Is there any Effect of Intracavitary Therapy for Superficial Bladder Tumors on Urethral Strictures?

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Abstract

Objectives: In this study, we aimed to find the answer to the question of whether intracavitary therapy administered for bladder tumor has any effect on the development of urethral strictures.

Methods: The patients who underwent transurethral resection of the bladder with the diagnosis of bladder tumor in our clinic were divided into two as the group with urethral strictures and the group without urethral strictures. Intracavitary therapies, follow-up, and recurrence data of the patients of both groups were recorded.

Results: The mean age of the patients with and without urethral stricture was 67.8 and 68.4 years, respectively. There was no significant difference between the T staging and grading of patients in the two groups. There was no statistically significant difference between the patients with and without urethral stricture in terms of intracavital therapy rates (p=0.943).

Conclusion: Although we demonstrated that intracavitary therapy administered for bladder tumors had no effect on the development of urethral strictures, we believe we need randomized controlled trials with larger patient series.

Keywords: Intracavitary therapy, urethral stricture, transurethral bladder resection

In a study, the incidence of urethral stricture was found to be 4% in patients who underwent TUR-B.6 Internal urethrotomy (IU) is the usual method to repair post-TUR-B urethral strictures. The risk of recurrence is high after urethral stricture operation, depending on the location and the patient. It was observed that using mitomycin C (MMC) to the area of strictures was very effective in the prevention of recurrence in urethral strictures as well as bladder neck contractures.7,8

In this study, we aimed to find the answer to the question of whether the incidence of urethral stricture will decrease or not, in patients who receive intracavitary treatment for bladder tumor.
Methods
The data of 237 patients underwent TUR-B and eventually diagnosed with bladder cancer in our clinic between May 2013 and May 2018 were retrospectively screened. Patients who underwent TUR-B due to primary bladder tumor and were followed-up at least for 1 year were included in the study. Those who underwent TUR-B in another center, or yielded T2 pathology of TUR-B, or those without follow-up data were excluded from the study.

All of the patients included were primary bladder cancer and they were diagnosed with TUR-B. In the follow-up, they were divided into two groups as the patients with urethral strictures and the patients without urethral strictures. Patients’ ages, T stages, and grades were recorded. The type and the number of intracavitary therapies administered were recorded. Tumor recurrences developed during the follow-up period were recorded. Urethral strictures were treated with IU or dilatation.

Statistical Analysis
IBM Statistical Package for the Social Sciences, Chicago, IL v20 program was used for statistical analysis. Differences between the groups were assessed by Chi-square test for categorical variables, by t-test or Mann–Whitney U-test for continuous variables. P<0.05 was considered statistically significant.

Results
In the follow-up, patients were divided into two groups as 81 patients with urethral stricture and 156 patients without urethral stricture. The mean age of the patients with urethral stricture was 67.8 (±9.1) years while that of the other group was (68.4±10.3) years. There was no statistically significant difference between the distribution of T stages and grades of both groups. Those with a previous history of ureteral intervention such as IU and TUR-B before the diagnosis of bladder tumor constituted 27.1% of the group with stricture and 29.4% of the other group without urethral stricture. With a previous history of ureteral intervention such as IU and TUR-B before the diagnosis of bladder tumor constituted 27.1% of the group with stricture and 29.4% of the other group without urethral stricture. Those with a previous history of ureteral intervention such as IU and TUR-B before the diagnosis of bladder tumor constituted 27.1% of the group with stricture and 29.4% of the other group without urethral stricture. Those with a previous history of ureteral intervention such as IU and TUR-B before the diagnosis of bladder tumor constituted 27.1% of the group with stricture and 29.4% of the other group without urethral stricture.

The mean number of interventions such as cystoscopy and TUR-B during the follow-up was 6.7 and 3.4 in the groups with and without urethral stricture, respectively. There was no statistically significant difference between the groups, despite the higher number in the group with stricture. Again, no significant difference was found in terms of recurrence between the two groups (p=0.086) (Table 1).

Discussion
Incidence for T stage and grade determined in our patients was similar to the results of other studies reported in literature.[9, 10] In previous studies on TUR-B, the incidence rate of urethral stricture was between 4% and 29%, which is considerably decreased today due to the improvements in surgical instruments and techniques.[11–13] In our study, however, about one-third of patients had a urethral stricture. We attribute this to the factors that can affect the recurrence of urethral strictures, such as cystoscopy or TUR-B, that are applied during follow-up.

