Orginal Article

Clinical outcome of Low dose intravesical BCG therapy for Non muscle invasive bladder cancer (NMIBC)

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Abstract

Introduction: Intravesical Bacillus Calmette-Guerin (BCG) is one of the most effective therapy for Non Muscle invasive bladder cancer (NMIBC), however, due to adverse effects many patients failed to continue treatment. Main objective of this study is to find out efficacy of low dose intravesical BCG in reducing adverse effect without compromising recurrence of tumor.

Methods: This is Cross sectional prospective study which include 39 patients who underwent trans-urethral resection of bladder tumor (TURBT) for bladder mass and histopathology (HPE) report is NMIBC receiving induction or maintenance intravesical BCG from 15th July 2025 to 30th November 2025 at Dhulikhel Hospital, Kathmandu university hospital.

Results: Mean age is 62.38 ± 10.74 years, 28 Male (71.79%) and 11(28.21%) Female patient. Majority of patients (82.05%) received 60mg intravesical BCG. Adverse effect was noted in 12.82% all are genitourinary symptoms. Recurrence is noted in 12.82% of patients.

Conclusion: Low dose of intravesical BCG for NMIBC is as effective as standard dose with similar recurrence rate and decreased adverse effects.

Keyword: Bacillus Calmette-Guerin (BCG), Non Muscle invasive bladder cancer (NMIBC), trans-urethral resection of bladder tumor (TURBT)

Introduction

Intravesical Bacillus Calmette-Guerin (BCG) is one of the most effective therapy for Non Muscle invasive bladder cancer (NMIBC).[1] NMIBC has high recurrence and around 10-20% progress to muscle invasive bladder cancer (MIBC).[2,3] BCG has shown both decrease in recurrence and progression in NMIBC.[4] Clear mechanism of BCG is poorly understood however it is definitely immune response mediated.[5] BCG therapy is usually affected by local and systemic adverse effects which are basically infective and irritative symptoms like cystitis, frequency, sepsis and hematuria which usually occur during induction and initial maintenance phase.[6,7] this symptoms accounts more than 60% leading to discontinue of treatment.[8] Several trial has been done to manage these adverse effect by using antibiotics, intravesical local anesthesia like lidocaine and anticholinergic drugs to decrease irritation.[9] Decreasing standard BCG dose can improve outcome by reducing BCG toxicity.[10,11]

Methods

This is Cross sectional prospective study among patients who underwent trans-urethral resection of bladder tumor (TURBT) and histopathology (HPE) report is NMIBC who were receiving induction or maintenance intravesical BCG from 15th July 2025 to 30th November 2025 at Dhulikhel Hospital, Kathmandu university hospital. Ethical clearance was obtained from Institutional review committee of Kathmandu university school of medicine (KUSMS) with reference number 178/25.

All the patient undergoing TURBT with HPE report of NMIBC above 18 years of age during study period were included in this study. Inclusion criteria were patient diagnosed urinary bladder mass without nodal and distant metastasis by CT abdomen and pelvis, age above 18 years and HPE report after TURBT is NMIBC.

American Urological Association (AUA) risk stratification was followed, low risk patients were not given intravesical BCG therapy.[12] Only intermediate and high risk patients were given BCG induction and maintenance therapy.

Low Risk	Intermediate Risk	High Risk
LG[a] solitary Ta ≤ 3cm	Recurrence within 1 year, LG Ta	HG T1
PUNLMP[b]	Solitary LG Ta > 3cm	Any recurrent, HG Ta
	LG Ta, multifocal	HG Ta, >3cm (or multifocal)
	HG[c] Ta, ≤ 3cm	Any CIS[d]
	LG T1	Any BCG failure in HG patient
		Any variant histology
		Any LVI[e]
		Any HG prostatic urethral involvement

[a]LG = low grade; [b]PUNLMP = papillary urothelial neoplasm of low malignant potential; [c]HG = high grade; [d]CIS=carcinoma *in situ*; [e]LVI = lymphovascular invasion

Southwest oncology group (SWOG) guideline was followed for induction and maintenance of intravesical BCG therapy. Onco BCG each vial containing 40mg was used. Each vial diluted with 40ml normal saline. BCG was installed via 60ml syringe through 14Fr or 16 Fr foley's catheter. After installation foley's catheter was clamped. Holding time less than 60 minutes was drop out from the study.

