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Intravesical Therapy in Urinary Bladder Carcinoma

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ABSTRACT: Urinary bladder carcinoma is associated with recurrence and metastasis. Various treatment modalities have been tried for treating this malignancy. However, there is variation in results reported in different studies. No particular treatment protocol has been reported to exhibit complete remission or limiting the progression of the disease. Intravesical chemotherapy is a novel technique that aids in preserving the urinary bladder from surgical mutilation while at the same time increases the disease free period and survival rates in these patients. The main challenge of intravesicle chemotherapy is patient selection process, and close monitoring of these subjects as there may be localized side-effects to this therapy.
This review article presents an overview of various published articles in the field of intravesical chemotherapy of urinary bladder carcinoma.

Keywords: Intravesical, therapy, urinary, bladder, metastasis, carcinoma

INTRODUCTION

Urinary bladder carcinoma is up to three times commonly reported among males when compared to females. It has incidences of 25:100,000 in males and 8:100,000 in females, respectively. Overall incidences of urinary bladder carcinoma are slowly increasing over the years. The median reported age at time of diagnosis is 65 years. Urinary bladder carcinoma has higher frequency of occurrence in urban areas when compared to rural areas, which can be due to environment associated factors. Occupation related exposures account for approximately 25% of all reported cases of urinary bladder carcinoma. Most significant risk-factor associated with occurrence of urinary bladder carcinoma is smoking of cigarettes, which alone is contributory to approximately 50% of malignancies among men and 33% among women (IARC, 1987).

Recurrent potential of urinary bladder carcinoma is due genetic alterations of an unstable type of urothelium that can facilitate continuous development of newer lesions or prevent implantation of carcinoma cells (Alfred *et al.*, 2017).

Urothelial carcinomas can be graded as per TNM staging system into- a) superficial, b) invasive and c) metastatic carcinoma. These stages have difference in their clinical behaviors, prognosis as well as management (Akaza *et al.*, 1987; Asahi *et al.*, 1980).

Superficially located tumors represent nearly 70% of all new cases. Recurrence or new malignancy development of urothelial carcinomas are reported within five years of resection in approximately 50 % to 70 % of treated patients. The superficially located tumors may undergo progression to advanced tumor stage. Thus, the aim of any therapeutic modality in superficial stage tumor is prevention of recurrence as well as progression to an advanced tumor stage (Nilsson *et al.*, 2001; Norming *et al.*, 1992).

Infiltration in underlying muscular layer has been associated with a greater risk of involvement of regional lymph nodes, which can subsequently undergo metastases to distant sites. Invasive urinary bladder carcinoma is reported in 20% to 25% of cases at diagnosis (Prout *et al.*, 1983; Rajala *et al.*, 1999; Reuter, 1990).

Multimodality type of approach are utilized for sparing any organ that has been diagnosed with a malignant condition. For example, breast carcinoma, head and neck carcinoma, cervical carcinoma, and anal carcinoma. These modalities of treatment generally include - limited amount of surgical resection and/or biopsy which is followed up by concurrent and/or sequential chemotherapy, and radiation therapy. On similar lines, the organ sparing approaches are followed up for urinary bladder carcinomas (Alfred *et al.*, 2017; Novara *et al.*, 2015).

Follow-up study data from Huland *et al.* (1990) indicated that mitomycin therapy protocol which was used as a short termed intense form of instillation

therapy combined with long-term maintenance therapy for instillation had beneficial effectiveness when compared to long-term instillation for maintenance, especially in patient's recurrent tumors (Huland *et al.*, 1990).

Masters *et al.* (1999), in their randomized study using intravesical therapy with standard dose at one mg/:ml) or double dosed epirubicin found, that epirubicin when used in double times standard dosage had no superiority with relation to tumoral response, time between recurrences, or rate of recurrence (Masters *et al.*, 1999).

