

Results of Postoperative Instillation of Mitomycin C in Non Muscle Invasive Bladder Cancer after Complete Resection Versus BCG (Recurrence and Progression)

ISMAIL SABER, M.Sc.*; ELSAYED MOUSA, M.D.** and AHMED FAHIM, M.D.**

The Departments of Urology, Maadi Military Hospital* and Department of Urology, Faculty of Medicine, Al -Azhar University**, Cairo, Egypt

Abstract

Background: Intravesical immunotherapy or chemotherapy for non-muscle invasive bladder cancer is a well-established treatment for preventing or delaying tumour recurrence after tumour resection. However, up to 70% of patients may fail. New protocols and new intravesical agents with improved effectiveness are needed

Aim of Study: Is to evaluate the oncological outcome as regard progression, local recurrence and side effects of non-muscle invasive transitional cell carcinoma of the urinary bladder managed by complete resection followed by postoperative intravesical instillation of Mitomycin C compared with BCG.

Patients and Methods: This is a prospective study that included 51 patients with non-muscle invasive TCC bladder (Ta and T1) at Urology Department, Al-Azhar University hospitals between 2011 and 2015. Patients divided into two groups, the Mitomycin group received immediate MMC and periodic 6 doses of MMC and the other group, BCG received 6 doses of BCG one dose per week. Follow-up by cystoscope for two years at 3th, 6th, 9th, 12th, 18th, 24th month to detect the recurrence, progression and side effects.

Results: The mean age of the patients was 60.58 (37 yrs. - 79 yrs.) in the MMC group and 61.76 (48 yrs-83 yrs) in the BCG group. The main comparison in this study is recurrence rate and progression rate of the tumor. Three patients (11.5%) had recurrence in the 1st year while four patients (15.4%) in the 2nd year with total recurrence seven patients (26.9%) in MMC group.

In the BCG group, patients who had a recurrence in the 1st year were, two patients (8%) and three patients (12%) in the 2nd year with total recurrence, five patients (20%).

The total progression in two years were 4 pts (15.38%) (One patient (3.8%) in the 1st year) (3 patients (11.5%) in the 2nd year) in the MMC group while were 4 pts (16%) (One patient (4%) in the 1st year) (year 3 patients (12%) in the 2nd year) in the BCG group.

Conclusion: Our study confirmed the positive effect of immediate Mitomycin C intravesical instillation in patients

who received periodic Mitomycin C instillation and either the positive effect of intravesical instillation of BCG in patients with non-muscle-invasive bladder tumors. Our present study showed that MMC and BCG equally reduced recurrence and progression in NMIBC patients while showed the superiority of MMC regarding to the adverse effects.

Key Words: Intravesical instillation – Mitomycin – Urinary bladder neoplasms.

Introduction

BLADDER cancer is the ninth most commonly occurring cancer globally. Seventy to eighty per cent of all bladder cancer patients initially present with non-muscle invasive [1]. Non-muscle invasive bladder cancers [Ta, T1 or carcinoma in situ (CIS)] are vary in terms of oncological outcome [2]. Worldwide, urothelial bladder cancer (UBC) is the seventh most common cancer in men and the 17th most common in women, but in developed countries bladder cancer is more common [3].

The main risk factor for UBC is smoking, which is thought to be responsible for at least one third of the cases. Males are three to four times more likely to develop UBC than their female counterparts. This discrepancy has been partially attributed to the higher proportion of smokers among males [4].

At presentation, approximately 70% have non-muscle-invasive UBC and 30% of patients have muscle-invasive UBC (cT2 or higher) [5]. Most cases are TCC and most new patients (65-75%) have Ta disease (mucosal only), T1 (lamina propria invasion), or carcinoma in situ (CIS) [6,7].

Both the natural history of non-muscle-invasive UBC and its treatment strategies are highly variable. Although some patients never experience disease recurrence, others experience disease progression

Correspondence to: Dr. Ismail Saber,
E-Mail: esmailsaber@yahoo.com, esmailsaber79@gmail.com

and eventually die of their disease [8]. Urothelial carcinoma of the bladder has become a major cause of morbidity, mortality, and health-related costs. There is still no standard instillation therapy against bladder cancer [9].

Generally, the initial approach for managing non-muscle invasive bladder cancer is cystoscopic transurethral resection [10]. After transurethral resection of the bladder tumor (TURBT) non-muscle-invasive bladder cancer (NMIBC) has a high risk of recurrence and of progression [11]. Since there is considerable risk of recurrence and progression, it is necessary to consider adjuvant intravesical therapy in most patients [12].

