Immediate post operative administration of intravesical Mitomycin in theatre for non-muscle invasive bladder cancer

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The administration of 1 immediate instillation of intravesical chemotherapy following transurethral resection of bladder tumour (TURBT) has been shown to decrease the risk of recurrence (1) and is recommended as standard practice following TURBT for new & recurrent tumours (2). In practice, administration of intravesical chemotherapy on the ward within 6 hours can often be difficult. At a recent interactive meeting on bladder cancer, 10% of the audience wished to but could not adopt this policy; 44% only administered intravesical within 24 hours (H.Mostafid, personal communication) even though administration should ideally be within 6 hours of TURBT (3).

In order to overcome many of the practical difficulties that prevent timely administration of intravesical therapy following TURBT, we have previously described the successful administration of intravesical MMC in theatre (4) using the Mito-In™ delivery system (Kyowa Hakko UK Ltd, Slough,UK).

The following items for reconstitution should be stored in a secure container in theatre:

- Mitomycin C 40mg vial
- Mito-In™ delivery system (Kyowa Hakko UK Ltd, Slough, UK)
- Sterile Bag to hold Mitomycin Vial (Comes with Mito-In™ packaging)
- Catheter connector (Comes with Mito-In™ packaging)
- 50 ml sterile luer lock syringe
- Sterile saline (0.9%)
- 21G green needle (luer lock compatible)
- Flip-Flo™ catheter valve (Bard Ltd., Crawley, UK)
- Catheter spigot
- Cytotoxic mask

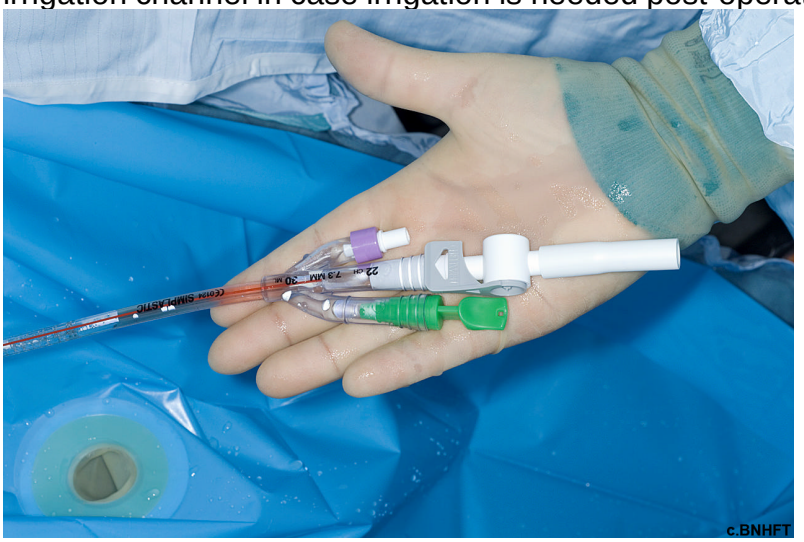
Reconstitution A trained, scrubbed nurse wearing suitable protection for cytotoxic handling, including protective eyewear should carry out the process of reconstitution. Any nurses supporting the process of reconstitution should also be wearing protective clothing and eyewear for the duration of this process. The reconstitution should be carried out in a well-lit and ventilated area.

Administration

1. Prior to start of TURBT procedure the scrub nurse and assistant should open all sterile items and place on sterile trolley for reconstitution. The assistant should Remove MMC from box, remove pink cap and place vial with top facing upwards in sterile bag (contained within the Mito-In™ packaging) held by scrub nurse (below left). This maintains sterility and also protects against spillage in case of vial breakage. The 2 MMC labels from the box should be detached and preserved for later use.

2. Reconstitute MMC using the Mito-In™ system by following instructions on Mito-In™ packaging

3. Upon completion of TURBT, a 3-way urethral catheter is inserted. A Flip-Flo™ valve in the closed position is inserted into the drainage channel. This maintains a closed system during administration and drainage of MMC. A spigot is inserted into the irrigation channel in case irrigation is needed post-operatively due to bleeding.



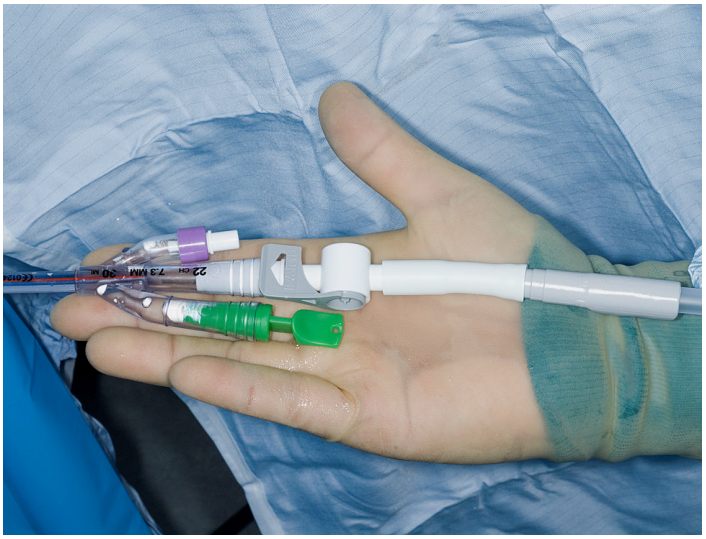
4. The Mito-In™ system is inserted into the Flip-Flo™ valve using the supplied catheter connector ensuring that the green clamp of the Mito-In™ system is closed.

