

V Edition of the Clinical Cases Contest on
non-surgical clinical management of Kidney Stones
Official template

Title: Urine alkalinization and measurement in patients undergoing Mitomycin instillations for intermediate risk non-muscle invasive bladder cancer.

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1. Abstract (no longer than 150 words).

Objective: To explore the urine alkalinization and its measurement in patients with intermediate risk NMIBC undergoing instillations with mitomycin.

Method: Two patients were given Lit-Control® pH Up 1-2 times a day with a target pH ≥ 6 during the weeks prior to the instillations. Every day, they measured their urine pH with lab sticks, recording the measurements and one patient used a digital pH-meter.

Results: Starting with a basal urine pH of 5 and 5.5, Lit-Control® pH Up was administered to alkalinize pH. pH was measured with dipsticks once a day. One patient used the Lit-Control® pH Meter one week after the instillations to record the pH.

Conclusions: Lit-Control® pH Up is a safe and tolerated option for improving the urine alkalinization, which reduces recurrence rates in patients undergoing mitomycin instillations. The digital pH-meter could give more information to the patient to guide the urine alkalinization

2. Introduction

Intermediate risk non muscle invasive bladder cancer (NMIBC) can be treated, after transurethral bladder resection (TURB), with instillations, being currently available a series of drugs ranging from BGC to mitomycin C (MMC), that can be used either as a single doses instillation just after the TURB, or also as a series of instillations, during some weeks, after TURB, as a therapeutical option to reduce de risk of recurrence in intermediate NMIBC (1,2).

A randomized controlled trial demonstrated a decrease of the recurrence rate of bladder cancer in patient that underwent urine alkalinization with bicarbonate (1.3 gr) the day before instillation of mitomycin, repeating it that same day and just before the instillation. There are no studies demonstrating the usefulness of potassium magnesium citrate and constant pH measurement for urine alkalinization to decrease recurrence rates during treatment of NMIBC treated with MMC instillation.

Our objective was the alkalinization of urine pH in patients with intermediate risk NMIBC, treated with MMC, and measure the urine pH.

3. Clinical Case description

Case 1:

a. Patient information / Medical records

77 year old man, with previous medical record of hypertension, dyslipidemia, hyperparathyroidism, right bundle branch block. As urological past medical history, he presented a low risk prostate adenocarcinoma for which he underwent a robotic radical prostatectomy in march 2018, with a pathology of prostate adenocarcinoma Gleason 2+2 pT2 Nx, with negative margins, currently with undetectable PSA.

b. Diagnostic support studies and results

In 2022, due to a hematuria, he is diagnosed after a transurethral bladder resection (TURB) of a low risk non-muscle invasive bladder cancer (pTaLG). He presents a recurrence in January of 2024, of 3 lesions <1cm in left bladder wall, trigone, and bladder neck. A TURB was carried out, with pathology compatible with a pTaLG (intermediate risk non muscle invasive bladder cancer)

He is referred to our center for a second opinion (no other treatment was offered at his local hospital).

c. Diagnosis

Intermediate risk non-muscle invasive bladder cancer

d. Treatment

After a careful oncological evaluation by the Uro-oncology unit, the patient is included in the mitomycin protocol. This protocol includes the instillation through a bladder catheter of mitomycin C 40 mg every week during 4 weeks, and then 1 instillation every month during 3 months (7 instillations in total). Lit-Control® pH Up was administered during the weeks in which the instillations were carried out, being the pH monitored by the patient every day with dipsticks.

e. Evaluation and progress

As the patient initial pH was 6 during first week after one pill of Lit-Control® pH Up, the team decided to maintain de treatment.

f. Clinical result

The patient tolerated the medication correctly. Control cystoscopy: Recurrence.

Case 2:

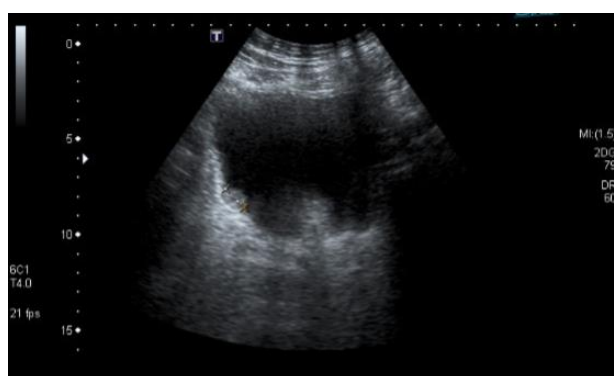
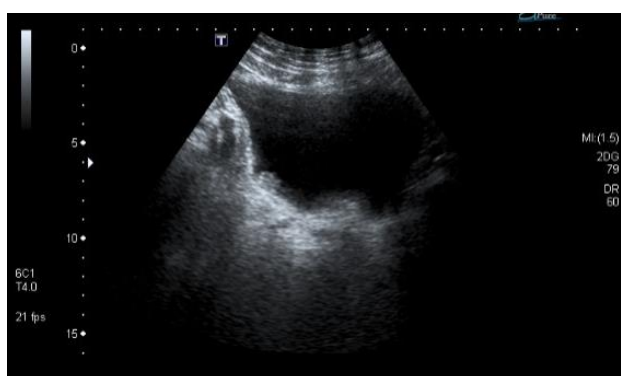
a. Patient information / Medical records

64 year old man, with a past medical history of myocardial infarction, high blood pressure, type II diabetes mellitus, and an abdominal aortic aneurism currently in follow up.

