ejpmr, 2022, 9(5), 45-49

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

OUTCOME OF MULTIPLE SESSION TRANSURETHRAL RESECTION OF BLADDER TUMOUR WITH INTRAVESICAL THERAPY IN COMPARISON WITH RADICAL CYSTECTOMY AND URINARY DIVERSION FOR HIGH GRADE (G3), STAGE T1 TRANSITIONAL CELL CAECINOMA OF URINARY BLADDER

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Article Received on 12/03/2022 **Article Revised on 02/04/2022** **Article Accepted on 22/04/2022**

ABSTRACT

Objectives: To observe the outcome between multiple session transurethral resection of bladder tumor with intravesical therapy vs radical cystectomy in case of high grade (G3) stage T1 transitional cell carcinoma of urinary bladder. **Methods:** Total 40 patients with T1G3 were selected by inclusion and exclusion criteria. Purposive sampling was done. Some patients (30) were treated with conservative approach and some patients (10) were treated with radical cystectomy and urinary diversion. This was a retrospective study. The study conducted in the department of urology of National Institute of Kidney Diseases and Urology, Dhaka from January 2015–dec 2015. All patients with TCC of urinary bladder. **Results:** Mean age and standard deviation of Group-A and Group-B patients were 61±10.33 and 58±6.74 respectively. There was no association between the patients treated by TURBT and intravesical therapy (Mitomycin-C or BCG) and radical cystectomy in case of male (36) and female (4). In relation to recurrence of disease the calculated value (i.e. 4.506) was greater than the tabulated value (i.e. 3.84). So the result was statistically significant. Percentage of recurrence was 100% and 20% in case of patients treated with conservative approach or radical cystectomy respectively. After radical cystectomy recurrence was occurred in the left lower ureter at the ureteroileal anastomotic site in one case and pelvic lymph nodes in another case. Disease progression was observed 4(30) and 2(10) patients in case of Group-A and Group-B. So the end point of my study to observe the recurrence and progression of disease in both groups. **Conclusion:** T1G3 transitional cell carcinoma of urinary bladder is an aggressive tumor. From my study it may be concluded that the recurrence rate of T1G3 TCC of urinary bladder is very high. In relation to recurrence of disease in high grade superficial bladder cancer TURBT and intravesical therapy is not a good treatment option. But early radical cystectomy and ileal conduit is the best treatment option to prevent recurrence. Certainly no definitive conclusions can be made regarding the impact of TURBT and intravesical therapy on progression from my study as the power of this study was limited by the small sample size. T1G3 is a deadly tumor, so proper follow-up protocol should be maintained.

KEYWORD:- Transurethral resection, Bladder tumor, Urinary bladder.

INTRODUCTION

Transitional cell carcinoma (TCC) of urinary bladder is a disease of middle age and elderly, though it can occur even in children, mean age at diagnosis of transitional cell carcinoma is 69 years in males and 71 years in females. Moreover the incidence of bladder cancer is also higher in elderly persons (Messing, 2002).[1] In man it is 2.5 times more common than in women, the 4th most common cancer after prostate, lung and colorectal malignancies, accounting for 6.2% of all cancer cases and in women it is the 8th most common cancer, accounting for 2.5% of all malignancies (Greenlee et al, 2000).[2]

More than ninety percent of bladder cancer is epithelial in origin. Out of that 90% are transitional cell carcinoma (Carrol, 2000).[3] About 70% of bladder cancer TCC present as superficial lesions at their initial presentation and 10% to 30% of these progress to muscle invasive lesion (Messing, 2002).[1] Superficial TCC refer to Ta,

T1, Tis lesions of any grade according to TNM staging system for bladder cancer which includes those tumors that involve bladder mucosa and invade up to lamina propria (Ro et al, 1992). Tumor grade and stage clearly have an influence on tumor recurrence and progression, Low grade (G1 & G2) Ta lesions recur at a rate of 50% to 70% and have a 5% chance of progression where as high grade (G3) T1 lesion recur in more than 80% of cases and progress to a higher stage in 50% of cases within 3 years.[4]