5. The Flip-Flo™ valve and green clamp of Mito-In™ system are opened and all 40ml of MMC are slowly instilled into the bladder

6. The Flip-Flo™ valve is closed to ensure MMC is held within the bladder

7. The green clamp on the Mito-In™ system is closed to prevent accidental leakage and the entire Mito-In™ system is disconnected from the Flip-Flo™ valve and discarded as cytotoxic waste.

8. A urine drainage bag is attached to the Flip-Flo™ valve to enable MMC and residual urine to be drained after 1 hour.



9. The first MMC label from the packaging is stuck to the urine drainage bag using yellow cytotoxic warning tape and the second MMC label is placed in the patient's records to warn staff of cytotoxic status of drainage bag contents.

10. The patient is transferred to the recovery area. Their bed is protected by incontinence pads in case of leakage around catheter.

11. If at any time the patient complains of pelvic or abdominal pain the urology team should be contacted to review the patient to exclude possible extravasation of MMC or bladder perforation.

12. If the patient bypasses MMC or the catheter comes out accidentally then signs of MMC spillage are looked for and the separate cytotoxic spillage protocol below should be followed.

13. After at 1 hour, the Flip-Flo™ is opened and the residual MMC is emptied into the patient's drainage bag maintaining a closed system.

14. The drainage bag is detached and disposed of in its entirety as cytotoxic waste. A new bag is attached to allow continuation of bladder drainage. The patient can then be transferred back to the urology ward.

Spillages

Full protective equipment (apron, double gloves, plastic sleeves, overshoes and eye protection) must be worn at all times when dealing with any spillage. If there is contact with skin, the area must be bathed immediately with sodium bicarbonate 8.4% and then washed with warm soapy water. If there is contact with eyes, they should be washed immediately with copious amounts of eyewash.

Spillage onto the floor should first be covered with liquid Milton or a solution of Presept, then mopped up with disposable adsorbent towels, starting at the outside of the spill and working inwards. When the entire spill has been mopped up, the floor should then be washed and dried at least three times with copious amounts of soapy water.

All affected linen and waste (including protective clothing) must be placed in a yellow clinical waste bag with a group D clinical waste sticker and some cytotoxic warning tape and a cytotoxic residue sheet.

Relative and Absolute exclusion criteria

After TURBT, the urologist should determine if it is safe to proceed with instillation;

Absolute exclusion criteria:	*Relative exclusion criteria:*
Known or suspected bladder perforation	Suspected invasive tumour
Heavy bleeding at the end of the procedure	Large resected area

Overall, approximately 16% of patients will fall into one of these categories (4).

Evidence of clinical efficacy and Adverse events

The rationale for this technique has already been discussed elsewhere (4) and we have reported a reduction in the tumour recurrence rate with this technique (5) that is similar to the reduction in recurrence rate in a meta-analysis of trials of single dose chemotherapy (1).

In our original report adverse events occurred in 2/177 (1%) of all cases. In total, over 300 patients have now received immediate instillation of MMC in theatre at our institution with only one further adverse event: a patient found the instillation uncomfortable in the recovery ward and the MMC had to released after 35 minutes. The technique has now been adopted in over 20 urology departments with careful monitoring of adverse events by the manufacturer. To date, no adverse events have been reported to the manufacturer.

Conclusion

The immediate administration of intravesical MMC in theatre following TURBT is simple, safe and effective. The technique provides the earliest and most certain prophylaxis against tumour cell re-implantation at TURBT.

References:

1. Sylvester RJ, Oosterlinck W, Van Der Meijden APM. A single immediate postoperative instillation of chemotherapy decreases the risk of recurrence in patients with stage Ta T1 bladder cancer: A meta analysis of published results of randomized clinical trials. J Urol 2004; 171: 2186-2190.

2. Babjuk M, Oosterlinck W, Sylvester R, Kaasinen E, Böhle A, Palou-Redorta J. EAU Guidelines on Non-Muscle-Invasive Urothelial Carcinoma of the Bladder. Eur Urol. 2008 Apr 30. [Epub ahead of print]

3. Rajala P, Kaasinen E, Raitanen M, Liukkonen T, Rintala E. and the Finnbladder Group. Perioperative single dose instillation of epirubicin or interferon-α after transurethral resection for the prophylaxis of primary superficial bladder cancer recurrence: a prospective randomized multicenter study- Finnbladder III long term results. J Urol 2002; 168:981-985.

4. Mostafid AH, Rajkumar RG, Stewart AB, Singh R. Immediate administration of intravesical mitomycin C after tumour resection for superficial bladder cancer. BJU Int. 2006 Mar; 97(3): 509-12.

5. Immediate intraoperative instillation of mitomycin-C following TURBT: An analysis of 195 instillations in 170 patients with non-invasive bladder cancer, including effect on recurrence rate. Mostafid H, Moon D, Biers S. Urology 2007; 68 (Suppl 5A): 152.