

THE USE OF ALPHA BLOCKERS IN TREATMENT OF LOWER URETERIC STONE

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الخلاصة: اعتمادا على حقيقة وجود مستقبلات الفا في الحالب, حاجز ألف (العقار تيرازوسين) أضيف إلى العلاج التقليدي للمغص الكلوي الناتج عن وجود حصاة في اسفل الحالب في مائة مريض, وذلك لتقييم فائدته في تعجيل نزول حصاة اسفل الحالب. المرضى إختيروا على اساس إمتلاك حصاة من سنتيمتر واحد أو أقل في أسفل الحالب إكتشفت بواسطة جهاز السونار. تمت اعادة فحص المرضى بالسونار بعد عشر أيام من العلاج ما لم تكون الحصاة قد نزلت قبل ذلك الوقت. ثمانية مرضى عانوا من آثار جانبية لاتطاق (دوخة وإنخفاض ضغط الدم) لذلك تم سحب التيرازوسين من علاجهم. كما ان عشرون مريضا لم يرجعوا مرة أخرى للمتابعة. هؤلاء المرضى إستثنوا من الدراسة. لقد نزلت الحصاة في ستة وستون مريضا, من الاثنان وسبعين مريضا الباقين , (91.6%). لقد حصل ذلك خلال عشر أيام. في خمسة عشر (22.7%) منهم نزلت الحصاة بعد ثلاثة أيام, وفي تسعة عشر (28.8%) منهم بعد خمسة أيام وفي ثمانية عشر (27.3%) مريضا بعد إسبوع واحد, وفي أربعة عشر (21.2%) مريضا أختفت الحصاة في فحص السونار اللاحق (بعد عشر أيام). لم تسقط الحصاة في ستة من المرضى (8.3%) حتى بعد تكرير العلاج. نستنتج من هذه الدراسة ان استعمال حاجز ألفا (تيرازوسين) بدأ مفيدا في تعجيل نزول حصاة اسفل الحالب.

Abstract: Depending on the fact that alpha adrenergic receptors are present in the ureter, the alpha blocker (terazosin) has been added to the conventional treatment of ureteric colic due to lower ureteric stone in hundred patients, to asses its advantage in hasting the passage of lower ureteric stone. The patients were selected on the bases of having a stone of one cm or less in the lower ureter discovered by sonography. The patients followed after ten days by sonography if the stone not pass before that. Eight patients developed intolerable side effects (dizziness and postural hypotension) so that terazosin was stopped and twenty patients not come back for follow up. Those patients were excluded from the study. Sixty-six patients, from the remaining 72 patients, (91.6%) pass the stone within ten days. *Fifteen* (22.7%) of them pass the stone after three days, *nineteen* (28.8%) of them did so after five days and *eighteen* (27.3%) patients after one week, in *fourteen* (21.2%) patients the stone disappear in the sonography taken after ten days. Six patients (8.3%) need urological interventions as the stone failed to pass even after two course of therapy. In conclusion, the use of alpha blocker (terazosin) seemed beneficial in hasting the passage of lower ureteral stone.

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Introduction:

Anatomically speaking, the ureter is divided into three parts:

- The upper ureter which extend from the pelvi-ureteral junction to the upper end of sacro-iliac joint.
- The mid ureter which extend from upper to lower end of sacroiliac joint.
- The lower ureter which extend from lower end of sacroiliac joint to ureteral meatus.⁽¹⁾

Morita and associate (1987) have provided evidence that the ureter is supplied by both adrenergic (sympathetic) and cholinergic (parasympathetic) neurons. Sympathetic nervous system appears to modulate ureteral activity by excitatory alpha adrenergic and inhibitory beta-adrenergic receptors. Norepinephrin, primarily an alpha – adrenergic agonist, increase the force of ureteral contraction. So alpha – adrenergic blockers will decrease the force of ureteral contraction and cause more relaxation resulting in less pain and enhance stone passage. Alpha-adrenergic receptors are more abundant in the lower ureter.^(1, 2, 3)

I depend on these facts in using alpha adrenergic blockers for hastening the passage of lower ureteric stone.