Transurethral resection of the bladder tumor (TURBT) followed by watchful waiting was usually performed for non-muscle-invasive bladder cancer in the past, but immediate intravesical chemotherapy has recently used more frequent in clinics [13].

The European Association of Urology (EAU) guideline recommends performing a one-time, immediate intravesical drug treatment after the surgery in all non-muscle-invasive bladder cancers, and intravesical chemotherapy is known to be effective in preventing cancer recurrence by suppressing implantation of the postoperative tumor cells wandering in the bladder after TURBT [13].

After TURBT, it requires waiting 1 to 2 weeks to begin the treatment with BCG; thus, it is possible that recurrence or progression could be affected during this period [14]. Therefore, we performed immediate post-TURBT Mitomycin C treatment in patients with non-muscle-invasive bladder Cancer periodic intravesical Mitomycin C instillation. The effect of the treatment MMC and BCG on the progression and recurrence of bladder cancer was investigated.

Patients and Methods

Between 2011 and 2015, this prospective study was performed on patients with non-muscle invasive transitional cell carcinoma (TCC) of the urinary bladder. Patients with single, primary tumors of sizes less than 3 cm and non-invasive tumors (Ta and T1), presenting at El Hussain University hospital were included. Individuals with muscle-invasive tumors or in situ bladder carcinoma on the pathological examination, non-transitional-cell carcinoma, invasion to the prostate or upper urinary tract, or a history of TURBT or intravesical chemotherapy were excluded. Pregnancy; women advised not to become pregnant while on therapy.

The study had local ethics committee approval and all patients signed a written informed consent, and were informed about the procedure and all possible complications.

All patients were evaluated by: Full medical history and clinical examination, Complete blood count, serum creatinine, serum urea, prothrombin concentration, SGOT and SGPT, Urine analysis and urine cytology, Abdomino pelvic ultrasound and Computerized tomography (CT) with contrast unless contraindicated.

The data of sex, age, history of smoking, size, stage, grade of the tumor were recorded. Following TURBT, the stage and grade of the tumor were determined using the TNM staging system (2009 system, American Joint Commission on Cancer in combination with the International Union Cancer Consortium).

Patients were divided into 2 groups:

The immediate Mitomycin C (I-MMC) group consisted of 26 patients who received one dose of Mitomycin C, 40mg diluted in 40ml of distilled water or saline, within 12 hours after TURBT and received periodic Mitomycin C instillation after 1 week (one dose per 1-week interval for 6 weeks). The BCG group patients received 90mg of BCG (Tice strain) diluted in 50mL saline instilled intravesically after 2 weeks of TURBT for 6 weeks (1-week interval). The instillation was retained for 1.5 to 2 hours by catheter and was then emptied out by self-voiding.

The follow-up schedule of our patients included a visit at 3th, 6th, 9th, 12th, 18th, and 24th months. During each visit, patients were evaluated by: Full clinical examination, complete blood count, serum creatinine, serum urea, prothrombin concentration, SGOT, SGPT and urine analysis. Patients were evaluated also by abdomino pelvic ultrasound, urine cytology and cystourethroscopy.

Primary end points were recurrence free interval (the period between initial transurethral resection and first recurrence). (Confirmed histologically), or severe degree of adverse effects of the drug. Secondary end points were disease-specific mortality.

Tumor grade, stage and the time of recurrence, progression and side effects of Mitomycin C and BCG were compared by Independent-samples *t*-test and chi square tests. Values were considered statistically significant at $p < 0.05$.

Results

Both groups (total of 51 patients), 26 patients in the Mitomycin C and 25 in the BCG group who were eligible for the study were comparable as regards clinical and pathological characteristics (Table 1). There were no statistically significant differences between the 2 groups.

Table (1): Patient characteristics.