A reduction in tumor recurrence from 55% till 27% was noted in 4 control drug trials on epirubicin by Ali-el-Dein *et al.* (1997a), Ali-el-Dein *et al.* (1997b), Oosterlinck *et al*. (1993) and Rajala *et al* (1999) (Ali-El-Dein *et al.*, 1997a; Ali-El-Dein *et al.*, 1997b; Oosterlinck *et al.*, 1993; Rajala *et al.*, 1999). Clinical efficacy of early therapy using epirubicin found that intervals between tumor recurrence was longer in these patients than those being treated with TUR-B therapy (36 Vs. 28 months).

Messing *et al.* (2018) in their study on lower grade non-muscle invasive urothelial carcinoma following post-resection intra-vesical Gemcitabine instillation reported significant reduction in recurrence risk for a period of 4 years (Messing *et al.*, 2018).

Yang *et al*. (2016) in their meta-analysis showed that use of peri-operative intra-vesicle chemotherapy improves chances of survival and reduces the rate of tumor recurrence in patients of urothelial carcinoma (Yang *et al.*, 2017).

Similarly, 2 prospective and independently conducted randomized controlled clinical trials by O'Brien *et al.* (2010) and Fang *et al.* (2013) showed that post-operative intra-vesicular mitomycin C either with or without cytosine arabinoside instillation, reduced recurrence risk of urinary bladder cancers following surgery (Fang *et al.*, 2013; O'Brien *et al*., 2011).

INTRAVESICAL CHEMOTHERAPY IN URINARY BLADDER CARCINOMA

Intravesical chemotherapeutic administration is done in as adjuvant therapy to trans-urethral resection or TUR-B in superficial lesions. This approach drastically reduces the short-term i.e., 1 to 3 years of rate of recurrence by around 20 %. Eight year period of follow-up have reported 8 % of total recurrences following intra-vesical chemotherapy (Nilsson *et al.*, 2001).

Long-term chemotherapy for maintenance by means of instillation per one year has not been shown to increase the interval between recurrence whether longer duration on comparison with immediate chemotherapy in a short-term post-operative period using intravesical chemotherapy (Malstrom *et al.*, 1996; Novara *et al.*, 2015; Nilsson *et al.*, 2001).

Majority studies have shown the intra-vesical therapy using 'Bacillus Calmette Guerin' or BCG) on comparison with intra-vesical use of chemotherapeutic agents demonstrate superior prevention of recurrent tumor. Intra-vesical chemotherapeutic regimens exhibit prolonged period of disease-free rate of survival with no chronic impact over progression of superficially localized urinary bladder carcinoma into infiltrating bladder of cancer in underlying muscle layer. There is no evidence available regarding benefit in rate of survival following use of adjuvant intra-vesical chemotherapy regimen (Krege *et al.*, 1996; Lundholm *et al.*, 1996).

Chemotherapeutic protocols with regimens using cisplatin produce objective tumor related response in approximately 50% patients suffering from metastatic carcinoma of urinary bladder. An increased period of survival with no disease and an overall survival with median duration of 2 to 3 months has been reported in patients after treatment with cisplatin based poly-chemotherapy when compared to those patients who were treated using cisplatin as single agent or with lesser intensive chemotherapeutic treatment (Byar and Blackard 1977; Burnand *et al*., 1976).

In clinical control randomized study trial performed in Scandinavia on high-risk tumors, adjuvant administration of mitomycin-C along with BCG has demonstrated better survival following a period free from disease, although, the rate of progression of malignancy had similarity in either of the study arms (Flamm *et al*., 1995).

Malstrom *et al.* (1999), in their follow-up study reported statistically significant (P = 0.04) in survival following BCG Tis (carcinoma in situ) disease. Also, no statistical difference in progression of tumor was observed between these arms (Malstrom *et al.*, 1996).

Rintala *et al.* (1991), in their study on patients who had frequent recurrence of Ta-T1 urinary bladder carcinomas reported BCG as a superior chemotherapy drug over mitomycin C in terms of responsiveness, survival with no disease and rate of recurrence. Though in present study, mitomycin C was observed to demonstrate superior effectiveness when compared to BCG patients suffering from Tis staged urinary bladder carcinoma (Rintala *et al.*, 1991).

Though BCG is accepted as a superior intra-vesical chemotherapeutic agent in superficial urinary bladder carcinoma, there are contradictory views regarding this (Tolley *et al.*, 1988; Witjes *et al.*, 1993).

