

Paper Alert

Topical Instillations of Chemotherapy for Renal Pelvic Urothelial Cancer

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Received 24 September 2020

Accepted 23 October 2020

Pre-press 21 November 2020

Published 14 December 2020

The management of upper tract urothelial cancer (UC) remains challenging; standard care being nephroureterectomy and bladder cuff excision (NU). However in the face of a solitary kidney or significant chronic kidney disease, NU will result in severe or total kidney dysfunction and likely need for dialysis. In this scenario, endoscopic therapies have often been utilized. However, ipsilateral local recurrence rates approaching 60% have been reported for endoscopic management alone [1]. To reduce the risk of recurrence, instillation of intra-renal pelvic topical chemotherapy, specifically of mitomycin C (MMC), has been reported in two recent publications [2, 3]. It should be noted that recurrences of UC within the bladder also are quite common after treatment of upper tract UC, and a single intravesical instillation of MMC shortly after NU has been shown to reduce intravesical recurrences in a randomized prospective clinical trial [4].

In one prospective study, Gallioli and coworkers [2] compared outcomes of patients receiving a single intra-renal pelvic instillation of MMC (40 mg/40 ml saline further diluted by 20 ml saline administered over an hour via a ureteral catheter [Single J stent], or 40 mg/40 ml saline diluted in 100 ml saline administered via a urethral Foley catheter with a double

J stent in place). Both were administered immediately after ureteroscopic management of upper tract UC. Twenty-five patients received one of these treatments versus 26 controls who were treated ureteroscopically without instillations. This study was not randomized, but treated patients and controls were well matched for demographics, tumor grade (> 50% low grade in both groups), prior upper tract UC, and comorbidities. MMC treatment reduced ipsilateral upper tract recurrences over a 20 month period of follow-up by nearly 50% (30% in controls versus 17.6% in treated patients), and overall UC recurrences including intravesical recurrences by over 50% (55.5% recurrences in controls versus 23.5% in treated patients). Some patients had concomitant bladder cancers, which were ablated/resected at the time of the index ureteroscopy. Complications, which were usually Clavian grade 1 or 2, occurred in less than a third of patients in each group. Risk of recurrence was higher with high grade upper tract UC and the authors felt that instillation via the ureteral catheter was more effective than through a urethral catheter, perhaps because there was more dilute MMC with the latter and that reflux via the double J stent was not necessarily assured.

In the second study, Kleinmann and colleagues [3] reported on 71 patients with low grade renal pelvic UC who received a MMC containing reverse thermal gel (UGN -101) instilled via a ureteral catheter. UGN-101 is in liquid form when instilled, but then turns

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to gel, and normal urine flow dissolves the gel over 4 to 6 hours. Patients with sterile urine and a marker lesion 5–15 mm in size were eligible if all ipsilateral ureteral, contralateral upper tract, and bladder tumors were ablated before entry. Sixty-one of the enrolled patients received all planned six weekly instillations of UGN-101 and then were evaluated for response by ureteroscopy. Monthly maintenance instillations for a year were planned for patients who achieved a complete response and while 71% received at least one maintenance instillation, the majority did not continue for a year. Forty-two of the 71 patients (59%) experienced a complete response (CR) at three months and >80% of these maintained their CR status at a year of follow up.

This treatment was not innocuous, with 26 (37%) having a “serious” procedure/drug-related adverse event including ureteral obstruction in 44% of the 71, urinary infection (32%), hematuria (31%) and flank pain (30%). Mild thrombocytopenia, anemia and leukopenia occurred in less than 13% of the patients, and were usually self-limited although one patient had transient severe pancytopenia. Twenty-four patients (34% of the 71) required ureteral stent placement and 11 (15.5% of the 71) required long-term stenting. Prior to instillations of UGN-101, renal pelvic volume has to be measured. UGN-101 (Jelmyto) has recently been approved for use by the Food and Drug Administration in patients with low-grade renal pelvic UC. However it is a costly treatment, so for it to be approved by payers all criteria for its administration must be met.

In summary, two approaches for administering chemotherapy for upper tract UC have been described and have significant short to intermediate-term efficacy. Particularly for patients with low-grade cancers with compromised renal function and/or a solitary kidney, either should be considered before moving to NU.

CONFLICTS OF INTEREST

The author has no conflicts of interest to report.

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