The initial critical step is to establish an accurate diagnosis. An inaccurate diagnosis, particularly understating, can adversely impact on the survival of the patient. Overtreatment affects the quality of life and possibly leads to unnecessary morbidity. So, it is not easy to make an accurate decision.[5]

Transurethral resection of the bladder tumor is a diagnostic and therapeutic procedure. Following TUR of a high-grade T1 tumor, the risk of recurrence approaches 80% and the risk of progression is 50% to 65%. The goals of adjuvant intravesical therapy are to decrease the rate of recurrence and ultimately decrease the chance of progression. Intravesical therapy with chemotherapeutic or immunologic agents in an adjuvant fashion after endoscopic resection has been shown to decrease the recurrence rate of stages Ta and T1 transitional cell carcinoma of the bladder. Radical cystectomy is the most appropriate option for patients who recur with high-grade or high-stage disease.[5]

Several groups recommend immediate or early cystectomy without a trial of adjuvant intravesical therapy with or without repeat TUR. Supporters of this approach argue that the 5-year survival rate of 90% may decrease to 50% to 60% if radical cystectomy is delayed until progression. Apart from this, there are several valid arguments that support both early and deferred cystectomy.[5]

J.D.T. Morgan *et. al* retrospectively reviewed those patients who underwent follow-up TURBTs within 6 weeks of the initial resection.[6] A total of 37% had persistent tumour on the second resection. Grimm et al similarly retrospectively reviewed 83 patients who underwent a repeat TURBT a mean of 7 weeks after the initial TURBT. Residual tumour was found in 33%.

OBJECTIVE

General objectives

To observe the outcome between multiple session transurethral resection of bladder tumor with intravasical therapy vs radical cystectomy in case of high grade (G3) superficial transitional cell carcinoma.

Specific objectives

- To see the rate of recurrence and progression after complete transurethral resection of bladder tumor and intravesical therapy.
- To see the complication of TURBT, intravesical therapy and radical cystectomy.

METHODOLOGY

Study design : A retrospective study
Study place : Department of Urology, NIKDU, Dhaka.
Period of study : Jan 2015-Dec 2015
Study population : All patients with TCC were admitted in this institute.
Sample size : A total of 40 cases were recruited with G3 superficial TCC. Some were treated with conservative approach and some were treated with radical cystectomy.
Sampling method : Purposive sampling

Selection criteria

Inclusion criteria

- Patients with high grade superficial TCC (pT1) of urinary bladder.

Exclusion criteria

- Muscle invasive / advanced TCC at initial presentation or at first resection.
- Grade I and grade II TCC
- Associated with upper tract TCC
- Associated with CIS (TCC)

Description of procedure

All patients, admitted in the Department of Urology, NIKDU with bladder tumor, were initially evaluated by taking history and clinical examination and investigation available with them. A good number of cases presented with definitive diagnosis and others were partially worked up or presented with recently developed urinary complaints. Ultrasonography of KUB and prostate were done to determine the size, number, and site of the growth in the bladder, to exclude bladder outflow obstruction, to exclude synchronous growth elsewhere in the urinary tract and/or other concomitant pathology. Urine analysis was done in all cases to see evidence of microscopic haematuria. Liver function test and coagulation profile was checked in all cases. Finally, only patients with T1G3 of TCC of urinary bladder were taken as sample. Total 40 patients were taken for the study fulfilling all criteria of inclusion. All of those patients and their relatives were counseled about the diagnosis, pathology, treatment option, recurrence and progression, complication and outcome of the disease.

Procedure of Preparing and Organizing materials

All collected questionnaire will be checked very carefully to identify the error in the data. Data processing work will consist of registration schedules, editing computerization, preparation of dummy table, analyzing and matching of data.

Data collection procedure

A questionnaire was administered for collecting data related to study.

Procedure of data analysis of interpretation

Data had been analyzed by using SPSS version 16. t-test and chi-square test was done.