In an EORTC randomized and prospective clinical trial that compared intra-vesical BCG-RIVM with mitomycin C in pTa, pT1 and pTis stage carcinomas, identical efficacy was observed with respect to recurrence of tumor. But mitomycin C had higher efficacy when compared to BCG in prevention of disease from progressing. However, the toxicity profiles on comparison were found to be non-significant (p=0.006) (Schulman *et al.*, 1982).

Another randomized controlled clinical trial on neo-adjuvant chemotherapeutic agents- methotrexate (MTX), cisplatin along with vinblastin or MCV prior to treating patients diagnosed with T_2 to$T_4aN_XM_0$ urinary bladder carcinoma with radiotherapy has been advocated by the 'Radiation Therapy Oncology Group'. No statistically significant differences were obtained in patients with distant metastases or in five year rate of survival. Hence, in this study it was noted that neo-adjuvant MCV intravesicular treatment had no

influence over clinical remission rate (Witjes *et al.*, 1998).

STUDIES ON SHORT TERM PREVENTION USING DIFFERENT CHEMOTHERAPEUTIC AGENTS USING INTRAVESICAL THERAPY IN RECURRENT URINARY BLADDER CARCINOMA

Ethoglucid has been studied as an adjuvant therapeutic intravesical agent along with endoscopic trans-urethral resection in a randomized clinical trial which comprised of 209 proven patients. This clinical study showed 59 % recurrence rate in control group, when compared with 28 % recurrence rate in patients who were treated using chemotherapy alone. Thus, a decrease of 31% rate of recurrence was observed when adjuvant intra-vesical chemotherapy was used (Kurth *et al.*, 1997).

On performing systematic analysis of studies which employed Mitomycin C as intravesical chemotherapeutic agent along with trans-urethral resection in 1774 confirmed patients, statistically significant improvement was observed in only 5 clinical trials. Recurrence rate was found to be 38 % in patient group that were treated using Mitomycin C in trans-urethral resection when compared to the group that was treated only with Mitomycin C chemotherapy (Huland and Otto 1983; IARC 1987; Kurth *et al.*, 1997; Lundholm *et al.*, 1996; Malstrom *et al.*, 1996; Novara *et al*., 2015; Norming *et al.*, 1992; Shabsigh *et al.*, 2009).

9 randomized clinical trials that comprised of a total of 1130 cases involving Thiotepa administration demonstrated statistically significant result in improving the reduced rate of recurrence using intravesical chemotherapy when compared with treatment using surgery alone (Nocks *et al.*, 1979; Prout *et al.*, 1983; Rajala *et al.*, 1999; Rubben *et al.*, 1990; Solsona *et al.*, 1999; Schulman *et al.*, 1982; Zincke *et al.*, 1983).

On comparing average incidences in recurrence in group where treatment was done through surgery alone and with Thiotepa chemotherapy, a 12% reduction in rate of recurrence was observed (Zincke *et al.*, 1983). Also, it was seen that the drug response was in proportion to its concentration in solution administered rather compared to bolus dose (Tolley *et al.*, 1988; Witjes *et al.*, 1993).

Randomized control trials using doxorubicin as intravesical chemotherapy agent have demonstrated statistically significant results in reducing risk of recurrence by up to 0.21 times (Niijima *et al.*, 1983; Nocks *et al.*, 1976; Zincke *et al.*, 1983).

A reduction in lowering of rate of tumor recurrence has been noted from 55 % to 27 % with intravesical therapy using epirubicin, specially during early installation of the drug. The average time for recurrence using Epirubicin was found to be 0.13 months when compared with 0.29 months in patients who were treated using trans-urethral resection only (Kim and Lee 1989; Koontz *et al.*, 1981; Minervini *et al.*, 1996; Medical Research Council Working Party on Urological Cancer 1994; Shipley *et al.*, 1998).

A controlled clinical trial using intra-vesical mitoxantrone demonstrated longer time for recurrence and an increase in period of disease-free survival or period of progression to advanced stage of disease when compared to patients who were treated only using transurethral resection therapy (Zincke *et al.*, 1983).