Urethral stricture recurrence within a short time is one of

| Variables                  | Urethral stricture (+) (n=81) | Urethral stricture (-) (n=156) | P      |
|----------------------------|-------------------------------|-------------------------------|--------|
| Age (average)              | 67.8                          | 68.4                          | 0.706  |
| T stage n (%)              |                               |                               |        |
| TA                         | 45 (55.5)                     | 72 (46.1)                     | 0.688  |
| T1                         | 36 (44.5)                     | 84 (53.9)                     | 0.504  |
| Grade n (%)                |                               |                               |        |
| Low                        | 59 (72.8)                     | 116 (74.3)                    | 0.188  |
| High                       | 22 (27.2)                     | 40 (25.7)                     | 0.188  |
| Previous history of ureteral intervention n (%) |                               |                               |        |
| Yes                        | 22 (27.1)                     | 46 (29.4)                     | 0.429  |
| No                         | 59 (72.9)                     | 120 (70.6)                    | 0.429  |
| Intracavitary therapy n (%) |                               |                               |        |
| Yes                        | 46 (56.7)                     | 73 (46.7)                     | 0.943  |
| No                         | 35 (43.3)                     | 83 (53.3)                     | 0.943  |
| BCG                        | 24 (52.1)                     | 34 (46.5)                     | 0.857  |
| MMC                        | 22 (47.9)                     | 39 (53.5)                     | 0.805  |
| Induction                  | 27 (58.6)                     | 41 (56.1)                     | 0.450  |
| Induction + maintenance    | 19 (41.4)                     | 32 (43.9)                     | 0.521  |
| Number of intracavitary therapies (average) | 6.1                          | 4.6                           | 0.745  |
| follow-up period (average) | 31.1                          | 27.7                          | 0.666  |
| Number of TURM (average)   | 3.4                           | 2.4                           | 0.780  |
| Number of cystoscopy (average) | 6.7                          | 5.7                           | 0.235  |
| Bladder tumor recurrence n (%) |                               |                               |        |
| Yes                        | 55 (67.9)                     | 105 (67.3)                    | 0.086  |
| No                         | 26 (32.1)                     | 51 (32.7)                     | 0.086  |
the major issues after the treatment of strictures by IU. Various systemically or locally applied substances were used to increase the success of the IU. Besides transurethral injection of triamcinolone, proposed for the first time by Hebert in 1972, systemic steroid administration or use of triamcinolone ointment was also tried. In a study by Hosseini et al., patients who underwent clean intermittent catheterization with triamcinolone ointment for 6 months following IU were compared against those who used a water-based lubricant and the rate of developing urethral stricture after a 12-month follow-up was slightly lower in the triamcinolone group, though no statistically significant difference was noted. In this study, we aimed to find out the effect of intracavitary therapy on the recurrence of urethral stricture in the patients with a bladder tumor.

When we reviewed the other studies in literature with a view to improve the success of the IU, we saw that MMC was used for its anti-fibroblast and anti-collagen properties and for preventing scar tissue formation. In the follow-up of the patients who were treated with submucosal MMC to the stenotic area following IU, we observed that strictures were less in comparison to the non-treated patients. In our study too, intracavitary MMC and BCG administration yielded no significant difference between the patients with and without urethral stricture. This can be the result of a failure in the administration of submucosal MMC to the region of stricture. Besides that, although there was no statistically significant difference, the number of TUR-B and cystoscopy was more in number among the patients with a urethral stricture in comparison to the patients without urethral stricture; hence, the incidence of strictures might be affected from this high number.

Intravesical administration of BCG executes its effect by a massive local immune response. BCG causes cytokine release in the bladder after it is adhered to urothelium and bladder cancer cells through fibronectin. The inflammatory process begins with the stimulation of the cellular immune response and continues. Immunological response activates cellular cytotoxic mechanisms, and tumor cells become the target of cellular immunity. In this study, it was shown that the immunoreaction generated by BCG did not affect the development of urethral stricture.

As for the limitations of the study, retrospective design and limited number of patients can be mentioned. To the best of our knowledge, this the first study conducted on this topic, which makes it valuable.

**Conclusion**

We concluded that intracavitary therapy administered for bladder tumor did not affect the development of urethral stricture. In the meantime, further randomized controlled studies are required to reach a more reliable result.

**Disclosures**

**Ethics Committee Approval:** The study was approved by the Local Ethics Committee.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – M.K.; Design – H.K., S.U., M.K.; Supervision – E.A.; Materials – E.A., S.U., H.T.; Data collection &/or processing – H.K., E.A.; Analysis and/or interpretation – S.U.; Literature search – S.U., M.K.; Writing – M.K.; Critical review – E.A.

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