

# Long-term Effect of Transurethral Resection of Bladder Tumour Combined with Intravesical Instillation of Pirarubicin on Immune Function in Superficial Bladder Cancer

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## Feng: Long-Term Effect of TURBT on Superficial Bladder Cancer

This study was aimed to explore the long-term effects of transurethral resection of bladder tumour combined with intravesical instillation of pirarubicin on immune function in superficial bladder cancer. Eighty four patients with bladder cancer admitted to the Linzi District People's Hospital from March 2016 to March 2017 were selected as research subjects and divided into 2 groups according to the digital table. The control group was treated with transurethral resection of bladder tumour. The study group was given intravesical instillation of pirarubicin in addition to the treatment given to the control group. There was no significant difference in recurrence rate between the study group and the control group, 6 mo after operation. However, the recurrence rate in the study group was lower than that in the control group 1 y after operation and the recurrence time of the study group was significantly shorter than that of the control group. There was no significant difference in the incidence of postoperative complications between the study group and the control group and the levels of IgM, IgG and IgA in the study group were significantly higher than those in the control group. In addition the levels of CD<sup>4+</sup>, CD<sup>4+</sup>/CD<sup>8+</sup> in the study group were significantly higher than those in the control group, while the CD<sup>8+</sup> in the study group was significantly lower than that in the control group. In conclusion, transurethral resection of bladder tumour combined with intravesical instillation of pirarubicin is effective in the treatment of bladder cancer and should be further popularized in clinic.

**Key words:** Transurethral resection of bladder tumour, pirarubicin, bladder perfusion, long-term effect, immune function

Bladder tumour is a common disease in urology which ranks as the 17<sup>th</sup> and 7<sup>th</sup> most common tumours in women and men, respectively<sup>[1]</sup>. More than 70 % of bladder tumours are noninvasive or superficially invasive at diagnosis. Transurethral resection of bladder tumour (TURBT) is the preferred treatment for these patients, but it usually leads to recurrence of tumours, so more active treatments are required<sup>[2]</sup>. Intravesical therapy may be another treatment for superficial bladder cancer. In the course of treatment, drugs are injected directly into the bladder through a catheter. It ensures high concentrations of drugs in bladder tissue, while reducing systemic exposure and adverse reactions. Immunotherapeutic and chemotherapeutic drugs are the most common drugs for intravesical use of bladder cancer<sup>[3]</sup>. The commonly used drugs in clinical practice include pirarubicin and doxorubicin. Pirarubicin, an analogue of adriamycin containing tetrahydro pyrrolidone, which can enhance its anticancer ability.

Pirarubicin prevents DNA replication and transcription in cancer cells, therefore, cancer cells are prevented from dividing, thereby reducing the risk of recurrence<sup>[4]</sup>. In this study, the long-term effects of TURBT combined with intravesical instillation of pirarubicin were explored on immune function in patients with bladder cancer in order to provide a basis for clinical practice.

Eighty four patients with bladder cancer admitted to the Linzi District People's Hospital from March 2016 to March 2017 were enrolled and divided into 2 groups according to the digital table method, with 42 cases in each group. The control group consisted of 28 males and 14 females with an average age of 58.3±2.3 y. Tumor stages<sup>[5]</sup> of the 42 cases are as follows, 24 cases in Ta stage and 18 cases in T1 stage. There were 27 males and 15 females in the study group, with an average age of 57.5±3.1 y. Tumour stages are, 25 cases in Ta stage and 17 cases in T1 stage. There was no significant difference between the 2 groups in

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terms of age, gender and tumour stage, as shown in Table 1. The patients in this study were informed about participating in the study before signing the consent form, which was approved by the Hospital Ethics Committee. Inclusion criteria were, patients diagnosed with superficial bladder cancer after clinical diagnosis; patients with no liver and kidney dysfunction, and patients with high postoperative compliance to complete subsequent treatment and follow-up. Exclusion criteria were, patients with severe urinary infection; patients who are intolerant to drugs in this study and patients who are not willing to participate in this study.

