



Malignant degree of tumor and degree of trauma after HOLBT and TURBT treatment of superficial bladder cancer

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ABSTRACT

Objective: To assess the malignant degree of tumor and degree of trauma after holmium laser resection of bladder tumor (HOLBT) and transurethral resection of bladder tumor (TURBT) treatment of superficial bladder cancer. **Methods:** A total of 76 cases of patients with superficial bladder cancer were included for study and divided into observation group 38 cases and control group 38 cases according to different surgical methods. Control group received TURBT, observation group received HOLBT, and then differences in the values of postoperative serum illness-related indicators, bladder cancer-related mRNA expression, bladder cancer tissue-related protein expression, surgical trauma-related indicators, etc. were compared between two groups. **Results:** Postoperative serum CIP2A, HGF, SE-cad, TSGF, DKK-1, YKL-40 and sFas values of observation group were lower than those of control group; postoperative focus *HSG*, *p16* and *MRP-1/CD9* mRNA expression levels of observation group were higher than those of control group while *Med-19* mRNA expression level was lower than that of control group; postoperative focus *ZEB1*, *Cripto-1*, *Sox2*, *Survivin*, *Livin* and zeste protein expression levels of observation group were lower than those of control group while E-cadherin expression level was higher than that of control group; early postoperative FBG and HOMA-IR values of observation group were lower than those of control group while PTA and FIB values were higher than those of control group. **Conclusions:** HOLBT can effectively remove superficial bladder cancer foci and reduce the malignant degree of tumor, causes less surgical trauma and is an ideal surgical treatment of superficial bladder cancer.

1. Introduction

There are many surgical ways for clinical treatment of superficial bladder cancer, holmium laser resection of bladder tumor (HOLBT) and transurethral resection of bladder tumor (TURBT) are the two with more clinical application, and they excise local tumor and the surrounding normal mucosa tissue to contain tumor invasion and progress. The two kinds of operation methods are with different core technology, so their clinical therapeutic effect is also different[1]. In the research, the malignant degree of tumor and degree of trauma after HOLBT and TURBT treatment of superficial bladder cancer were mainly assessed, hereby reported as follows.

2. Materials and methods

2.1. General information

A total of 76 cases of patients with superficial bladder cancer were included for study, and the time range of treatment was from January 2014 to December 2015. According to different surgical methods, all included patients were divided into observation group 38 cases and control group 38 cases. Control group included 21 male cases and 17 female cases, they were 37-76 years old and the average was (59.27±8.59) years; observation group included 20 male cases and 18 female cases, they were 39-74 years old and the average was (58.46±8.08) years. Differences in gender, age and other baseline information were not statistically significant between two groups ($P>0.05$).

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2.2. Surgical treatment

Observation group received HOLBT, specifically as follows: patients took lithotomy position after epidural anesthesia, cystoscope was placed in the bladder through urethra, saline was used to flush the bladder and make it in half full state, and the tumor size, location and other basic information were determined. Holmium laser optical fiber entered into the bladder by cystoscope operation hole, and the laser parameters were set as follows: energy 1.0 J, frequency 20 Hz and power 30 W. Holmium laser optical fiber cut the tumor at 1 cm of the base and changed to push type when it reached muscle layer, tumor tissue was flushed with water and lifted, normal mucosa tissue within 2 cm of the tumor was removed, and urethral catheter was routinely indwelled after operation. 5 d after operation, urethral catheter was removed, and 7 d after operation, pirarubicin was infused in the bladder, 50 mg each time.

Control group patients received TURBT treatment, specifically as follows: normal saline was used before operation to half-fill the bladder, patients received epidural anesthesia and took lithotomy position, Olympus continuous perfusion resectoscope was put inside bladder under direct vision, the basic information of tumor was determined, and parameters were set as follows: electric resection function 140 W and electric coagulation power 60 W. When tumor was removed to muscle layer, electric coagulation was used to deal with normal mucosa tissue within 2 cm of the tumor, and urethral catheter was routinely indwelled after operation. One week after operation, pirarubicin was infused in the bladder, 50 mg each time.

