DOI:10.2478/jbcr-2022-0009

Original Article

# INTRAVESICAL THERAPY OF SUPERFICIAL UROTHELIAL BLADDER CANCER WITH BCG AND EPIRUBICIN 50 MG - COMPARATIVE ANALYSIS

**Nikolay I. Nikolov,**
**Vladislav R. Dunev,**
**Angel A. Anatoliev,**
**Nikolay H. Kolev,**
**Martin B. Stoykov,**
**Boyan S. Atanasov**

*Clinic of Urology,*
*University Hospital "St. Marina" - Pleven*
*Medical University - Pleven*

**Corresponding Author:**
Nikolay I. Nikolov
Department of Urology,
University Hospital "St. Marina"
Bulgarian aviation Str.,
Pleven, 5800
Bulgaria
*e-mail: dr_niknikolov@abv.bg*

**Received:** January 18, 2022
**Revision received:** February 01, 2022
**Accepted:** May 11, 2022

## Summary

Bladder cancer is a heterogeneous disease in molecular, histological and clinical aspects. Treatment should also be considered from different angles - surgery, intravesical chemo- or immunotherapy, radiation therapy and lifestyle changes. Intravesical treatment of superficial bladder cancer with Epirubicin or Bacillus Calmette-Guérin (BCG) is a continuation of surgical treatment to reduce or eliminate further recurrence.
**Keywords:** bladder cancer, intravesical therapy, epirubicin, BCG

## Introduction

Epirubicin is an anthracycline cytotoxic agent. It is known that anthracyclines can affect a number of biochemical and biological functions in eukaryotic cells. The exact mechanisms of cytotoxicity and/or antiproliferative properties of epirubicin are not fully understood. BCG has been used to treat non-muscular invasive bladder cancer for more than 30 years. It is one of the successfully used molecules for biotherapy in cancer. Despite the long clinical experience with BCG, the mechanism of its therapeutic effect is still under investigation. Available data suggest that urothelial cells and immune system cells play a crucial role in the therapeutic anti-tumor effect of BCG. Immune system cells that have a potential role in BCG therapy include CD4+ and CD8 lymphocytes, natural killer cells, granulocytes, macrophages and dendritic cells. Bladder cancer cells are killed by the direct cytotoxicity of these cells, by secretion of soluble TRAIL (tumor such as TRAIL necrosis factor binding apoptosis-inducing ligand) and, to some extent, by the direct action of BCG. There are still several gaps in our knowledge that need to be addressed in future efforts to understand this cancer biotherapy [5]. Transurethral (TUR) resection is the gold standard for treatment of patients with superficial bladder cancer with histological verification Ta, T1, Tis. Intravesical



© Medical University Pleven

application of BCG and Epirubicin has been shown to reduce tumor recurrence and prevent or delay progression to muscle invasion and metastasis. However, a comparison of the efficacy and safety of Intravesical BCG and Epirubicin in bladder cancer has not been studied yet [3].The use of BCG for 6 weeks or Epirubicin 50mg for 6 weeks reduces the risk of recurrence compared with a group of patients who underwent only transurethral surgery.

## Materials and Methods

Seventy-five patients with superficial bladder carcinoma were followed from October 10 2020 to October 10 2021. All these patients underwent transurethral surgery. The histological picture corresponding to Ta, Tis, T1 transitional cell carcinoma with low to moderate risk. Intravesical chemo- or immunotherapy was given to 57 patients. The remaining 18 patients were not followed-up. The follow-up examinations were at 3, 6, 9 and 12 month. Cytological examination of urine for tumor cells, imaging, urethrocystoscopy, white light and NBI (narrow bind imaging) were performed in all of them. The data were summarized and a comparative analysis was made. Patients were divided into three groups: Group A - without subsequent chemotherapy (18 patients); Group B - with Intravesical application of BCG (22 patients); and Group C - with Intravesical application of Epirubicin 50 mg (35 patients). Intravesical infusions of BCG or Epirubicin were performed using a 16 ch nelaton catheter. The time without urination was between 100, 150 minutes, average of 120 min. The treatment course was 6 weeks, followed by treatment once a week and subsequent course of 6 months, followed by treatment once a month. Before each intravesical therapy, patients were examined for PC, urea, creatinine, and urine exography of the abdominal organs and pelvis was performed.