RESULTS

Table 1: Age distribution of patients.

Age (years)	Group-A (Treated by TURBT and intravesical therapy)	Group-B (Treated by cystectomy and urinary diversion)	Mean $\bar{x}_1$	Mean $\bar{x}_2$	Standard deviation (SD) Group-A	Standard deviation (SD) Group-B	't'
40-50	4	1	61	58	10.33	6.74	1.053
50-60	10	5					
60-70	10	4					
70-80	5						
80-90	1						

In this study age of patients were found ranging from 40 years to 90 years. 't' calculated value was smaller than 't' tabulated value at 5% level (0.05) of significant. So there was no significant difference between mean age of patients treated by TURBT and intravesical therapy and mean age of patients treated by cystectomy and urinary diversion.

Table 2: Sex distribution of patients.

Sex	Group-A (Treated by TURBT and intravesical therapy)	Group-B (Treated by cystectomy and urinary diversion)	X^2
Male	28	8	1.481
Female	2	2	

Now referring the X^2 table, value of 1 degree of freedom at 5% level of significance was 3.84. The calculated value (i.e. 1.48) was less than the tabulated value (i.e. 3.84). So there was no association between the patients treated by TURBT and intravesical therapy and radical cystectomy in case of male and female.

Table 3: Clinical presentation.

Symptoms	Number of patients	Percentage (%)
Haematuria	36	90
Frequency	12	30
Urgency	10	25
Dysuria	8	20
Urinary retention	2	5

Most of the patients (36) presented with haematuria (90%). Only 2 patients presented with retention of urine.

Table 4: Complication after intravesical therapy (Total patients: 30).

Complication	Patients numbers	Percentage
Frequency, Urgency, Dysuria	12	40%
Hemorrhagic cystitis	0	0%
BCG osis	0	0%

12(30) patients were suffered from irritative bladder symptom.

Table 5: Complication after TURBT or cystectomy and diversion.

Complication	Group-A (Treated by TURBT and intravesical therapy)	Group-B (Treated by cystectomy and urinary diversion)
Per operative hemorrhage needed blood transfusion	4	6

Post operative haematuria needed blood transfusion	8	
Clot retention	4	
Sexual problem		2
Recurrent UTI	5	6
Metabolic complication	2	3
Stoma related complication		3

Postoperative haematuria was the most common complication.[14] Recurrent UTI and electrolyte imbalance were presented in both groups.

Table 6: Recurrence of disease.

Groups	Total number of patients	Number of recurrence	Percentage (%)	X^2
Group-A (Treated by TURBT and intravesical therapy)	30	30	100	4.506
Group-B (Treated by cystectomy and urinary diversion)	10	2	20	

Now referring the X^2 table, value of 1 degree of freedom at 5% level of significance was 3.84. The calculated value (i.e. 4.506) was greater than the tabulated value (i.e. 3.84). So the result was statistically significant. Percentage of recurrence was 100% and 20% in case of patients treated with conservative approach or radical cystectomy respectively. Recurrence was occurred in the left lower ureter at the ureteroileal anastomotic site in one case and pelvic lymph nodes in another case.

Table 7: Progression of disease.

Groups	Total number of patients	Number of progression	X^2
Group-A (Treated by TURBT and intravesical therapy)	30	4	0.1875
Group-B (Treated by cystectomy and urinary diversion)	10	2	

Now referring the X^2 table, value of 1 degree of freedom at 5% level of significance was 3.84. The calculated value (i.e. 0.1875) was less than the tabulated value (i.e. 3.84). In case of Group-A, T1 TCC was progressed to T2 disease in 4(30) patients. Local progression was occurred in 2(10) patients in Group-B where T1 TCC extend to pelvic lymph node in one case and left lower ureter in another case. So, in both groups diseases progression were observed.

DISCUSSION

Transurethral resection of bladder tumors is a diagnostic and therapeutic procedure. It aims not only to determine the type and extent of disease, but also to eradicate all macroscopic superficial and if possible invasive tumors. Transurethral resection should also provide adequate specimens for pathological evaluation of tumor grade and stage.