CONCLUSIONS

Despite prolonging disease-free period of survival, neo-adjuvant intra-vesical chemotherapy has failed to show no distinct findings in long term or in preventing progression of superficial malignancy into invasive urinary bladder carcinoma. Also, there is limited data representing survival rate intra-vesical chemotherapy using any of the known chemotherapeutic agents.

SCOPE OF STUDY

The cumulative findings of this paper are suggestive of necessity regarding continued work on intravesicle chemotherapy as a treatment modality or as an adjunctive therapy in patients of urinary bladder carcinoma.

FUTURE SCOPE

Studying the effect of intravesical therapy in urinary bladder carcinoma will enhance treatment modalities in more effective manner.

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REFERENCES

Alfred, W. J., Lebret, T. and Comperat, E. M. (2017). Updated 2016 EAU guidelines on muscle-invasive and metastatic bladder cancer. *Eur Urol.*, *71*(3), 462-475.

Akaza, H., Isaka, S. and Koiso, K. (1987). Comparative analysis of short-term and long-term prophylactic intravesical chemotherapy of superficial bladder cancer. Prospective, randomized, controlled studies of the Japanese Urological Cancer Research Group. *Cancer Chemother Pharmacol.*, (Suppl 20), 91-96.

Ali-El-Dein., B., El-Baz., M. and Aly, A.N.M. (1997). Intravesical epirubicin versus doxorubicin for superficial bladder tumors (Stages pTa and PT1): a randomized prospective study. *J Urol.*, 1*58*, 68–74.

Ali-El-Dein., B., Nabeeh, A. and El-Baz, M (1997). Single-dose versus multiple instillations of epirubicin as prophylaxis for recurrence after transurethral resection of T1 transitional–cell bladder tumours: a prospective, randomized controlled study. *Br. J. Urol.*, *7*, 731-735

Asahi, T., Matsumura, Y. and Tanahashi, T. (1980). The effects of intravesical instillation of thiotepa on the recurrence rate of bladder tumors. *Acta Med Okayama*, *34*, 43-49.

Byar, D. and Blackard, C. (1977). Comparisons of placebo, pyridoxine, and topical thiotepa in preventing recurrence of stage I bladder cancer. *Urol.*, *10*, 556-561.

Burnand, K. G., Boyd, P. J. R. and Mayo, M. E. (1976). Single dose intravesical thiotepa as an adjuvant to cystodiathermy in the treatment of transitional cell bladder carcinoma. *Br J Urol.*, *48*, 55-59.

Fang, D., Li, X. S., Xiong, G. Y., Yao, L., He, Z. S. and Zhou, L. Q. (2013). Prophylactic intravesical chemotherapy to prevent bladder tumors after nephroureterectomy for primary upper urinary tract urothelial carcinomas:

a systematic review and metaanalysis. *Urologia internationalis*, *91*(3), 291-296.

Flamm, J., Donner, G. and Oberleitner, S. (1995). Adjuvant intravesical mitoxantrone after transurethral resection of primary superficial transitional cell carcinoma of the bladder. A prospective study. *Eur J Cancer*, *31*, 143-146.

Huland, H., Kloppel, G. and Feddersen, I. (1990). Comparison of different schedules of cytostatic intravesical instillations in patients with superficial bladder carcinoma: Final evaluation of a prospective multicenter study with 419 patients. *J. Urol.*, *144*, 68–72.

Huland, H. and Otto, I. J. (1983). Mitomycin instillation to prevent recurrence of superficial bladder carcinoma. Results of a controlled, prospective study in 58 patients. *Eur Urol.*, *9*, 84-86.

IARC (1987). Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42. In: IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans (Suppl 7). *Lyon*, IARC.

Kurth, K., Tunn, U. and Ay. R. (1997). Adjuvant chemotherapy for superficial transitional cell bladder carcinoma: Long-term results of a European Organization for Research and Treatment of Cancer randomized trial comparing doxorubicin, ethoglucid and transurethral resection alone. *J Urol*, *158*, 378-384.