2.3. Observation indicators

Level of serum illness related indicators: cancerous inhibitor of

protein phosphatase 2A (CIP2A), hepatocyte growth factor (HGF), soluble E-cad (SE-cad), tumor-specific growth factor (TSGF), Dickkopf 1 (DKK-1), YKL-40 and soluble Fas (sFas).

Lesion specimens were obtained by cystoscope after operation, and bladder cancer-related mRNA expression was detected by RT-PCR method: proliferation-inhibiting gene *HSG*, tumor suppressor gene *p16*, *Med-19* gene and *MRP-1/CD9* gene.

Lesion specimens were obtained by cystoscope after operation, and bladder cancer-related protein expression was detected by Western-blot method: zinc finger E-box binding homeobox 1 (ZEB1), E-cadherin, Cripto-1, Sox2, Survivin, Livin and zeste.

Serum trauma-related indicators were detected: fasting blood glucose (FBG), insulin resistance index (HOMA-IR), prothrombin activity (PTA) and fibrinogen (FIB).

2.4. Statistical methods

SPSS 23.0 software was used to input and analyze the data in the research, measurement data was in terms of Mean \pm SD, comparison between two groups was performed by *t* test, and $P < 0.05$ indicated statistical significant differences.

3. Results

3.1. Serum illness-related indicators

Results showed that postoperative serum CIP2A, HGF, SE-cad, TSGF, DKK-1, YKL-40 and sFas values of observation group were lower than those of control group ($P < 0.05$), shown in Table 1.

Table 1

Comparison of serum illness-related indicator values between two groups.

Groups	CIP2A ($\mu\text{g/L}$)	HGF ($\mu\text{mol/L}$)	SE-cad (ng/mL)	TSGF (u/mL)	DKK-1 (ng/mL)	YKL-40 (pg/mL)	sFas ($\mu\text{g/L}$)
Observation group	5.37 \pm 0.49	2.73 \pm 0.29	1.93 \pm 0.15	65.38 \pm 5.89	5.12 \pm 0.52	87.36 \pm 9.05	7.12 \pm 0.69
Control group	11.28 \pm 1.76	4.05 \pm 0.34	5.14 \pm 0.49	101.27 \pm 10.83	7.85 \pm 0.76	115.64 \pm 10.58	13.65 \pm 1.47
<i>t</i>	7.384	6.023	7.485	12.384	6.325	9.283	8.273
<i>P</i>	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

3.2. Bladder cancer-related mRNA expression

Results showed that postoperative focus *HSG*, *p16* and *MRP-1/CD9* mRNA expression levels of observation group were higher than those of control group while *Med-19* mRNA expression level was lower than that of control group ($P < 0.05$), shown in Table 2.

Table 2

Postoperative bladder cancer-related mRNA expression of two groups.

Groups	<i>HSG</i>	<i>p16</i>	<i>Med-19</i>	<i>MRP-1/CD9</i>
Observation group	113.28 \pm 10.59	132.93 \pm 12.57	75.38 \pm 7.11	119.62 \pm 12.53
Control group	75.32 \pm 6.95	90.25 \pm 8.59	98.75 \pm 9.05	85.37 \pm 8.34
<i>t</i>	8.293	11.283	9.283	9.724
<i>P</i>	<0.05	<0.05	<0.05	<0.05

3.3. Bladder cancer tissue-related protein expression

It showed that postoperative focus ZEB1, Cripto-1, Sox2, Survivin, Livin and zeste protein expression levels of observation group were lower than those of control group while E-cadherin expression level was higher than that of control group ($P < 0.05$), shown in Table 3.

3.4. Surgical trauma-related indicators

It showed that early postoperative FBG and HOMA-IR values of observation group were lower than those of control group while PTA and FIB values were higher than those of control group ($P < 0.05$), shown in Table 4.

Table 3

Comparison of postoperative bladder cancer tissue-related protein expression between two groups.

Groups	ZEB1	E-cadherin	Cripto-1	Sox2	Survivin	Livin	Zeste
Observation group	75.38±7.11	115.37±10.59	65.38±7.11	58.39±6.09	73.27±6.39	75.16±8.54	94.27±8.05
Control group	129.75±13.64	75.32±8.53	91.27±8.56	98.77±8.54	112.37±10.58	104.26±10.38	143.83±13.25
<i>t</i>	13.284	11.235	9.232	9.834	11.732	10.389	14.273
<i>P</i>	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Table 4

Comparison of surgical trauma-related indicator values between two groups.