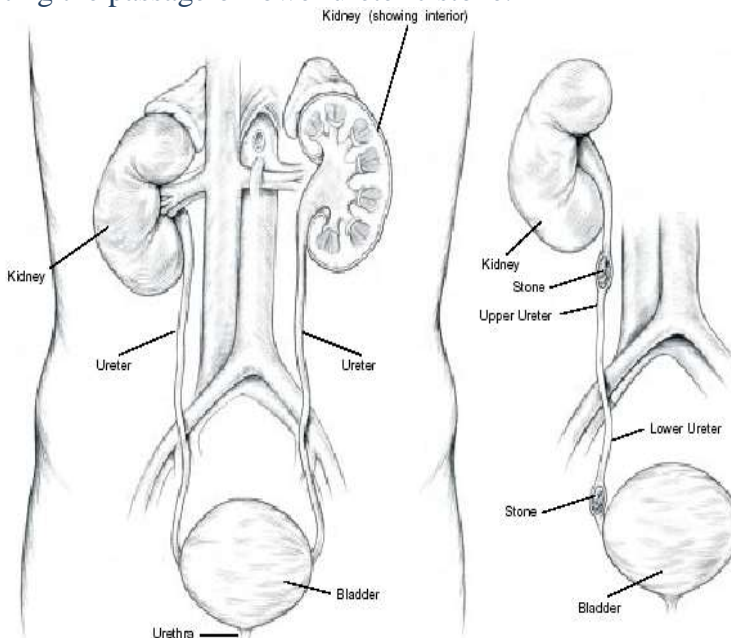


Figure (1): anatomy of ureter.

- Ureteric stone can be divided into primary and secondary stone.

- Primary stone arises in the ureter it self, usually in dilated segment of the ureter as in ureterocele or in a prestenotic segment; here urinary stasis and infection will occur and predispose for stone formation.
- Secondary stone is more common, originate in the kidney and descend down into the ureter and impact at narrow points in the ureter like pelviureteric junction, where the ureter crosses the iliac vessels, where the ureter crossed by the vas deferens or uterine artery, the ureteral hiatus and orifice. ⁽⁴⁾

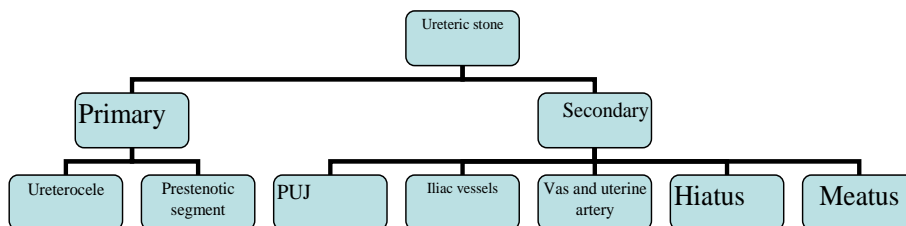


Figure (2): types of ureteral stone

Calculi in the last three positions (distal ureter) were involved in the study. Calculi in the lower ureter often cause pain that radiate to groin and testicle in males and the labia majora in females.

The patient presenting with acute ureteral colic typically in severe pain, attempting to find relief in different, frequently bizarre positions. Systemic components of renal colic may be obvious, with tachycardia, sweating, and nausea often prominent. Costovertebral angle tenderness may be apparent.

Non contrast spiral CT scan is now the imaging modality of choice in patient presented with acute renal colic. In our country, spiral CT not available for emergency use and restricted for cold cases and on an appointment. For this fact we still depend on ultrasonography for diagnosing ureteric stone .Hydronephrosis and proximal hydroureter is obvious in patient with acute ureteric colic. Lower ureteric stone easily visualized through the acoustic window of a full bladder.

Most ureteral stone pass spontaneously depending on stone size, shape, location, and period of impaction. Medical intervention involve the treatment of ureteric colic using NSAID, narcotic analgesic and recently antidiuretic hormone (ADH) .dissolution agents may be used for ureteral stone as potassium bicarbonate and citrate. Obstructing ureteral stone, especially if associate with infection requires emergency drainage via retrograde or percutaneous rout. ESWL (extracorporeal shock wave lithotripsy) can be used for ureteral stone fail to pass with conservative therapy except those poorly visualized or overlying

sacroiliac joint. Ureteroscopic stone extraction is highly efficacious for lower ureteral calculi. Ureterolithotomy can be used for extraction of ureteral stone impacted for long period or those not accessible for endoscope and ESWL. ^(1,2,4)

Aim of the study:

To assess the advantage of using alpha-adrenergic blockers in hastening the passage of lower ureteric stone.