Krege, S., Giani, G. and Meyer, R. (1996). A randomized multicenter trial of adjuvant therapy in superficial bladder cancer: transurethral resection only versus transurethral resection plus mitomycin C versus transurethral resection plus bacillus Calmette-Guerin. Participating clinics. *J Urol.*, *156*, 962-966.

Kim, H. H. and Lee, C (1989). Intravesical mitomycin C instillation as a prophylactic treatment of superficial bladder tumor. *J Urol.*, *141*, 1337-1339.

Koontz, W. W. Jr., Prout, G. R. Jr. and Smith, W (1981). The use of intravesical thiotepa in the management of non-invasive carcinoma of the bladder. *J Urol.*, *125*, 307-312.

Lundholm, C., Norle´n, B. J. and Ekman, P. (1996). A randomized prospective study comparing long-term intravesical instillations of mitomycin C and bacillus Calmette-Guerin in patients with superficial bladder carcinoma. *J Urol.*, *156*, 372-376.

Malstrom, P. U. and Wijkstrom, H., Lundholm, C. (1996). 5-year follow-up of a randomized prospective study comparing mitomycin C and Bacillus Calmette-Guerin in patients with supeficial bladder carcinoma. *J Urol.*, *161*, 1124-1127.

Masters, J. R., Popert, R. J. M. and Thompson, P. M (1999). Intravesical chemotherapy with epirubicin: a dose response study. *J Urol.*, *161*, 1490–1493.

Messing, E. M., Tangem, C. M., Lerner, S. P., Sahasrabudhe, D. M., Kopple, T. M. and Wood, D. P. (2018). Effect of intravesical instillation of Gemcitabine VS Saline immediately following resection of suspected low-grade non-muscle invasive bladder cancer on tumor recurrence. *JAMA*, *319*(18), 1880-1888.

Minervini, R., Felipetto, R. and Vigano, L. (1996). Recurrences and progression of superficial bladder cancer following long-term intravesical prophylactic therapy with mitomycin C: 48-month follow-up. *Urol Int*, *56*, 234-237.

Medical Research Council Working Party on Urological Cancer, Subgroup on Superficial Bladder Cancer (1994). The effect of intravesical thiotepa on tumour recurrence after endoscopic treatment of newly diagnosed superficial bladder cancer. A further report with long-term follow-up of a Medical Research Council randomized trial. *Br J Urol*, *73*, 632-638.

Niijima, T., Koiso, K. and Akaza, H. (1983). Randomized clinical trial on chemoprophylaxis of recurrence in cases of superficial bladder cancer. *Cancer Chemother Pharm*, (Suppl 11), 79-82.

Nocks, B. N., Nieh, P. T. and Prout, G. R. (1979). A longitudinal study of patients with superficial bladder carcinoma successfully treated with weekly intravesical thiotepa. *J Urol*, *122*, 27-29.

Novara, G., Catto, J. W. F. and Wilson, T. (2015). Systematic review and cumulative analysis of perioperative outcomes and complications after robot-assisted radical cystectomy. *Eur Urol.*, *67*(3), 376-401.

Nilsson, S., Ragnhammar, P., Nygren, P., Glimelius, B. (2001). A Systematic Overview of Chemotherapy Effects in Urothelial Bladder Cancer. *Acta Oncologica*, *40*, 371-391.

Norming, U., Nyman, C. R., Gustafsson, H. (1992). Deoxyribonucleic acid profile and tumor progression in primary carcinoma in situ of the bladder: A study of 63 patients with grade 3 lesions. *J Urol*, *147*, 11-15.

O'Brien T., Ray, E., Singh, R., Coker, B., Beard, R., British Association of Urological Surgeons Section of Oncology (2011). Prevention of bladder tumours after nephroureterectomy for primary upper urinary tract urothelial carcinoma: a prospective, multicentre, randomised clinical trial of a single postoperative intravesical dose of mitomycin C (the ODMIT-C Trial). *European Urol*, *60*(4), 703-710.

Oosterlinck, W., Kurth, K. H. and Schroder, F (1993). A prospective European Organization for Research and Treatment of Cancer Genitourinary Group randomized trial comparing transurethral resection followed by a single intravesical instillation of epirubicin or water in single stage Ta, T1 papillary carcinoma of the bladder. *J Urol.*, *149*, 749–752.

