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Effect of alpha blockers on duration of urinary leakage post-percutaneous nephrolithotomy (PNL): a prospective randomized study

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Abstract

Background Urinary leakage after removal of the nephrostomy tube post-percutaneous nephrolithotomy (PNL) is a common complication which could be secondary to ureteral stone fragments, blood clots, ureteral edema at the ureteropelvic or ureterovesical junction, or rupture calyx. Unfortunately, it could impact the patient's hospital stay causing it to be lengthy, delaying time to return to work, and the negative psychological effect. The current study aimed at assessing the role and effectiveness of alpha blockers (tamsulosin) in minimizing the duration of urinary leakage post-percutaneous nephrolithotomy (PNL).

Methods In this prospective randomized clinical study, 62 cases of PNL were included. Physical examination, laboratory investigations and radiological work up (KUB and plain computed tomography) were done. Cases were randomized into two equal groups: Group A (31 cases) received tamsulosin perioperatively; Group B (31 cases) did not receive tamsulosin. The two groups were followed postoperatively as regards duration of urinary leakage, urinary catheterization and hospital stay.

Results Duration of urinary leakage was statistically significantly shorter in group A (10.61 ± 6.66 h) compared to group B (21.48 ± 12.41 h) (*p*-value ˂ 0.001). Similarly, duration of hospital stay was shorter in group A (2.52 ± 0.72 days) compared to group B (3.10 ± 0.98) (*p*-value 0.020).

Conclusions In patients undergoing PNL for renal stones and receiving tamsulosin, the duration of urinary leakage, and eventually hospital stay was shorter compared to those not receiving tamsulosin.

Keywords Percutaneous nephrolithotomy, Urinary leakage, Nephro-cutaneous fistula, Alpha blockers

1 Background

Renal stone disease is a significant and worldwide medical problem with a marked increase in prevalence over the past 20 years

Such increasing prevalence of kidney stones resulted in development of new minimally invasive techniques, but also led to resurgence of the already established methods such as percutaneous nephrolithotomy (PNL). PNL is accepted as a standard treatment for staghorn and large-volume renal calculi, as well as upper tract calculi refractory to other modalities, difficult lower pole stones, cystine nephrolithiasis, and calculi in anatomically abnormal kidneys [1]. PNL is typically a safe and well-tolerated procedure in properly selected patients [2] with success rate exceeding 90% [3].

A percutaneous nephrostomy tube (PCN) is usually placed following PNL to provide external drainage

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of urine, hemostasis, time for resolution of edema, and preservation of the antegrade access if the presence of residual stones necessitates a second look procedure [4, 5]. This is removed once it is no longer necessary and there is adequate ureteral drainage down to the bladder [6].

Urinary leakage after removal of the nephrostomy tube is common following PNL which could be secondary to ureteral stone fragments, blood clots, ureteral edema at the ureteropelvic junction or ureterovesical junction or rupture calyx. Unfortunately, the duration of urinary leakage could impact the patient's hospital stay causing it to be lengthy, delaying time to return to work, and further necessitating a secondary procedure like placement of an indwelling ureteric stent. not to mention the psychological burden that is added to the patient from such delayed hospital discharge and the misery of foul odor from leaking urine and the impact of the macerated skin affected by such leakage, and finally the bothersome irritative LUTS (lower urinary tract symptoms) associated with the DJ (double J) ureteric stent placed (if needed) to accelerate the healing of the tract.

Alpha blockers have been routinely used for effective expulsion of ureteric stones and even clots causing distal obstruction. Similarly, they are used in cases post SWL (shock wave lithotripsy) to avoid accumulation of residual stones along the ureter where the alpha blockers exert their effect on the ureter especially the distal ureter to reduce ureteral spasm and relax the ureter in the region of and distal to the stone [7].

In the current study, therefore we tried to evaluate whether the administration of alpha blocker namely, tamsulosin has an influence on duration of urinary leakage (DUL) post removal of the nephrostomy tube after PNL procedure.

2 Methods

The current study is a prospective randomized double blinded clinical trial (experimental study) that was conducted at our tertiary care center in the period between December 2019 and May 2020 to assess the role and effectiveness of alpha blockers (Tamsulosin) on the duration of urinary leakage post-percutaneous nephrolithotomy (PNL). The study included 62 patients with different configurations of renal stones.