Groups	FBG (mmol/L)	HOMA-IR	PTA (%)	FIB (g/L)
Observation group	5.36±0.52	0.68±0.07	76.27±7.13	2.73±0.23
Control group	7.19±0.75	1.19±0.14	62.05±6.11	1.65±0.14
<i>t</i>	6.983	5.723	8.293	5.783
<i>P</i>	<0.05	<0.05	<0.05	<0.05

4. Discussion

Superficial bladder cancer can be excised by minimally invasive surgery, and the treatment effect is good. Current operation methods for clinical resection of superficial bladder cancer are mainly HOLBT and TURBT, which can not only keep the bladder function, but can also promote the early postoperative recovery[2,3]. Both HOLBT and TURBT are with the advantages such as high efficiency, less complications and rapid postoperative recovery, but the effect of the two on the treatment of bladder cancer differs. In order to define the differences in clinical application effect of HOLBT and TURBT, patients with superficial bladder cancer were selected as research subjects of the research, they received HOLBT and TURBT treatment respectively, and the differences in postoperative tumor malignancy, trauma, etc, in patients were mainly evaluated.

CIP2A is necessary to malignant transformation of human cells, it has been found that CIP2A expression is up-regulated in squamous cell carcinoma, gastric cancer, colon cancer and other specimens, and it is speculated that CIP2A may widely exist in human malignant tumors and is an important marker in the development of tumor[4]. HGF has many biological functions, and it is combined with receptor c-met to activate downstream signal product phosphorylation and stimulate tumor metastasis. As the tumor staging and grading increase, HGF content increases. Structure and function of the tumor cell surface are damaged, which can lead to decreased and even lost adhesion between tumor cells as well as enhanced tumor cell invasion and metastasis activity. Degraded extracellular SE-cad fragment enter the blood circulation in dissociated way, leading to increased serum SE-cad content[5,6]. TSGF can promote massive proliferation of tumor and surrounding capillaries, is released into the blood in early malignant transformation of cells, is considered as the specific marker for malignant tumor, and is an effective indicator for early diagnosis of tumors. DKK-1 belongs to the human DKK family and has important effect on the regulation of cell proliferation and polarity. DKK-1 has strong Wnt signaling pathway-inhibiting activity, has been found to be highly expressed in lung cancer, liver cancer, ovarian cancer and other malignant tumors, and is considered to be one of the new tumor markers. YK-40 is a potential

tumor marker, and many in vitro studies have confirmed that YKL-40 is highly expressed in osteosarcoma cell lines, colon cancer cell lines and prostate cancer cell lines[7]. Some scholars put forward that YKL-40 may be directly involved in tumor proliferation, differentiation and anti-apoptosis process, and YKL-40 gene knockout can significantly inhibit the process of tumor angiogenesis. sFas plays a regulating role in cell apoptosis, and the combination of sFas and FasL can reversely inhibit cell apoptosis and lead to tumor immune privilege. The research results showed that postoperative serum CIP2A, HGF, SE-cad, TSGF, DKK-1, YKL-40 and sFas values of observation group were lower, indicating that HOLBT could more thoroughly remove bladder cancer tissue and reduce the levels of related factors produced by tumor tissue and secreted into the blood circulation.