Prout, G. R. Jr., Koontz, W. W. Jr. and Coombs, L. J. (1983). Long-term fate of 90 patients with superficial bladder cancer randomly assigned to receive or not to receive thiotepa. *J Urol*, *130*, 677-680.

Rajala, P., Liukkonen, T. and Raitanen, M. (1999). Transurethral resection with perioperative instillation of interferon-a or epirubicin for the prophylaxis of recurrent primary superficial bladder cancer: a prospective randomized multicenter study – Finn bladder III. *J Urol*, *161*, 1133-1136.

Rubben, E. J., Graf-Dobberstein, C. and Ostwald, R. (1990). Prospective randomized study of adjuvant therapy after complete resection of superficial bladder cancer; mitomycin C vs BCG Connaught vs TUR alone. In: de Kernion JB, Mazema E, eds. Immunotherapy of Urological Tumours. Ch. 3, *New York: Churchill Livingstone*, 27-36.

Rintala, E., Jauhiainen, K. and Alftan, O. (1991). Intravesical chemotherapy (mitomycin C) versus immunotherapy (bacillus Calmette-Gue´rin) in superficial bladder cancer. *Eur Urol*, *20*, 19-25.

Reuter, V. (1990). Pathology of bladder cancer: Assessments of prognostic variables and response to therapy. *Semin Oncol*, 17, 524-532.

Shabsigh, A., Korets, R. and Vora, K. C. (2009). Defining early morbidity of radical cystectomy for patients with bladder cancer using a standardized reporting methodology. *Eur Uro*, *55*(1), 164-174.

Shipley, W. U., Winter, K. A. and Kaufman, D. S. (1998). Phase III trial of neoadjuvant chemotherapy in patients with invasive bladder cancer treated with selective bladder preservation by combined radiation therapy

and chemotherapy: Initial results of Radiation Therapy Oncology Group 89-03. *J Clin Oncol*, *16*, 3576-3583.

Solsona, E., Iborra, I. and Rico´s, J. V. (1999). Effectiveness of a single immediate mitomycin C instillation in patients with low risk superficial bladder cancer: short and long-term follow-up. *J Urol*, *161*, 1120-1123.

Schulman, C. C., Robinson, M. and Denis, L. (1982). Prophylactic chemotherapy of superficial transitional cell bladder carcinoma. An EORTC randomized trial comparing thiotepa, an epipodophyllotoxin (VM26) and TUR alone. *Eur Urol*, *8*, 207-212.

Tolley, D. A., Hargreave, T. B. and Smith, P. H. (1988). Effect of intravesical mitomycin C on recurrence of newly diagnosed superficial bladder cancer: interim report from the Medical Research Council Subgroup on Superficial Bladder Cancer. (Urological Cancer Working Party). *Br Med J*, *296*, 1759-1761.

Witjes, J. A., van der, Meiden. A. P. and Witjes, W. P. (1993). A randomized prospective study comparing intravesical instillations of mitomycin-C, BCG-Tice, and BCG-RIVM in pTa-pT1 tumours and primary carcinoma in situ of the urinary bladder. *Eur J Cancer*, *29*, 1672-1676.

Witjes, J. A., van der, Meijden. A. P. and Sylvester, R. (1998). Long-term follow-up of an EORTC randomized prospective trial comparing intravesical bacille Calmette-Gue´rin-RIVM and mitomycin C in superficial bladder cancer. EORTC GU Group and the Dutch South East Cooperative Urological Group. *Urology*, *52*, 403-410.

Yang, X., Li, P., Deng, X., Dong, H., Cheng, Y. and Zhang, X (2017). Perioperative treatments for resected upper tract urothelial carcinoma: a network meta-analysis. *Oncotarget*, *8*(2), 3568-3580

Zincke, H., Utz, D. C. and Taylor, W. F. (1983). Influence of thiotepa and doxorubicin instillation at time of transurethral surgical treatment of bladder cancer on tumor recurrence: a prospective, randomized, double-blind, controlled trial. *J Urol*, *129*, 505-509.

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