The control group was subjected to TURBT. The specific procedure is as follows, the patient underwent epidural anaesthesia and took the lithotomy position. After confirming the success of anaesthesia, the Wolf resectoscope was placed through the urethra to confirm the location of bladder tumours. For patients with small basal tumours, the electrosurgical parameters were set to 60 J electrocoagulation power and 100 J electric power. For patients with large basal tumours, the tissue covering the tumour pedicle was removed first, and then the tumour was completely removed. Then, 2 cm of tissue was burnt around the tumour pedicle to prevent postoperative recurrence<sup>[6]</sup>. Patients in the study group were given intravesical instillation of pirarubicin in addition to the treatment received by the control group. Specific details are as follows, the operation method was the same as that of the control group. After the operation, 30 mg pirarubicin was dissolved in 50 ml sterilized water for perfusion (Chinese medicine quasi character H10930105, Shenzhen Wan Le Pharmaceutical Co., Ltd). The first perfusion was performed on d 2 after operation, and once a week for 8 w. Then the perfusion period was adjusted to once a month for 1 y<sup>[7]</sup>.

The postoperative recurrence rate was recorded in the 2 groups 6 mo and 1 y after operation in the follow-up. The incidence of postoperative complications in the 2 groups was statistically analysed, including

**TABLE 1: COMPARISON OF GENERAL CHARACTERISTICS BETWEEN THE 2 GROUPS**

Groups	N	Gender		Age	Tumor stage	
		Male	Female		Ta stage	T1 stage
Control group	42	28	14	58.3±2.3	24	18
Study group	42	27	15	57.5±3.1	25	17
X <sup>2</sup> /t	/	0.053		0.342	0.049	
P	/	>0.05		>0.05	>0.05	

myelosuppression, ureteral injury, bladder perforation and urinary irritation symptoms. The levels of serum IgM, IgG and IgA, which represent the humoral immunity, were measured using the enzyme-linked immunosorbent assay in both groups. Flow cytometry was used to detect and analyse CD<sup>4+</sup>, CD<sup>8+</sup> as well as the ratio of CD<sup>4+</sup>/CD<sup>8+</sup>, which represent the cellular immunity in the 2 groups.

The data was analysed using SPSS 18.0, in which the count data was subjected to Chi-square test (%), while the measurement data was subjected to t test ( $\bar{x}\pm s$ ).  $p < 0.05$  indicated significant difference. There was no significant difference in the recurrence rate between the study group and the control group 6 mo after operation, as shown in Table 2. There was no difference in the incidence of complications, including myelosuppression, ureteral injury, bladder perforation, urinary irritation symptoms and total rate, between the study group and the control group, as shown in Table 3. The levels of IgM, IgG and IgA in the humoral immunity of the study group were higher than those of the control group, as shown in Table 4.

The levels of CD<sup>4+</sup>, CD<sup>4+</sup>/CD<sup>8+</sup> in the cellular immunity of the study group were significantly higher than those of the control group, while the CD<sup>8+</sup> in the cellular immunity of the study group was significantly lower than that of the control group, as depicted in Table 5. Bladder cancer is a malignant tumour, which has a serious impact on people's quality of life, mainly including superficial bladder cancer<sup>[8]</sup>. At present, TURBT is the main treatment for this disease, but it has a relatively high recurrence rate in clinical practice, which seriously limits its therapeutic utility<sup>[9]</sup>. Although some therapeutic strategies such as systemic immunotherapy/chemotherapy and radiotherapy have been adopted recently, the overall survival rate has not improved and the incidence and even mortality of bladder cancer are very high. Therefore, it is clear that alternative treatment for bladder cancer is still needed<sup>[10]</sup>. Researchers have found that postoperative intravesical instillation can effectively improve the treatment outcome and reduce the recurrence rate<sup>[11,12]</sup>. The drugs