As urological past medical history, he was being followed by the Stone unit for bilateral microlithiasis in a Horseshoe kidney. In control ultrasound a 13mm exophytic lesion was observed.

b. Diagnostic support studies and results

Ultrasound images:



c. Diagnosis

Possible bladder tumour

d. Treatment:

In May 2024 a transurethral bladder resection of the tumour is performed, being observed in the cystoscopy various tumors <2cm, with an anatomy compatible with a non muscle invasive bladder cancer Ta Low Grade.

The patient was included in mitomycin C protocol. This protocol includes the instillation through a bladder catheter of mitomycin C 40 mg every week during 4 weeks, and then 1 instillation every month during 3 months (7 instillations in total).

Lit-Control® pH Up was administered during the weeks in which the instillations were carried out, being the pH monitored by the patient every day with urine strips.

e. Evaluation and progress

As patient initial pH was 5 during first week after two pills of Lit-Control® pH Up, the team decided to give the patient twice a day, until urine medium pH of 6.5 is reached.

This patient also recorded during some days, after the treatment, his urine pH using a Lit-Control® pH Meter.

f. Clinical result

Control cystoscopy: no recurrence.

Table 1: urinepH of patient 1

Week	pH (lab-stick)
1	5.5
2	6
3	6
4	5
5	6
6	6
7	6

Table 2 urine pH of patient 2

Week	pH (lab-stick)
1	5
2	6
3	7
4	7
5	6
6	6
7	7
Lit-Control® pH Meter (after instillations)	5-5.5

4. Discussion:

75% of bladder cancers are not muscle invasive at the moment of the diagnosis. According to a series of pathological and clinical factors, patients can be grouped in different risk groups of progression. Intermediate risk non muscle invasive bladder (NMIBC) cancer can be treated, after transurethral bladder resection, with instillations, being currently available a series of drugs such as mitomycin C, according to EAU guidelines (5).

Mitomycin C can be used as a single immediate postoperative instillation, and also as a series of instillations during weeks after the diagnosis (2,3). Several factors have been analyzed to try to enhance its local effect. Various studies have concluded that inadequate drug delivery, for example due to high residual urine in the bladder can difficult the penetration of the drug in the deep muscle, due to the fact that mitomycin C is unstable in acid urine pH (1). This could lead to a reduction in its efficacy.

A randomized controlled trial also demonstrated the lower recurrence of bladder cancer in patients who underwent urine alkalization before instillation of mitomycin (4), using sodium bicarbonate, administered the day before, the same morning and just before the instillation. Thus, urine alkalization is specially interesting in this group of patients. In our center, our protocols establish that patients should be given oral bicarbonate prior to instillations of MMC. In our study, we used Lit-Control® pH Up to produce an alkalization of urine pH, in contrast to the sodium bicarbonate of the original study.

Several studies have demonstrated the importance of monitoring urine pH during modification, which can be managed amongst many methods, with dipsticks, or lately, using a Lit-Control® pH Meter. Angerri et al. (6) demonstrated that although dipstick test is a largely employed method, it can be highly subjective in its interpretation, specially in older patients with macular degeneration, or neurologic disorders. It also presents a high variability of interpretation between brands. Moreover, there are brands of dipstick that can be accurate to differentiate pH <5 or >8, but are not good measuring pH 5.5-8 (7). This, specially in the case of our patients, could be a serious limitation, even after being trained to interpret the dipstick by our nursery team. In the same study, the Lit-Control® pH Meter was superior to dipstick after a global analysis in terms of precision and accuracy (6). This could have solved the problem of variability mentioned above, enabling an objective pH measurement and recording (it can be written manually or automatically recorded in the mobile application), although patients must be well trained to be performed. In the case of our patients, we used dipsticks to monitor the pH, which enabled us to increase the doses if the pH was too low, as it happened with one of the patients. The Lit-Control® pH Meter that one of the patients used some days after the treatment could have helped guide the urine alkalization better than the dipsticks. Although one of the patients presented a recurrence, the current evidence does not suggest that it can be due to urine alkalization, but rather to the tendency towards recurrence of bladder cancer.

It has been demonstrated, as we extensively mentioned above, that urine alkalization is interesting in intermediate risk NMIBC. The administration of Lit-Control® pH Up in these patients has been well tolerated, and it produced urine alkalization the weeks in which the instillations were going to be performed. The pH was monitored using dipsticks, but by using a Lit-Control® pH Meter, the team may be able to guide the patient better in the need to maintain or increase the doses in order to achieve the correct urinary pH to increase the efficiency of the MMC, and with this, decrease the recurrence of the bladder cancer.

5. Conclusions:

Lit-Control® pH Up is well tolerated and can alkalize urine in patient who required the MMC instillation to improve the efficiency of Mitomycin C instillations to decrease bladder tumor recurrence. The pH Lit-Control® pH Meter could be a good alternative, in contrast to urine dipstick, to monitor more accurately and guide the modification of urinary pH.

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