	MMC group	BCG group	p-value
No. of patients	26	25	
No. of tumors	26	25	
<i>Sex:</i>			
Male	22/26 (84.6%)	21/25 (84%)	0.952
Female	4/26 (15.4%)	4/25 (16%)	
Mean age (yr.)	60.58±8.72	61.76±8.24	0.621
<i>Smoking:</i>			
Yes	19/26 (73.1%)	16/25 (64%)	0.485
No	7/26 (26.9%)	9/25 (36%)	
<i>Clinical stage:</i>			
Ta	19/26 (73.1%)	17/25 (68%)	0.691
T1	7/26 (26.9%)	8/25 (32%)	

The recurrence rate and progression of the tumor. As demonstrated in (Table 2), three patients (11.5%) had recurrence in the 1st year while four patients (15.4%) in the 2nd year in MMC group. BCG group, patients who had a recurrence in the 1st year were, two patients (8%) and three patients (12%) in the 2nd year. The total recurrence in two years were seven patients (26.9%) in MMC group while were five patients (20%) in the BCG group. So, the efficacy of MMC in our study as regard recurrence was 73.1% (19 pts) in two years, while the efficacy of BCG was 80% (20 patients). From these results there are no significant difference between two groups in the recurrence rate.

Table (2): Recurrence and progression in each group according to follow-up period.

	MMC group	BCG group	p-value
<i>Recurrence:</i>			
1st year	3 (11.5%)	2 (8%)	0.671
2nd year	4 (15.4%)	3 (12%)	0.725
<i>Total:</i>			
Yes	7/26 (26.9%)	5 /25 (20%)	0.959
No	19 /26 (73.1%)	20/25 (80%)	
<i>Progression:</i>			
1st year	1 (3.8%)	1 (4%)	0.977
2nd year	3 (11.5%)	3 (12%)	0.959
<i>Total:</i>			
Yes	4/26 (15.38%)	4 /25 (16%)	0.952
No	22/26 (84.62%)	21/25 (84%)	

MMC group, one patient (3.8%) had a progression in the 1st year while 3 patients (11.5%) in the 2nd year. In BCG group one patient (4%) had a progression in the 1st year, while in the 2nd year 3 patients (12%). The total progression in two years were 4 pts (15.38%) in MMC group while were 4 pts (16%) in the BCG group. So, the efficacy of MMC in our study was 84.62% (22 pts) in two years, while the efficacy of BCG was 84% (21 patients). From these results there are no significant difference between two groups in the progression rate.

As regard side effects:

Table (3): Side effects.

	MMC group (n=26)	BCG group (n=25)	X ²	p	Sig.
<i>Dysuria:</i>					
Yes	5 (19.2%)	12 (48%)	4.747	0.029	S
No	21 (80.8%)	13 (52%)			
<i>Urgency:</i>					
Yes	6 (23.1%)	13 (52%)	4.561	0.033	S
No	20 (76.9%)	12 (48%)			
<i>Hematuria:</i>					
Yes	5 (19.2%)	11 (44%)	3.932	0.048	S
No	21 (80.8%)	14 (56%)			
<i>Fever:</i>					
Yes	2 (7.7%)	6 (24%)	2.563	0.109	NS
No	24 (92.3%)	19 (76%)			
<i>Frequency:</i>					
Yes	7 (26.9%)	15 (60%)	5.985	<0.01	HS
No	19 (73.1%)	10 (40%)			

S: Significant. NS: Non significant. HS: Highly significant.

Discussion

Post-TURBT intravesical chemotherapy has been used for non-muscle-invasive bladder cancer for more than 40 years. Thiotepa, Adriamycin, Epodyl, Epirubicin, and Mitomycin C have been used for the periodic intravesical chemotherapy [15].

There have been several reports about the timing to begin the intravesical chemotherapy. Soloway and Masters reported in a study that post-TURB intravesical chemotherapy was effective even though it was performed after 24 hours [16], whereas Pan et al., insisted that intravesical chemotherapy was effective only when it was performed within 1 hour after the surgery [17].

As regard the periodic intravesical post TURBT MMC, Kaasinen et al., reported that the relative risk of recurrence was reduced to half when the first instillation of the periodic Mitomycin C treatment was performed within 24 hours after TURB

[18]. We believe that immediate instillation of Mitomycin C within 12h after TURBT offers the earliest and most effective prophylaxis against tumor cell implantation, and had less early side effects.

The significant reduction in early recurrence in our study with one dose of Mitomycin C strongly supports the hypothesis of cell implantation as a recurrence mechanism, 3 pts (11.5%) in the first year and total 7 pts (26.93%) after 2 years of follow up. Our results similar to the result of study by Jung et al., [19]. In Jung et al., study, one group received an immediate MMC plus periodic 6 doses as in our study but the dose of MMC was 30mg and the follow-up was 3 years.

Our study had the standard duration of BCG retention, which defined as dwell time, is 1-2h, as originally proposed by Morales et al., The original 6-week induction schedule proposed by Morales remains in wide clinical use and is supported by guidelines [20].