In western countries it is generally a disease of middle age or elderly persons, with the median ages at diagnosis for TCC being 69 years in males and 71in females. A conservative approach with TURBT and inrtavesical therapy was done by Pansadoro *et. al.* in 1996.[7] Mean age at diagnosis was as old as 73 years among their patients with stage T1 tumors.

In standard text incidence of bladder tumor has been reported 5:2 in male and female.[2] In my study incidence in female was lower than that (9:1). This discrepancy may be due to low incidence of disease, under reporting of the case among women as a result of poor socioeconomic condition, position in society/ family, cultural and religious background and smoking habit of our population with male preponderance.

Mike B. Siroky et. al. stated that in case TCC of urinary bladder approximately 80% of patients present with gross, painless haematuria.[8] Approximately 20% of patients with bladder cancer present solely with microscopic haematuria. Ten percent of patients present with symptoms secondary to metastases. Dysuria and irritative symptoms are present in up to 30% of patients. Secondary urinary infection may be present in about 30% of patients.

The largest series of complications from BCG included over 2600 patients. The most common were irritative lower urinary tract symptoms (LUTS) (27%-95%), fever greater than 39.5ºC (2.9%), hematuria (1.0%), granulomatous prostatitis (0.9%), granulomatous pneumonitis or hepatitis (0.7%), arthralgia (0.5%), epididymitis (0.4%), and severe disseminated BCG sepsis (0.4%), as well as very rare rashes, ureteral obstruction, bladder contraction, and renal abscesses (all<0.3%).[9] In my study 12(30) patients, 40% were suffered from irritative bladder symptom. Hemorrhagic cystitis, BCG sepsis was not observed in any patient.

Furthermore the potential for disease recurrence and progression even in the long term typically requires and necessitates lifelong follow-up.[10] Although a variety of different follow-up strategies have been advocated, the most common approach has included patient assessment every three months in the first two years after initial diagnosis followed by every six months for the subsequent two to three years, and then annually thereafter.[10]

Selected patients with T1G3 disease can be managed conservatively with excellent long-term outcomes. A study from Italy reported a progression rate of 15%, recurrence rate of 33% and overall bladder-cancer specific death rate of 6% in 81 patients with T1G3 tumors treated with TURBT and maintenance BCG with median follow-up of 76 months.[7] A recent combined analysis from seven European trials demonstrates that for T1G3 disease, the five-year probabilities for recurrence after TUR are 46%. The risk increases with increasing number of tumors, tumor size, prior recurrence rate and concomitant CIS.[11]

The progression rate in superficial G3 tumors treated with TURBT along is roughly 40%. The progression rate for patients with recurrent disease in the bladder becomes 60%. This statistic is supported by Lutzeyer *et al.* (1982), who showed in a large study that the risk of progression in T1 disease was about double for a recurrent tumor compared with a primary one.[13] This level of risk would, for many, justify a prophylactic cystectomy.

In this study at 5% level of significance, the calculated value (i.e.0 .1875) was less than the tabulated value (i.e. 3.84). In case of Group-A, T1 TCC was progressed to T2 disease in 4(30) patients. Local progression was occurred in 2(10) patients in Group-B where T1 TCC extend to pelvic lymph node in one case and left lower ureter in another case. So, in both groups diseases progression were observed.

CONCLUSION

From my study it may be concluded that the recurrence rate of T1G3 TCC of urinary bladder is very high. In relation to recurrence of disease in high grade superficial bladder cancer TURBT and intravesical therapy is not a good treatment option. Second transurethral resection to eradicate local residual disease and to get additional information about depth of invasion of tumor suggests a different approach. But early radical cystectomy and ileal conduit is the best treatment option to prevent recurrence. Certainly no definitive conclusions can be made regarding the impact of TURBT and intravesical therapy on progression from my study as the power of this study was limited by the small sample size. T1G3 is a deadly tumor, so proper follow-up protocol should be maintained.

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