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Paper Alert

Neoadjuvant Intravesical Chemotherapy for Non-muscle Invasive Bladder Cancer

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Immediate post transurethral resection of bladder tumor (TURBT) intravesical chemotherapy with a variety of agents is considered the standard of care for treating non-muscle invasive bladder cancers (NMIBC) [1, 2]. However, at times it cannot be administered because of depth of resection and fear of extravesical extravasation or there is too much hematuria to safely clamp a catheter for an hour dwell time. This is a judgement "call" but most urologists would prefer not to have patients experience such potentially disastrous consequences. This occurs about 15% of the time after TURBT [2]. Also, there are numerous logistical issues which make getting the chemotherapeutic agents delivered to the operating or recovery room for same day administration a challenge which requires extra effort on the part of urologic surgeons to accomplish [3, 4]. Unfortunately, this treatment is far easier to accomplish when a research nurse hands the surgeon syringes of study drug and then sits with the patient in the post-anesthesia care unit (PACU) so that recovery room nurses are not confronted with a post-operative patent with a clamped catheter [3, 4].

The hypothesized mechanisms of action of immediate post-operative intravesical chemotherapy are to kill tumors too small to be seen or are overlooked at the index TURBT; an incomplete resection of visible tumor (which should recur in the site of the original tumor); implantation of perturbed (from the TURBT) tumor cells; and new tumor formation [2, 5]. If the chemotherapy is administered after the TURBT the first three should be addressed, while tumor implantation and new tumor formation will not be if drug is given before the TURBT.

Despite that, in a small randomized study of preoperative administration of Mitomycin C (MMC) Lee, et al. reported a non-statistically significant reduction in tumor recurrence at one-year follow-up, 97% recurrence- free survival in the intervention group vs 89% in the control group ($p = 0.11$) [5]. In this study, stage progression occurred in three patients in the control group vs none in the intervention group. MMC was administered one day before and four hours before the index TURBT in the intervention group, while in the control group no placebo was used, and hence no preoperative catheterization was done. The patients were well matched with > 90% in both groups having primary tumors and 58% (intervention) and 53% (control) having AUA high risk tumors [6].

Besides the lack of blinding/double blinding, and the small study sample, additional treatments beyond standard TURBT, including blue light cystoscopy for the index TURBT in all patients, and courses of post-operative intravesical therapy (BCG or MMC) in 88% of patients in the intervention group (and

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87% of controls) were administered. Additionally, 64% of patients in the intervention group and 63% of controls underwent re-TURBT (presumably without blue light cystoscopy, or neoadjuvant or post TURBT intravesical instillation chemotherapy) four to six weeks after their index TURBT. These treatments of course are effective in reducing recurrence rates, making interpretation of the effects of the neoadjuvant MMC instillations alone very challenging.

Furthermore, I could not find the rationale for administering two neoadjuvant instillations of intravesical chemotherapy or why these time points were chosen. It is probable that in South Korea patients are admitted to the hospital a day before TURBT, making the administration of both doses feasible, but in the US, TURBTs are performed on an outpatient basis making the "day before" instillation impractical. However, even as an outpatient, a single immediate preoperative instillation can be done. It should be noted that while outcome results are uninterpretable (for all the reasons mentioned) the treatments were well tolerated and did not complicate the surgery.

In summary, this is an intriguing trial although were it to be done in the US, a single preoperative intravesical instillation is all that would be given. Additionally, participants would be restricted to likely low or low-intermediate risk groups to reduce the effects of additional therapies, and perhaps another treatment group (immediate post TURBT intravesical therapy) would be added [1, 2].

CONFLICTS OF INTEREST

The author has no conflicts of interest to report.

REFERENCES

[1] Bosschieter J, Nieuwenhuijzen JA, Vis AN, et al. An immediate, single intravesical instillation of mito-mycin C is of benefit in patients with non-muscle-invasive bladder cancer irrespective of prognostic risk groups. Urol Oncol. 2018;36(9):400.e7-400.e14.

[2] Messing EM, Tangen CM, Lerner SP, et al. Effect of intravesical instillation of gemcitabine vs. saline immediately following resection of suspected low-grade non-muscle-invasive bladder cancer on tumor recurrence: SWOG S0337 randomized clinical trial. JAMA. 2018;319(18):1880-8.

[3] Steinmetz AR, Gantz J, Fiscella K, Messing EM, Improving rates of immediate postoperative intravesical chemotherapy for low grade bladder cancer: an implementations analysis. Urol Pract. 2022;9:47-55.

[4] Messing, EM. Implementing a new standard of care. Bladder Cancer. 2022;8.

[5] Hye Won Lee, Hyung Ho Lee, Eun Young Park, et al. Clinical Efficacy of Neoadjuvant Intravesical Mitomycin-C Therapy Immediately Before Transurethral Resection of Bladder Tumor in Patients with Nonmuscle-invasive Bladder Cancer: Preliminary Results of a Prospective, Randomized Phase II Study. JUrol. 10.1097.

[6] Chang SS, Boorjian SA, Chou R, et al. Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline. JUrol. 1962;196(4):1021-9.