Patients with the following criteria were included: age 16–65 years, patients admitted for a PNL procedure with renal stones of different configurations (pelvic, calyceal and PUJ stones) were included in the study (Fig. 1), while Exclusion criteria were: Patients who were expected to require an indwelling DJ stent post PNL (e.g.: solitary kidney), previous open renal stone surgery (due to possible adhesions that might impair healing), patient with renal impairment in addition to patients with marked hydronephrosis and decreased parenchymal thickness, and patients who had placement of an indwelling DJ stent due to an intraoperative complication, e.g.: perforation.

Patients were randomized into two equal groups (31 patients each). Randomization was done by closed envelopes method. Neither the surgeon nor the data collector knew the patient's group. Group A received tamsulosin 3 days before PNL and continued for 2 weeks post PNL, while Group B received the conventional treatment without receiving any tamsulosin.

Preoperatively, patients were evaluated by detailed history and physical examination. Radiological work up (plain urinary tract Xray "KUB", and plain computed tomography of the urinary tract CTUT). Laboratory tests included complete blood count, coagulation profile, renal function tests, liver function tests, urine analysis and culture.

A standard technique of prone PNL was done in both groups.

Ureteric catheter 6F was initially placed in the lithotomy position; access obtained under fluoroscopy guidance.

Coaxial Alkan dilators with 32F Amplatz sheath with pneumatic lithotripter for stone fragmentation.

Intraoperative parameters were monitored including estimated blood loss, any encountered complications, operative time and number of percutaneous accesses,

The patients were followed up postoperatively for the presence and duration of urinary leakage post PNL. (The dressing was exposed every hour after removal of nephrostomy tube and endorsed).

Postoperatively on day 1, KUB was done for assessment of the presence of any residual stone fragments. This was replaced by CTUT in case of radiolucent stones. In addition, postoperative Hemoglobin and creatinine were checked.

Postoperatively the following were recorded: degree of pain, analgesic needs, fever, need for blood transfusion, time to open the PCN (if initially closed for tamponade effect) and time of PCN removal (removed once the output is clear) duration of ureteric catheterization, (removed on the morning after the nephrostomy site is dry) and hospital stay.

Follow-up of the patients was continued for 2–3 weeks for assessment of any delayed postoperative complications. Of main concern was urinary leakage post hospital discharge which could be caused by residual fragments that might obstruct the ureter, as well as late onset hematuria.