## Results

The results of the control examinations were summarized. Table 1 presents the number of patients with local recurrence at 3, 6, 9 and 12 month of the three control groups. It can be seen that the largest relative share is in group A - without Intravesical Therapy. (Figure 1)

**Table 1.** Patients with relapse at month 3, 6, 9 and 12

| Group | 3rd month | 6th month | 9th month | 12th month |
|---|---|---|---|---|
| A | 1 | 2 | 4 | 5 |
| B | 0 | 0 | 2 | 3 |
| C | 0 | 2 | 3 | 3 |

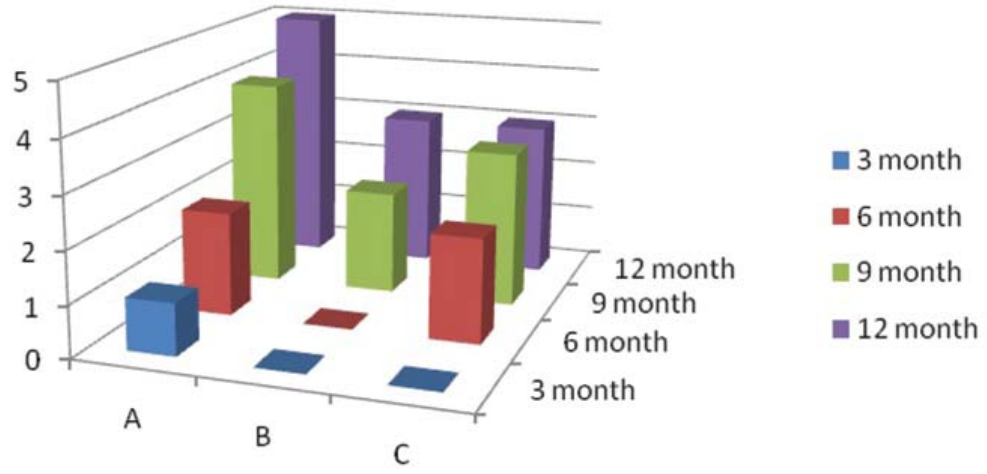


**Figure 1.** Number of patients with local recurrence at 3rd, 6th, 9th and 12th month in the three control groups



© *Medical University Pleven*

There was an increase in patients with relapse in group A by 27.78 % compared with group B - 13.64 % and group C - 8.57 % (Table 2).

In group B and group C, there was a slight increase in local recurrence, as compared with group A. (Figure 2)

The total number of patients with local recurrence in groups B and C was insignificant. In patients in group A the recurrence rate was three times that of groups B and C. (Figure 3)

**Table 2.** Distribution of patients with relapse by percentage

| Group | 3rd month | 6th month | 9th month | 12th month |
|---|---|---|---|---|
| A | 5.56% | 11.11% | 22.22% | 27.78% |
| B | 0% | 0% | 9.09% | 13.64% |
| C | 0% | 2.86% | 8.57% | 8.57% |