Patient and method:-

From 2004 to 2006, alpha blocker (terazosin) has been added to the conventional treatment of lower ureteric stone in one hundred adult patients with ureteral colic due to lower ureteric stone (74 male and 26 female). Those patients usually come to me with acute ureteral colic, Diclofenac 75 mg used first to relieve pain, if they not get relief; pethidine 100 mg or tramadol 50 mg is used. Glucose saline is used to replace fluid lost by vomiting. When the symptoms relieved, they sent for ultrasonography. Ultrasonography will detect a stone in the lower ureter with dilated pelvi-caliceal system and upper ureter. The patients involved in the study were selected on the following bases:

1. Have a ureteral stone of one cm or less.
2. The stone located in the lower ureter.
3. Have systolic blood pressure not less than 100 mm Hg.
4. Have no indications for urgent intervention like:-
 - a. Severe intractable pain.
 - b. Fever and sepsis.
 - c. Complete obstruction of a solitary kidney or bilateral ureteral stone (anurea).

Selected patients were given 2 mg terazosin (prostanor) in addition to other drugs usually used for treatment of urinary stone as, allopurinol 100-300 mg, rowtenex, alkalization agents, and analgesics. We advised the patients to take prostanor at bed time to avoid the common side effects of alphas blockers (dizziness and postural hypotension). The patients instructed to:

1. Increase fluid intake and motility.
2. Watch their urine for stone.
3. Come back once the stone pass.
4. Come back if intolerable adverse effects occurred.
5. Come back after ten days if none of the above occurred.

If the patient come back carrying his stone, it will be send for stone analysis. If the patient can not tolerate alpha blocker side effects,

prostanor will be stopped and he will be excluded from the study. If the patient come back ten days later, ultrasonography is requested again to follow up the stone.

Results:

Eight patients, 3 male and 5 female, presented after one or two days with severe dizziness and postural hypotension, prostanor was removed from their medication immediately. Unfortunately, twenty patients disappear and not comeback for follow up.

Those 28 patients were excluded from the study and only 72 patients who complete the course of therapy and come back for follow up were included in the evaluation, from them sixty-six patients (91.6%) pass the stone within ten days.

Fifteen (22.7%) patients pass the stone after three days, *nineteen (28.8%)* patients did so after five days, *eighteen (27.3%)* patients pass the stone after one week and in *fourteen (21.2%)* patients the stone disappear in the sonography taken after ten days, they not notice the passage of stone.

Six patients (8.3%) fail to pass the stone which still appear in ultrasonography, even after another ten days of same therapy. Those patients required urosurgical intervention.

Table (1): Results of the study.

Pass the stone				Fail	S.E	Run
3 days	5 days	7 days	10 days	6	8	20
15	19	18	14			

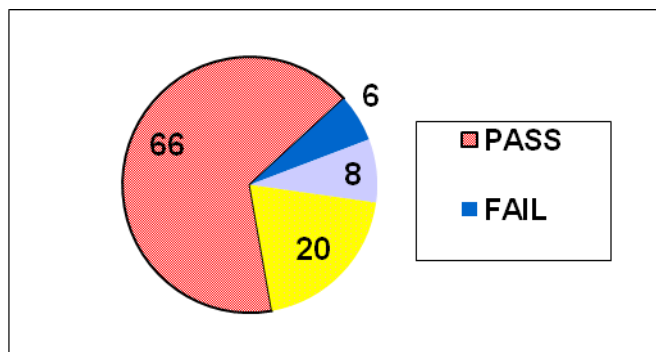


Figure (3): Result of the study in number of patients.

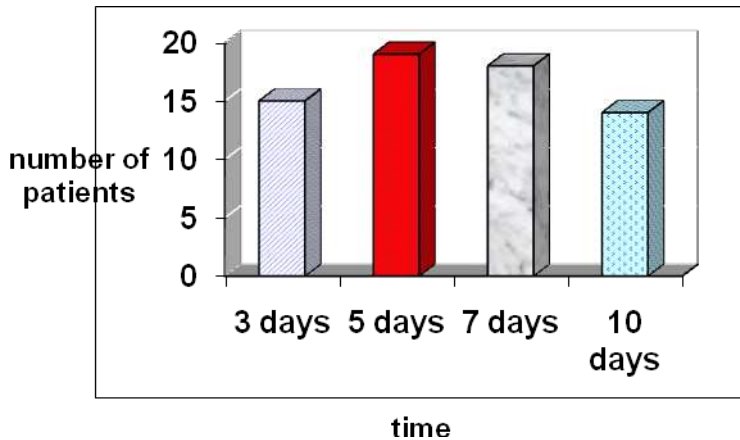


Figure (4): the numbers of patients pass the stone in different periods.