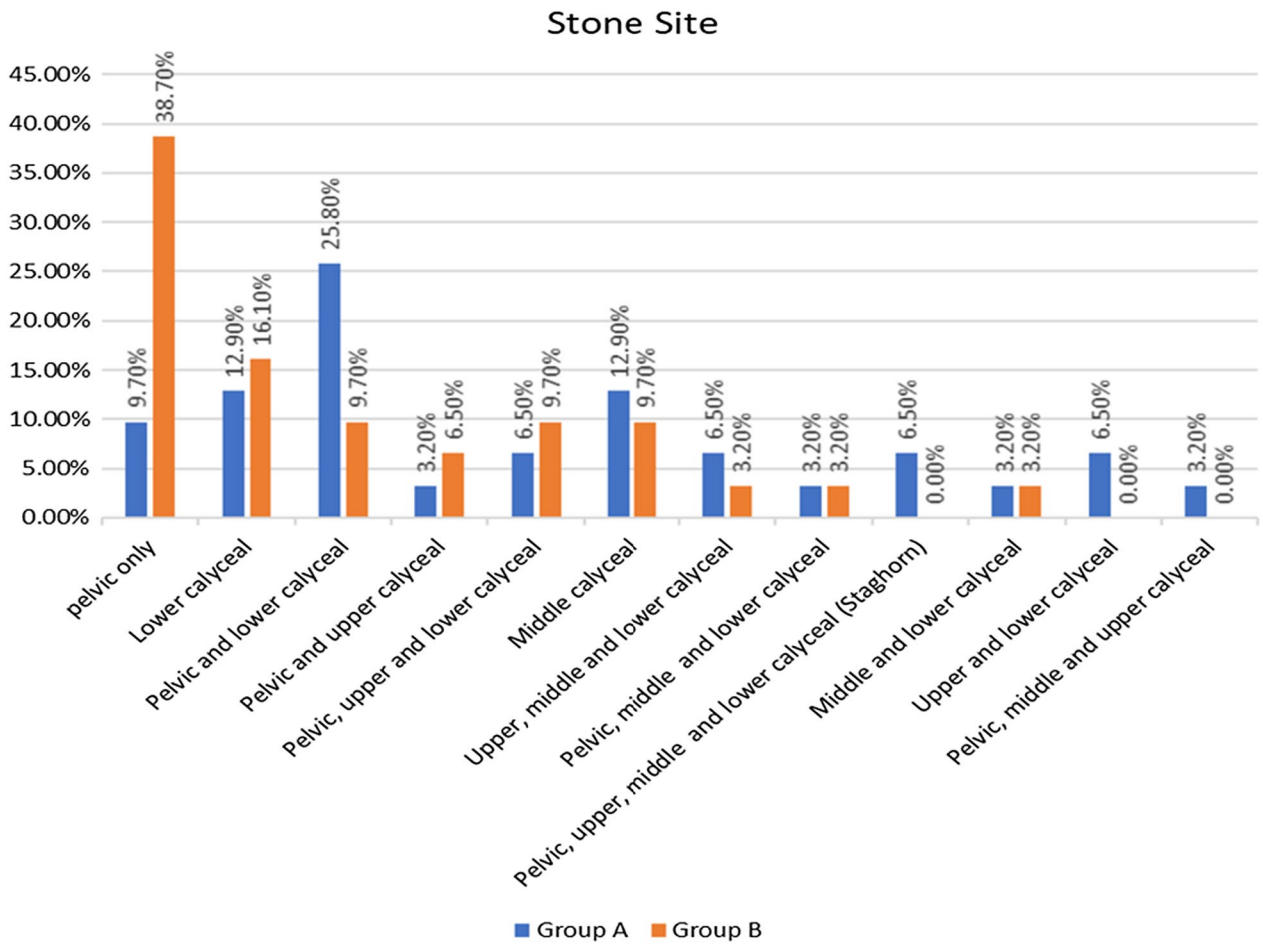

Fig. 1 Stone site in both groups

3 Statistical analysis

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA).

Data were summarized using mean, standard deviation, median, minimum, and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data.

Comparisons between quantitative variables were done using the nonparametric Mann–Whitney test [8]. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5 [9].

P-value of (≤ 0.05) was considered statistically significant.

4 Results

Group A consisted of 31 cases who were planned for conventional PNL with ureteral catheter and nephrostomy tube (28 F) and who received tamsulosin 0.4 mg once daily (3 days preoperative and continued for 2 weeks postoperatively).

Group B included 31 cases who underwent conventional PNL also with ureteral catheter and nephrostomy tube insertion but no tamsulosin was given.

No significant differences in preoperative parameters were noted between the two groups (Tables 1, 2).

Mean stone size for group A was 2.64 ± 1.29 cm^3 (0.0.9–6 cm^3)), while in group B mean stone size was 2.58 ± 1.002 cm^3 (1.3–5 cm^3). For stratification purposes, the stone burden was further classified into two groups whether >2.5 cm^3 or ≤ 2.5 cm^3 total stone burden whether single or multiple). Accordingly, there were 26 cases (41.9%) where the stone burden was >2.5 cm^3, and

Table 1 Quantitative data regarding our study

	Group										*P* value
	Group A					Group B					
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Age	43.00	13.87	41.00	17.00	73.00	41.10	14.96	43.00	18.00	66.00	0.647
Pre Hb	13.35	1.70	13.40	10.10	16.20	13.40	1.90	13.20	10.00	17.00	0.916
Pre Creat	1.07	0.27	1.02	0.60	1.70	1.03	0.25	1.00	0.60	1.60	0.591
Op. time (hours)	1.78	0.71	1.50	0.50	3.00	1.50	0.63	1.50	0.67	3.33	0.088
Postop Hb	12.24	1.62	12.00	9.50	14.90	12.62	1.96	12.80	8.10	16.20	0.331
Postop creat	1.17	0.27	1.20	0.66	1.60	1.04	0.28	1.00	0.70	1.70	0.060
Duration of PCN clamping (Hours)	11.42	9.34	18.00	0.00	24.00	11.03	8.91	18.00	0.00	24.00	0.849
Duration of PCN (Hours)	27.42	12.87	24.00	4.00	50.00	29.94	14.19	30.00	6.00	48.00	0.611
Duration of Ureteric catheter (Hours)	36.94	16.62	36.00	6.00	72.00	50.84	21.32	48.00	18.00	114.00	0.010
Postoperative hospital stays (days)	2.52	0.72	3.00	1.00	4.00	3.10	0.98	3.00	2.00	6.00	0.020
Hours till dry (after removal of PCN)	10.61	6.66	10.00	2.00	30.00	21.48	12.41	18.00	2.00	72.00	< 0.001