BCG immunotherapy after TURBT is effective in preventing tumor recurrence in Ta and T1 bladder tumors. Five patients of 25 pts (20%) in our study had recurrence within two years, this efficacy may be changed with long duration of follow-up. Although patients in our study did not receive BCG maintenance, the recurrence rate was not higher than expected. Han et al., [21], used the same regimen of ours in the BCG group and gave progression rate (33.6% ±4.7%).

The effect of BCG in reducing tumor progression in our study after two years of follow-up was 16% which is close to results of Dalbagni [22] and relatively distant to Mohanty et al., [23] who reported that 8.75% only had progression.

In our study, although the recurrence appeared in 5 patients (20%) in the BCG group which less than the MMC group (7 patients equal 26.9%), we found that no significant difference between the two groups in the recurrence rate which is the same of Shelley, [24].

With regard to disease progression, the result for BCG versus MMC are less clear [25]. Sylvester et al., [26] were able to demonstrate a statistically significant advantage of BCG versus MMC for disease progression.

The progression in our study, reported in 4 patients (15.4%) and 4 patients (16%) in MMC and BCG groups respectively. Accordingly, our

present study shows that MMC and BCG equally reduced recurrence and progression in NMIBC patients, whereas several RCT studies on a slightly higher-risk cohort reported that BCG is superior to chemotherapy the benefit was greater, but not significant.

Reports and reviews have shown that local and systemic side effects are more frequent with BCG than with MMC, our study agree with these results.

Conclusion:

Considering the clinical factors of our study and the non-significance between the two groups in age, Sex, size, grade and stage, we had a powerful point in comparison between recurrence, progression in our study. Our study confirmed the positive effect of a single, immediate mitomycin C instillation in patients with non-muscle-invasive bladder tumors who received periodic mitomycin C instillation. This benefit was limited to early recurrence and was not maintained with long-term follow-up.

Our present study shows that MMC and BCG equally reduced recurrence and progression in NMIBC patients, whereas several RCT studies on a slightly higher-risk cohort reported that BCG is superior to chemotherapy. The benefit was greater, but not significantly different. Our study revealed that the superiority of MMC regarding to the adverse events especially the local side effects.

References

- 1- WITJES J.A., PALOU J., SOLOWAY M., et al.: Current clinical practice gaps in the treatment of intermediate- and high-risk non-muscle-invasive bladder cancer (NMIBC) with emphasis on the use of bacillus Calmette-Guérin (BCG): Results of an international individual patient data survey (IPDS). *BJU. Int.*, 112: 742-750, 2013.
- 2- JIANG S.J., YE L.Y. and MENG F.H.: Comparison of intravesical bacillus Calmette-Guerin and Mitomycin C administration for non-muscle invasive bladder cancer: A meta-analysis and systematic review. *Oncol. Lett. Apr.*, 11 (4): 2751-2756, 2016.
- 3- FERLAY J., SHIN H.R., BRAY F., et al.: Cancer incidence and mortality worldwide: IARC Cancer Base no. 10, 2008 [Internet]. Lyon, France: International Agency for Research on Cancer. Available at <http://globocan.iarc.fr> ; 2010 [accessed 6 May, 2012].
- 4- PARKIN DM: The global burden of urinary bladder cancer. *Scand. J. Urol. Nephrol. Suppl.*, 218: 12-20, 2008.
- 5- KIRKALI Z., CHAN T., MANOHARAN M., et al.: Bladder cancer: epidemiology, staging and grading, and diagnosis. *Urology*, 66: 4-34, 2005.
- 6- MALKOWICZ S., BRUCE VAUGH DAVID J. and WEIN A.J.: Adult genitourinary cancer-prostate and bladder. In:

- Hanno P.M., editor. Penn Clinical Manual of Urology. Saunders; Philadelphia, pp. 523-570. Ch. 15, 2007.
- 7- KANDEEL W., ABDELAL A., ELMOHAMADY B., et al.: Comparative study between full-dose and half-dose intravesical immune bacille Calmette-Guérin injection in the management of superficial bladder cancer. Arab. J. Urol. Dec., 13 (4): 233-237, 2015.
 - 8- SYLVESTER R., VAN DER MEIJDEN A., KURTH K., et al.: Predicting recurrence and progression in individual patients with stage Ta T1 bladder cancer using EORTC risk tables: A combined analysis of 2596 patients from seven EORTC trials. Eur. Urol. 49: 466-475, 2006.
 - 9- CUI J., WANG W., CHEN S., et al.: Combination of Intravesical Chemotherapy and Bacillus Calmette-Guerin Versus Bacillus Calmette-Guerin Monotherapy in Intermediate- and High-risk non muscle Invasive Bladder Cancer: A Systematic Review and Meta-analysis. Medicine (Baltimore). Jan., 95 (3), 2016.
 - 10- SHELLEY M., JONES G., CLEVES A., et al.: Intravesical gemcitabine therapy for non-muscle invasive bladder cancer (NMIBC): A systematic review. BJU. Int., 109: 496-505, 2012.
 - 11- ODDENS J., BRAUSI M., SYLVESTER R., et al.: Final results of an EORTCGU Cancers Group Randomized Study of maintenance bacillus Calmette-Guerin in intermediate- and high-risk Ta, T1 papillary carcinoma of the urinary bladder. One-third dose versus full dose and 1 year versus 3 years of maintenance. Eur. Urol., 63: 2-47, 2013.
 - 12- LOGAN L., BROWN M. and HAYNE D.: Intravesical therapies for bladder cancer indications and limitations. BJU. Int., 110: 12-21, 2012.
 - 13- JUNG S.J., CHANG H.S., PARK C.H., et al.: Effectiveness of an Immediate Mitomycin C Instillation in Patients with Superficial Bladder Cancer Receiving Periodic Mitomycin C Instillation. Korean. J. Urol., 52: 323-326, 2011.
 - 14- SEO K.W., KIM B.H., PARK C.H., et al.: The efficacy of the EORTC scoring system and risk tables for the prediction of recurrence and progression of non-muscle-invasive bladder cancer after intravesical bacillus calmette-guerin instillation. Korean. J. Urol., 51: 165-70, 2010.
 - 15- BARGHI M.R., RAHMANI M.R., HOSSEINI MOGH-ADDAM S.M., et al.: Immediate intravesical instillation of Mitomycin C after transurethral resection of bladder tumor in patients with low-risk superficial transitional cell carcinoma of bladder. Urol. J., 3: 220-4, 2006.
 - 16- SOLOWAY M.S. and MASTERS S.: Urothelial susceptibility to tumor cell implantation: influence of cauterization. Cancer, 46: 1158- 63, 1980.
 - 17- PAN J.S., SLOCUM H.K., RUSTUM Y.M., et al.: Inhibition of implantation of murine bladder tumor by thiotepa in cauterized bladder. J. Urol., 142: 1589-93, 1989.
 - 18- KAASINEN E., IONTALA E., HELLSTRÖM P., et al.: Factors explaining recurrence in patients undergoing chemo immunotherapy regimens for frequently recurring superficial bladder carcinoma. Eur. Urol., 42: 167-74, 2002.
 - 19- JUNG S.J., CHANG H.S., PARK C.H., et al.: Effectiveness of an Immediate Mitomycin Receiving Periodic Mitomycin C Instillation. Korean. J. Urol., 52: 323-326C Instillation in Patients with Superficial Bladder Cancer, 2011.
 - 20- LOGAN L., BROWN M. and HAYNE D.: Intravesical therapies for bladder cancer indications and limitations. BJU. Int., 110: 12-21, 2012.
 - 21- HAN K.S., YOU D., JEONG I.G., et al.: Is Intravesical Bacillus Calmette-Guérin Therapy Superior to Chemotherapy for Intermediate-risk Non-muscle-invasive Bladder Cancer? An. Ongoing. Debate. J. Korean. Med. Sci., 30: 252-258, 2015.
 - 22- DALBAGNI G.: The management of superficial bladder cancer Nature clinical practice Urology May, Vol. 4, No. 5, 254-260, 2007.
 - 23- MOHANTY N.K., RAJIBA L., NAYAK M.S., et al.: Intravesical gemcitabine in management of BCG refractory superficial TCC of urinary bladder Urologic Oncology: Seminars and Original. Investigations, 26: 616-619, 2008.
 - 24- SHELLEY M.D., WILT T.J., COURT J., et al.: Intravesical bacillus Calmette-Guerin is superior to Mitomycin C in reducing tumor recurrence in high-risk superficial bladder cancer: A meta-analysis of randomized trials. BJU. Int., 93: 485-490, 2004.
 - 25- DALBAGNI G.: Is Intravesical Bacillus Calmette-Guérin Better than Mitomycin for Intermediate-Risk Bladder Cancer? Eur. Urology, 56: 257-259, 2009.
 - 26- SYLVESTER R., VAN DER MEIJDEN A. and LAMM D.: Intravesical bacillus Calmette-Guerin reduces the risk of progression in patients with superficial bladder cancer: A meta-analysis of the published results of randomized clinical trials. J. Urol., 168: 1964-1970, 2002.