HSG is a proliferation-inhibiting gene that acts on the outer membrane of mitochondria, and it plays an important role in maintaining mitochondrial morphology and other aspects. HSG is directly involved in the proliferation and apoptosis of tumor passage cell lines, and its abnormal expression or function deletion can promote tumor development[8,9]. P16 is a tumor suppressor gene that directly regulates the cell cycle, it can block the Rb protein phosphorylation process, block cell stage from G phase to S phase and finally realize the inhibition of cell proliferation, and abnormal p16 expression or deletion has been found in a variety of malignant tumor cells. *Med-19* gene plays an important role in the process of gene transcription, and is closely related to the regulation of cell growth cycle. In human body, *Med-19* gene has been defined as tumor metastasis-related gene, and highly expressed *Med-19* genes can be found in many malignant tumors such as gastric cancer and lung cancer. *MRP-1/CD9* gene belongs to the transmembrane 4 superfamily, and it forms complexes with other transmembrane proteins and then regulates cell adhesion, migration and signal transduction. Research has shown that *MRP-1/CD9* gene is expressed in paraffin-embedded bladder cancer tissue, and *MRP-1/CD9* gene is not usually expressed in highly malignant tumors; mildly malignant tumors often express *MRP-1/CD9*, and are not easy to develop into more aggressive tumors[10,11]. The research results showed that postoperative focus *HSG*, *p16* and *MRP-1/CD9* mRNA expression levels of observation group were higher while *Med-19* mRNA expression level was lower, indicating that HOLBT could effectively remove superficial bladder tumor and kill its activity, and this was because that HOLBT operation process didn't need to directly remove tumor tissue and reduced tumor tissue implantation, metastasis, etc.

ZEB1 can promote the invasion and metastasis of tumor cells, and ZEB1 high expression has been found in squamous cell carcinoma of the lung. E-cadherin belongs to cadherin family, it has been found

that its expression decreases in a variety of malignant tumor tissues, and it is associated with the invasion and metastasis of tumor[12]. ZEB1 can be combined with E box on E-cadherin to down-regulate its transcription and induce tumor invasion. *Cripto-1* and *Sox2* belong to stem cell-related genes, and are associated with the malignant potential of tumors. *Cripto-1* belongs to epidermal growth factor-CFC family, is located in the cell membrane and can enter into tissue and play the role under the effect of GPI-phospholipase D. Study has shown that *Cripto-1* can activate the ras/raf/MAPK signal transduction pathway and promote tumor growth and invasion. *Sox2* is a member of the SOX family, and it has been found that *Sox2* can promote cervical cancer cell growth and influence breast cancer G₁/S phase cell proliferation[13]. Survivin and Livin are newly discovered apoptosis-inhibiting proteins, activated Survivin can inhibit Caspase activity, inhibit Caspase cascade and achieve the effect of suppressing cell to perform apoptosis process. At present, it has been found that Livin shows high expression in a variety of malignant tumor cells, and can promote infinite tumor cell proliferation. Zeste homologue is considered to be associated with tumor cell proliferation, infiltration and distant metastasis, and high expression of Zeste is one of the signs of highly malignant tumor. The research results showed that postoperative ZEB1, *Cripto-1*, *Sox2*, Survivin, Livin and zeste protein expression levels of observation group were lower while E-cadherin expression level was higher, indicating that HOLBT had more advantages in effectively killing tumor activity and inhibiting tumor recurrence.

At the same time of excising superficial bladder tumor, HOLBT and TURBT can bring different degree of trauma to patients. There is malnutrition or immunosuppression in patients with malignant tumor, surgical trauma can cause further impact on the patients, and excessive trauma can even cause reduced body autoimmunity to tumor and accelerated tumor expansion[14]. Detection of surgical trauma-related indicators of two groups can indirectly reflect the degree of body damage, and in addition to the tumor resection effect, the damage to patients from different surgical methods was further analyzed. FBG can rise sharply in traumatic stress state, which is mainly because catecholamine stimulates the glycogen decomposition. At the same time of increased blood glucose, in order to maintain the body blood glucose balance in the central nervous system, insulin secretion increases, the binding ability of too much insulin with receptor reduces, causing relative insulin resistance and elevated insulin resistance index (HOMA-IR). Both PTA and FIB can reflect the status of the body's blood coagulation, surgical trauma can act as stressor to cause nerve-humoral factor disorder and lead to early blood coagulation dysfunction, and lower PTA and FIB values are the signs of blood coagulation dysfunction[15]. The research results showed that postoperative FBG and HOMA-IR values of observation group were lower while PTA and FIB values were higher, indicating that HOLBT caused less bleeding during operation and less trauma to the body.

To sum up, it is concluded that HOLBT can effectively remove superficial bladder cancer foci and reduce the malignant degree of tumor, causes less surgical trauma, is an ideal surgical treatment of superficial bladder cancer, and is worth popularization and application in clinical practice in the future.

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