**TABLE 2: COMPARISON OF RECURRENCE RATE BETWEEN THE 2 GROUPS**

Groups	N	Recurrence after operation	
		6 mo	1 y
Control group	42	2 (4.8 %)	8 (19.0 %)
Study group	42	1 (2.4 %)	2 (4.8 %)
X <sup>2</sup>	/	0.346	4.086
P	/	>0.05	<0.05

**TABLE 3: COMPARISON OF POSTOPERATIVE COMPLICATIONS BETWEEN THE 2 GROUPS**

Groups	N	Myelosuppression	Ureteral injury	Bladder perforation	Urinary irritation symptoms	Total rate
Control group	42	0 (0.0)	2 (4.8)	1 (2.4)	1 (2.4)	4 (9.5)
Study group	42	2 (4.8)	1 (2.4)	0 (0.0)	1 (2.4)	4 (9.5)
X <sup>2</sup>	/	2.049	0.346	1.012	0	0
P	/	>0.05	>0.05	>0.05	>0.05	>0.05

**TABLE 4: COMPARISON OF HUMORAL IMMUNITY BETWEEN THE 2 GROUPS**

Groups	N	Time	IgM (g/l)	IgG (g/l)	IgA (g/l)
Control group	42	Before treatment	0.3±0.1	3.1±1.5	0.2±0.1
		After treatment	0.8±0.2 <sup>a</sup>	10.4±1.5 <sup>a</sup>	0.9±0.2 <sup>a</sup>
Study group	42	Before treatment	0.3±0.2	3.1±1.5	0.2±0.1
		After treatment	1.9±0.7 <sup>ab</sup>	13.7±3.9 <sup>ab</sup>	1.7±0.9 <sup>ab</sup>

<sup>a</sup>p<0.05 vs. before treatment, <sup>b</sup>p<0.05 vs. after treatment in the control group

**TABLE 5: COMPARISON OF CELLULAR IMMUNITY BETWEEN THE 2 GROUPS**

Groups	N	Time	CD <sup>4+</sup> (%)	CD <sup>8+</sup> (%)	CD <sup>4+</sup> /CD <sup>8+</sup> (%)
Control group	42	Before treatment	12.3±5.3	8.3±2.3	1.5±0.2
		After treatment	36.7±4.3 <sup>a</sup>	17.4±2.9 <sup>a</sup>	2.1±0.6 <sup>a</sup>
Study group	42	Before treatment	12.3±5.3	8.3±2.1	1.5±0.3
		After treatment	40.1±3.2 <sup>ab</sup>	14.3±3.5 <sup>ab</sup>	2.7±0.5 <sup>ab</sup>

<sup>a</sup>p<0.05 vs. before treatment, <sup>b</sup>p<0.05 vs. after treatment in the control group

for bladder perfusion are mainly divided into biological agents and chemotherapeutic drugs. However, the side effects of biological agents in the clinical application are very large<sup>[13]</sup>. Therefore, chemotherapeutic drugs have become the main drugs for bladder perfusion. Currently, the commonly used drugs in clinical practice include pirarubicin and doxorubicin<sup>[14]</sup>. Pirarubicin can prevent DNA replication and transcription in cancer cells, thus, cancer cells are prevented from dividing, thereby reducing the risk of recurrence<sup>[4]</sup>.

In this study, pirarubicin perfusion was given to patients treated with TRUBT. Subsequently, it was found that the recurrence rate of the study group was lower than that of the control group, and it did not increase the incidence of postoperative complications. In addition, the immune status of patients was also compared between the study group and the control group and the results revealed that immune status of the study group was better than that of the control group. In summary, in the treatment of bladder cancer, TURBT combined with pirarubicin bladder infusion can effectively reduce the recurrence rate and improve patient's immune status, which should be further promoted and applied clinically.

### Conflict of interest:

No conflict of interest between any of the authors.

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