تقييم استخدام عقار المايتومايسين سى كعلاج داخل المثانة ما بعد إستئصال الأورام السطحية بالمنظار بالمقارنة مع عقار البى سى جى

تعتبر الأورام السرطانية بالمثانة من الأورام الأكثر شيوعاً فى الجهاز البولى التناسلى وعلاجها أيضاً ذو تكلفة عالية مما يجعلها عبئاً على المريض.

تمثل الأورام السرطانية بالمثانة ٧٠٪ : ٨٠٪ من أورام المثانة، ٨٠٪ منها يقتصر ظهورها فى الأغشية المخاطية بينما ٢٠٪ يقتصر على الطبقة الملاصقة للأغشية المخاطية دون العضلات.

إن الخطوة الأولى والأساسية فى علاج أورام المثانة وتحديد مراحل تقدمه هو إستئصاله الكامل بالمنظار.

ورغم الإستئصال الكلى للورم يظل معدل إرتجاعه قائماً بنسبة تتراوح من ٤٨٪ : ٧٠٪ وكذلك معدل تقدم مراحلها تتراوح من ٧٪ : ٤٠٪ وذلك طبقاً لخصائص الورم. وطبقاً لهذه المعدلات فمن الضرورى الوضع فى الاعتبار اللجوء إلى العلاج الكيماوى المساعد الموضعى بالمثانة ومن أشهر العقارات المستخدمة عقار المايتومايسين وعقار البى سى جى.

لقد أثبتت الأبحاث السابقة أن الحقن الفورى (خلال ٢٤ ساعة من إستئصال الورم بالمنظار) لعقار المايتومايسين فى المثانة وكذلك حقن عقار البى سى جى من الطرق الفعالة لمنع إرتجاع الورم.

إن بعض الأبحاث أثبتت أفضلية عقار البى سى جى على عقار المايتومايسين فى معدلات إرتجاع الأورام، بينما أثبت البعض الآخر عدم أفضلية أى منهم على الآخر، ومن ثم فإن الهدف الرئيسى لهذا البحث هو المقارنة بين العقارين فى علاج أورام المثانة السطحية عن طريق الحقن بالمثانة. وكان التركيز الأساسى على تأثير كل منهما على نسب ومعدلات إرتجاع الورم وكذلك معدلات تقدم مراحلها.

لقد أظهرت نتائج هذا البحث أن:

- نسبة إرتجاع الورم فى المرضى الذين تم علاجهم لعقار المايتومايسين كانت ٢٦.٩٪ بينما مع عقار البى سى جى ٢٠٪.
- نسبة تقدم مراحل الورم مع إرتجاعه كانت ١٥.٤٪ مع عقار المايتومايسين بينما كانت ١٦٪ مع عقار البى سى جى.
- أما بالنسبة لآثار الجانبية: تراوحت النسبة ما بين ١١.٥٪ إلى ٢٦.٩٪ مع عقار المايتومايسين بينما تراوحت بين ٤٠٪ إلى ٦٠٪ مع عقار البى سى جى.

ومن هذه النتائج يتضح الآتى:

- إن الحقن الفورى للمثانة بإستخدام عقار المايتومايسين مضافاً إليه الحقن الدورى لمدة ٦ أسابيع من نفس العقار فى نفس المريض له فائدة كبيرة من حيث منع الإرتجاع المبكر لأورام المثانة السطحية.
- إن عقارى المايتومايسين والبى سى جى يؤثران بفاعلية كبيرة وبشكل متقارب على تخفيض معدلات إرتجاع الأورام السطحية وكذلك تقدم مراحلها.
- إن عقار المايتومايسين هو الأقل تأثيراً من عقار البى سى جى من حيث الإضرار الجانبية على المريض.

إن الألام بمواصفات العقار المستخدم فى العلاج ومعرفة طريقة عمله ومميزاته والمضاعفات الناتجة من أستخدامه على العوامل الرئيسية لتحقيق الفائدة العظمى للعلاج وتخفيض الآثار السلبية له على المريض.