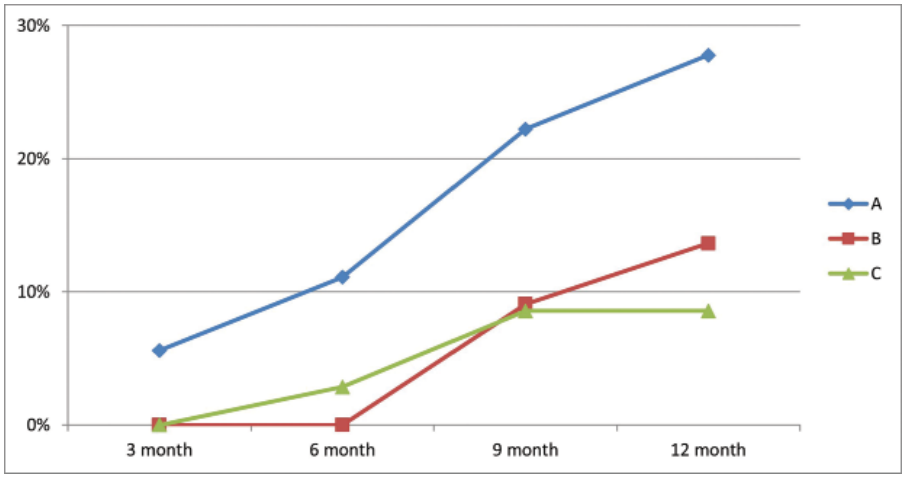


**Figure 2.** Distribution of patients with relapse by percentage

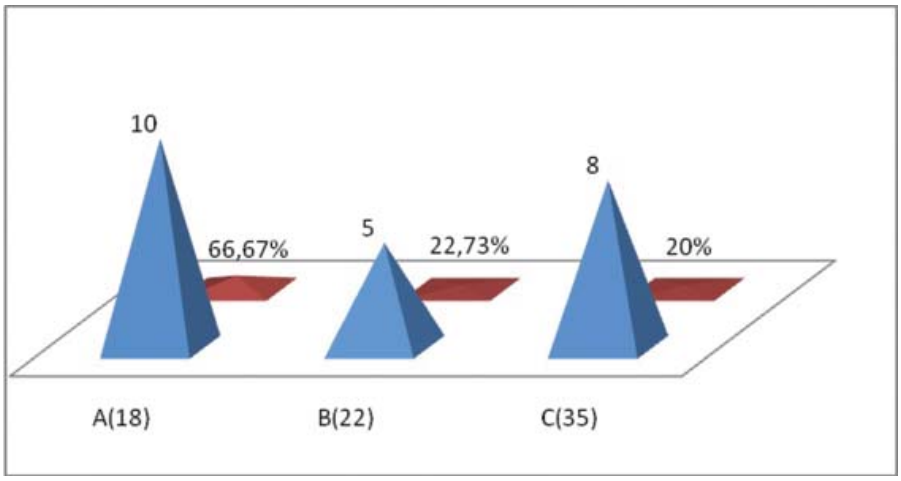


**Figure 3.** Total number of patients with local recurrence

## Discussion

Bladder cancer is the most common tumor of the urinary system. The male:female ratio varies from 6:1 to 2:1. In recent years, more and more young people are getting sick, which requires a new strategy for its diagnosis and treatment. Superficial or non-muscular invasive bladder cancer is found in approximately 70% of patients. It is not an immediate life-



© Medical University Pleven

threatening condition, unlike its muscle-invasive counterpart, but it is characterized by significant levels of relapse of 50 %-80% and a potential for progression of 10%-45% [6]. Surgical treatment of superficial urothelial bladder cancer alone cannot be definitive. Intravesical therapy with BCG or Epirubicin is a step up, in terms of its treatment and prevention of recurrence. Immediate application (up to 24 hours) of a local chemotherapeutic was found to reduce the risk of recurrence by 35% and the five-year recurrence rate by 44.8% to 58.8%.The lack of response to intravesical chemotherapy in patients with non-muscular invasive bladder cancer is known to be due to two factors: lack of sensitivity of the neoplasm to intravesical chemotherapy and inadequate drug delivery to the tumor. In high-risk patients, BCG has been shown to be superior to Epirubicin in preventing recurrence after TUR [1, 2, 4]. The relative efficacy of Epirubicin and BCG after TUR in low-risk patients is still unclear. Intravesical Epirubicin has been found to be better tolerated than BCG. Immunotherapy has a long-term effect than the risk of relapse, but has more side effects.

## Conclusion

The application of chemotherapy and immunotherapy leads to a reduction in local recurrences and the progression of urothelial carcinoma of the bladder. In high- risk patients, BCG has shown to be superior to Epirubicin in preventing recurrence after TUR, but Epirubicin is better tolerated by patients.

## References

1. Ganev T, Petkova L, Statelov T, Stamboliyski V, Hinev A, Evtimov N. Clinical experience in the treatment of invasive bladder cancer. Uronet. 2011;3:29-34.
2. Evtimov N, Ganev T, Stamboliyski V. Complications in the choice of laparoscopic surgical technique. Urology. 2015:2;36-41.
3. Arends TJ, Nativ O, Maffezzini M. et al. Results of a Randomised Controlled Trial Comparing Intravesical Chemohyperthermia with Mitomycin C Versus Bacillus Calmette-Guérin for Adjuvant Treatment of Patients with Intermediate- and High-risk Non-Muscle-invasive Bladder Cancer. Eur Urol. 2016 Jun;69(6):1046-52.
4. Chou R, Selph S, Buckley DI. et al. Intravesical Therapy for the Treatment of Nonmuscle Invasive Bladder Cancer: A Systematic Review and Meta-Analysis. J Urol. 2017 May;197(5):1189-99.
5. Redelman-Sidi G, Glickman MS, Bochner BH. The mechanism of action of BCG therapy for bladder cancer - a current perspective. Nat Rev Urol. 2014 Mar;11(3):153-62.
6. Porten SP, Leapman MS, Greene KL. Intravesical chemotherapy in non-muscle-invasive bladder cancer. Indian J Urol. 2015 Oct-Dec;31(4): 297-303.



© *Medical University Pleven*