Table 2 Categorical data regarding our study

		Group A		Group B		*P* value
		Count	%	Count	%	
Sex	Male	23	74.2	20	64.5	0.409
	Female	8	25.8	11	35.5	
Side (CT/KUB)	Right	16	51.6	15	48.4	0.799
	Left	15	48.4	16	51.6	
Size (CT/KUB)	≤ 2.5 cm	19	61.3	17	54.8	0.607
	> 2.5 cm	12	38.7	14	45.2	
Hydronephrosis (CT/KUB) (SFU grading system)	none	9	29.0	7	22.6	0.288
	mild	16	51.6	14	45.2	
	moderate	4	12.9	7	22.6	
	Mild to moderate	1	3.2	0	0	
	minimal	0	0.0	3	9.6	
	marked	1	3.2	0	0.0	
KUB	Radiopaque	25	80.6	25	80.6	1
	Faint radiopaque	3	9.7	2	6.5	
	Radiolucent	3	9.7	4	12.9	
Est. blood loss (cc)	≤ 200 cc	18	58.1	16	51.6	0.191
	200–500 cc	13	41.9	11	35.5	
	> 500 cc	0	0.0	4	12.9	
Number of PCN	1 PCN	30	96.8	31	100.0	1
	2 PCNs	1	3.2	0	0.0	

36 cases (58.1%) with a stone burden ≤ 2.5 cm^3. Stone location is detailed in Fig. 1.

No significant difference could be elicited between the two groups regarding intraoperative blood loss. One case encountered intraoperative bleeding and hypotension in group A, yet the patient resuscitated immediately, and the procedure was continued. However, 2 cases required blood transfusion postoperatively in group A and only one case in group B.

Residual stone fragments (> 4 mm) were found in 5 cases (16.1%) in group A, while in group B only one case

was associated with residual stone fragments (3.2%). Yet, none of these cases required second look PNL.

Postoperative low-grade fever developed in 8 cases in group A while 11 cases had low grade fever in group B.

There was a statistically significant difference between the two groups regarding duration after which ureteric catheter was removed (36.94 ± 16.62 h in group A and 50.84 ± 21.32 h in group B) (*p*-value 0.010).

Regarding the effect of tamsulosin on duration of urinary leakage, our primary outcome was the number of hours till dry after removal of PCN. The time till dry was significantly shorter in the group receiving tamsulosin at 10.61(± 6.66) hours, compared to 21.48(± 12.41) hours in group B (*p*-value < 0.001). Consequently, postoperative hospital stay was also shorter in group A (2.52 ± 0.72 days) compared to (3.10 ± 0.98 days) in group B (*p*-value 0.020).

5 Discussion

Urinary leakage after removal of the nephrostomy tube is common following PNL. Unfortunately, it could impact the patient's hospital stay causing it to be lengthy, delaying time to return to work, in addition to the negative psychological effect, and further necessitating a secondary procedure like placement of an indwelling ureteric stent [10], this is in addition to the psychological burden that is added to the patient from such delayed hospital discharge and the misery of foul odor from leaking urine and the impact of the macerated skin affected by such leakage, and finally the bothersome irritative LUTS associated with the DJ stent placed(if needed) to accelerate the healing of the tract.

Tubeless PNL had emerged as a new modification of the standard PNL aiming to avoid post PNL leakage, less postoperative pain and early hospital discharge but cannot be applied in all cases of PNL where fixation of nephrostomy tube is preferable. (Bleeding, perforation, and residual stones necessitate staged procedure).

In the current study we tried to evaluate whether administration of an alpha blocker, namely tamsulosin, could have an influence on duration of urinary leakage (DUL) post removal of the nephrostomy tube.