Patient were followed up after 2 weeks, then as per SWOG guideline for maintenance BCG and check cystoscopy.

The data were entered in Microsoft excel 2013 and then exported to IBM SPSS version 20 for statistical analysis. Categorical variables were expressed as frequency and percentages. Continuous variables were expressed as mean with standard deviation or median with inter quartile range. We measured only descriptive outcome.

Results

There was total 39 cases with 11 females (28.21%) and 28(71.79%) males. The age ranged from 35 years to 84 years with mean age 62.38 ± 10.74 years.

Mean BMI was 23.35±2.04 kg/m2.

Most of the patients received 60mg intravesical BCG 82.05%, 17.95% received 40mg intravesical BCG.

Adverse effect was noted in 12.82% of patients, out of which frequency was noted in 1(2.56%), burning micturition in 2(5.13%) and UTI in 2(5.13%) patient. All those patients were managed in OPD basis.

Check cystoscopy was done as per SWOG guideline, recurrence was noted only in 5(12.82%) patient who underwent Re-TURBT. Inflamed urothelium was noted in 2(5.13%) patients.

Table 1: Demographic and clinical characteristics

Variables	Total (n=39)
Mean age (years)	62.38± 10.74
Gender Male Female	28 (71.79%) 11 (28.21%)
BMI	23.35±2.04
BCG dose 60mg 40mg	 32(82.05%) 7(17.95%)
Side effects Burning Micturition Frequency UTI	5(12.82%) 2(5.13%) 1(2.56%) 2(5.13%)
Check cystoscopy findings Inflamed urothelium Recurrence normal	 2(5.13%) 5(12.82%) 32(82.05%)
HPE CIS Ta T1	 1(2.56%) 15(38.46%) 23(58.98%)
Tumor Grade Low Grade (LG) High Grade (HG)	 12 (30.77%) 27 (69.23%)

Histopathological findings were: CIS 1(2.56%), Ta 15(38.46%) and T1 23(58.98%).

Most of the tumor were of HG (69.23%).

Discussion

Intravesical BCG therapy is the mainstay of treatment to decrease recurrence and progression of NMIBC. However, due to adverse effects of BCG therapy many patients have to abandoned from this treatment. Many trials have been

conducted to decrease this adverse effect like antibiotic prophylaxis, concurrent use of interferon and dose reduction of BCG.[13,14,15] Decreasing BCG dose has shown improve outcome by reducing BCG toxicity.[10,11]

Though intravesical BCG is mainstay of treatment for NMIBC in intermediate and high risk patient, it carries adverse effect which has be life threatening also.[16] The rate of adverse effect is reported to be less than 5% as per EAU 2024 guidelines and intravesical BCG decrease recurrence and progression in high and intermediate risk patients.[17]

In a study conducted by Larsen et al., only 1% BCG related side effect was noted of which 78.4% was genitourinary symptoms which was much lower than in our study which has shown 12.82% adverse effect but in our study also most of them were genitourinary symptoms.[18] In a study conducted by Vijjan et al, 28.6% and 54% adverse effect noted in 40mg and 80mg group respectively with 5 patients having grade 3 toxicities requiring inpatient management which was unlike our study where all adverse effect were grade 1 and 2 as per NCCN CTC guideline which were managed as outpatient basis.[19]

In a study conducted by Grajales et al., 5.2% of patients dropped out from treatment due to BCG toxicity, however in our study no patient dropped out from treatment except 2 patients with UTI were deferred from treatment until UTI was treated and intravesical therapy was resumed after that.[20]

In our study recurrence rate was 12.82% which correlates with study by Luitel et al. 13% recurrence in low dose intermediate risk group and Vijjan et al. Showing 13.5% recurrence in 80mg group.[19,21]

Immediate post TUR intravesical mitomycin was given in our all cases of TURBT unless contraindicated. In a study conducted by Mian et al., immediate post TUR mitomycin C intravesical vs delayed mitomycin C immediate group has shown to decrease recurrence rate 27% vs 36%.[22]

Study Limitations

This was short duration study. Longer duration of treatment course and follow up would reflect exact recurrence and adverse effect. Sample size of this study is very small and this is single centre study.

Conclusion

Low dose intravesical BCG for NMIBC is as effective as standard dose with similar recurrence rate and decreased adverse effects.

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