Discussion:

Most of the obstacles in the ureter are found in the lower part. ^(1, 5) A stone descending down from the kidney may impact in the lower ureter causing severe loin pain that radiated to the testis or labia and may associated with Irritative voiding symptoms. Some time we can diagnose lower ureteric stone from these symptoms. ^(2, 6)

Ultrasonography is the investigation of choice to prove diagnosis especially if done with full bladder as lower ureteric stone can be seen through the acoustic window of full bladder. Associated hydroureteronephrosis may aid the diagnosis. ⁽⁴⁾

Alpha-adrenergic receptors are more abundant in the lower ureter, so the use of alpha-adrenergic blockers in treatment of lower ureteric stone is more logic and more successful than upper and mid ureter. ^(1, 3)

Most ureteral stone pass spontaneously depending on stone size, shape, location, and period of impaction. Ureteral calculi 4-5 mm have 40-50% chance of spontaneous passage .In contrast stone > 6 mm have < 5% chance of spontaneous passage. Fifty percent of distal ureteral calculi pass spontaneously, in contrast to a 25 % and 10 % chance in the middle and proximal ureter respectively. ^(4, 5, 7)

Once the stone pass outside the ureter it will readily pass outside the bladder. ^(1, 4)

The vast majority of stone that pass do so within a 6 weeks period after the onset of symptoms.

Although most of distal ureteral stone will pass spontaneously, it is preferable not to wait 6 week for it's descend as:

1. Recurrent attack or ureteral colic is annoying to the patient.
2. Return of renal function after relief of partial or complete obstruction is not guarantee after this long period.

To hasten lower ureteral stone passage I add alpha blockers to the conventional treatment of urinary lithiasis. Terazosin is long acting, non-selective alpha blocker used in treatment of benign prostatic hyperplasia. It cause relaxation of smooth muscle fibers of the prostate and reduces outlet resistance of urethra so that urinary stream and BPH symptoms improved. In case of lower ureteral stone, terazosin results in relaxation and dilatation of lower ureter and that will relief pain and aid in the passage of ureteral stone.

We use terazosin for adult (Children were excluded), male and female, with a systolic blood pressure of more than 100mm Hg to avoid intolerable postural hypotension.

In spite of that, eight patients come back the second or the third day of therapy with intolerable dizziness and postural hypotension that interfere with their daily activity, in those patient terazosin was removed from their medication immediately and they excluded from the study. In addition twenty patients who not come back for follow up were excluded also, so only 72 patients remain for assessment, 66 patients (91.6%) of them pass the stone within ten days with a mean of 6.25 days.

Fifteen (22.7%) of the patient brought back the stone after three days of therapy, nineteen (28.8%) of them brought back the stone a after five days and eighteen (27.3%) patients after one week, those fifty-two patient brought back the stone intact and about the same size reported in the sonography, that is to say it not pass merely by the dissolving action of other drugs used .The stones were sent for chemical analysis in order to start preventive therapy.

In fourteen (21.2%) patients the stone disappear in the sonography done in the next visit, it may be dissolved or they not notice the passage of stone.

Six patient (6%) when came back for follow up , still having the initial symptoms, examination reveal lower abdominal tenderness, and ultrasonography still showing the stone in the lower ureter ,in those patient treatment repeated ,no trial to increase the dose of alpha blocker for the fear of adverse effects. However further course of treatment also fail and they required urosurgical intervention. It seems that alpha-adrenergic blockers to be effective it did so within ten days or never did.

So as compared to generally 50% spontaneous descend within 6 week, I got 91.6% descend within ten days.

As compared to ESWL, American association of urologist report an 85% stone free rate after ESWL for a stone less than 1cm in the lower ureter, but a 4% complications rate and 10% of unplanned second surgical intervention, and as compared to ureteroscopy, AUA report an 89% stone free rate after ureteroscopy for a stone less than 1cm in the lower ureter, but with 9% complications rate and 7% unplanned second surgery.⁽⁸⁾ So I got better stone free rate and with out complications or unplanned second surgery.

In comparison to similar study done in the Department of Urology, Gazi University School of Medicine, Ankara, Turkey ,they use tamsulosin and they got 46% stone free rate in CT scan taken after 15 days.⁽⁹⁾

But they don't say whether the patients pass the stone intact or it dissolved by over- hydration they used.

Another study done in BERKELEY, CA (Urotoday Inc.) used tamsulosin 0.4 mg for a maximum of 28 days plus deflazacort 30 mg (a steroid) for up to 10 days, resulted in stone passage in 85% of patients within a mean of 7.9 days (and an outer range of 15 days),⁽³⁾ so we got 91.6% stone free rate with adding alpha blocker alone and in a mean of 6.25 days.

Conclusion:

The addition of alpha-adrenergic blockers to conventional treatment of lower ureteral stone seemed beneficial. It increases stone free rate and in a short time. It avoids the use of ESWL and ureteroscopy and their associated complications.

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