The duration of urine leakage (DUL) following removal of the nephrostomy tube after PNL varies significantly depending on various factors and this has the potential to extend hospital stay. Few studies have evaluated the relationship between prolonged DUL and the demographic and clinical characteristics of patients. With the primary stone burden, stone free rate, degree of hydronephrosis, and parenchymal thickness are the most important predictors of DUL [11].

The rationale of our study is that alpha blockers could provide distal ureteric unobstructed pathway to allow rapid healing of the nephrostomy tract. The idea is based on previous proved efficacy of alpha blockers as a medical expulsive therapy in naïve ureteric stones or post ESWL ureteric stones.

In the current study, no significant difference was found between the 2 groups regarding, preoperative parameters, intraoperative blood loss and postoperative hemoglobin drop or creatinine rise. Postoperative residual stone fragments were found in 5 cases in group A and one case in group B, and they did not need further intervention or second look PNL. This substantiated the role of tamsulosin which might facilitate stone passage thus possibly minimizing the duration of urinary leakage and subsequently the hospital stay and eventually this would favorable impact patients experience and QOL. Our results showed a statistically significant difference between the two groups regarding hours till dry after removal of PCN (10.61 ± 6.66 h in group A and 21.48 ± 12.41 h in group B; *p*-value < 0.001). This was reflected in the hospital stay (2.52 ± 0.72 days in group A, and 3.10 ± 0.98 days in group B; *p*-value 0.020), and all of this was reflected on QOL. Accordingly, we can conclude that tamsulosin has a favorable effect in reducing the duration of urinary leakage. This can be explained by the relaxing effect of alpha blockers on the ureter (preventing spasm) [12] which allows for better drainage so that the nephro-cutaneous tract heals faster leading to a faster hospital discharge and better QOL.

In our study all patients were drained by a urethral catheter along with the ureteric catheter which might be considered a confounding factor. In fact, it is a common observation that in some cases the nephro-cutaneous tract may dry earlier when the ureteric catheter is removed (due to blockage of ureteric catheter). Further studies are needed to assess the effect of alpha blockers on DUL post PNL without the ureteric catheter to make sure that the effect of alpha blocker is genuine and not a result of the ureteric catheter. However, we should note that ureteric catheters were left in place in both groups until the tract dried out and yet there was a statistically significant difference between the group that received tamsulosin as opposed to the control group regarding duration of urinary leakage and hospital stay. This may be explained by the effect of preoperative administration of tamsulosin and or relaxing effect on ureteral wall around the ureteric catheter based on this prospective trial, with an adequate sample size, we feel justified to recommend administration of alpha blockers 3 days prior to PNL and continuing for 2 weeks postoperatively to allow for passage of small residual fragments. We think that this will minimize the duration of urinary leakage from the nephro-cutaneous tract following removal of the percutaneous nephrostomy and allow for faster

hospital discharge with an advantageous effect on QOL. The shorter hospital stays and early return to work will provide economic benefits that outweigh the added cost of medication and the minimal potential side effects of tamsulosin.

The main limitation of the current study is the small number of the study population as our manuscript is a preliminary study with a paucity of research on this aspect of consequences of percutaneous nephrolithotomy (nephron cutaneous fistula). We recommend performing further studies on this issue with larger number of patients.

6 Conclusions

In patients undergoing PNL for renal stones and receiving tamsulosin, the duration of urinary leakage, the duration of urethral catheterization and eventually hospital stay are shorter compared to those not receiving tamsulosin and this would favorable impact patients experience and QOL. However, further studies are needed to determine stones characteristic that may benefit from perioperative alpha blocker therapy.

Abbreviations

PNL	Percutaneous nephrolithotomy.
KUB	Kidney, Ureter and Bladder (Xray)
PCN	Percutaneous nephrostomy tube
LUTS	Lower urinary tract symptoms)
SWL	Shock wave lithotripsy)
DUL	Duration of urinary leakage DUL

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Author contributions
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Declarations

Ethics approval and consent to participate
The study was approved by the research ethical committee of faculty of medicine, Kasr- Alainy Hospital, Cairo university (code: MS-316-2019). All patients signed informed consent.

Consent for publication
All patients signed informed consent for use of their data in publication.

Competing interests
No competing interest.

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