with the data obtained after medication becomes more clear. Therefore, it is very necessary to detect the gene before medication. The contents of three enzymes in the case group and the experimental group before medication are shown in Figure 2.

As shown in Figure 2, before treatment, the number of ALT enzyme was higher than that of the control group,

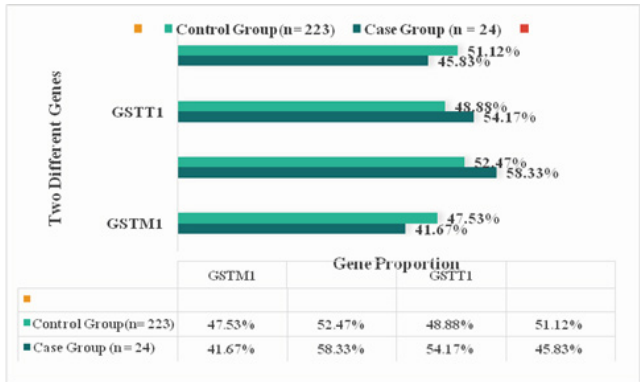

Figure 1. The gene deletion ratio of the two groups.

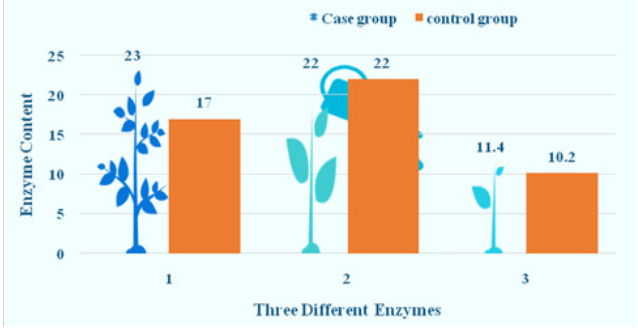

Figure 2. The ratio of the three enzymes before and after treatment.

while TBIL was the same in the two groups. In AST, the difference between the case group and the control group was small.

Gene Content in Gallbladder Carcinoma

The distribution frequency of the GSTM1 genotype in the case group and the control group was studied. The results of 247 patients showed that 135 (57.5%) patients had no GSTM1 genotype deletion, and 112 (42.5%) patients showed deletion genotype. After medication, 85 cases (26.7%) of 247 patients with gallbladder cancer showed no GSTM1 genotype deletion, while 162 (73.3%) patients had genotype deletion. The genotype frequency distribution of cystic carcinoma was significantly different before and after the experiment ($x^2 = 30.27$, $P < 0.0001$), and the gene frequency distribution is shown in Figure 3.

As shown in Figure 3, the frequency of GSTM1 gene deletion in the normal group is higher than that in the experimental group. In this case, the observation of gallbladder cancer is unfavorable.

Generally speaking, gallbladder cancer is more insidious, and in the early clinical diagnosis, symptoms are very common, not typical. With the progress of science and technology, now in the etiology, molecular biology, diagnosis and treatment methods continue to deepen, constantly to improve the detection of special tumor markers, which is very helpful in the early diagnosis of gallbladder cancer. Adjuvant therapy provides a favorable technology for improving the survival rate of patients with gallbladder cancer, and molecular targeted drugs are a new treatment method (25,26). When the gene distribution frequency of cholecystitis is low, the development trend of cholecystitis will be easier in the experiment. Therefore, after the use of drugs, the content of various enzymes in the body changes greatly, and the three enzymes also show a trend of gradual decrease. The trend of the three enzymes after the medication is shown in Figure 4.

It can be seen from Figure 4 that the enzyme content in the body decreases sharply after medication, which can make us more clearly observe the development trend of gallbladder cancer, which also provides great help for the

Table 2. Before and after treatment, the contents of various enzymes in the two groups were tested.

	Before Medication			After Medication		
Group	ALT/(U/L)	TBIL/(imol/L)	AST/(U/L)	ALT/(U/L)	TBIL/(imol/L)	AST/(U/L)
Case Group	23	22	11.4	172	83	12.8
Control Group	17	22	10.2	24	26	9.1
p	0.095	0.147	0.095	0.001	0.001	0.073

Figure 3. The frequency of gene distribution in normal controls and gallbladder cancer.

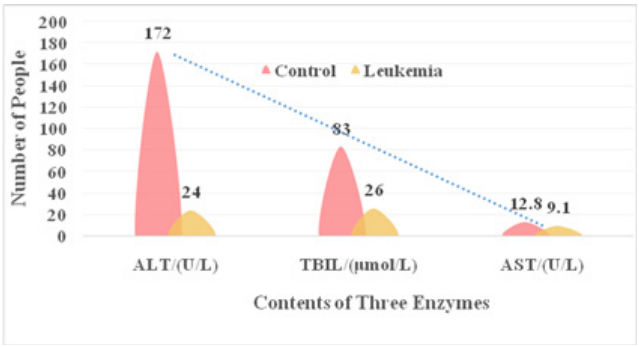

Figure 4. The trend of enzyme content after treatment.

treatment of gallbladder cancer. Because the scope of operation is larger, the mortality rate is high, and it is difficult to achieve radical resection, the possibility of surgical treatment can only be considered after multidisciplinary comprehensive discussion. Therefore, laparoscopic surgery is not included in the selection scope, but laparoscopy can be used as a means of exploration or pathological biopsy.

Conclusion

In recent years, surgical technology has been greatly improved in many aspects. Doctors' medical skills even include technology-assisted robots. In the past, minimally invasive surgery for gallbladder cancer has been regarded as taboo laparoscopic surgery by many people. Due to the development of science and technology, more and more experts and scholars in the field of medicine are paying attention to it, and the scope of clinical application is also growing. At present, the treatment of gallbladder cancer mainly adopts surgery or chemotherapy, mainly with surgery combined with drug treatment. In the treatment of gallbladder cancer, the use of drugs that control and cure the disease at the same time will also cause many other adverse reactions. In view of this, the treatment of gallbladder cancer needs continuous progress and constantly overcoming many unknown challenges. Gallbladder cancer surgery must be more cautious.

In this paper, 247 cases of gallbladder cancer after operation were selected, including 187 males and 60 females aged 43-67 years, with an average age of 54.95 years. They were divided into two groups, the experimental group and the control group. The frequency of gene deletion in gallbladder cancer was registered before the experiment, and then the frequency of gene deletion in medication was compared. Using a logistic regression model to analyze the observed data and compare the results, we can clearly find that the gene frequency of gallbladder cancer was too high before the experiment, which hindered the observation of the experiment. After medication, the decrease of gene frequency deletion is very helpful to the accuracy of our experimental results.

The study of the relationship between GSTM1 and GSTT1 gene polymorphism and gallbladder cancer can help us to explain the genetic mechanism and principle of gallbladder cancer and provide very important information for the medical field of prevention and treatment of this disease, and it is also very helpful in reducing the incidence of adverse reactions of gallbladder cancer. How to develop a standardized treatment plan for gallbladder cancer smoothly while reducing or avoiding other parts of the body is also very important. Therefore, we need to understand the internal situation of gallbladder cancer more clearly through GSTM1 and GSTT1 Genes so as to improve the clinical treatment effect.

Acknowledgments

Not applicable.

Interest conflict

The authors declare that they have no conflict of interest.

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