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Comparison of safety and efficacy of tamsulosin, tadalafil, combinations and deflazacort in lower ureteric orifice negotiation by large size ureteroscope (8/9.8 Fr) prior to intracorporeal lithotripsy

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Abstract

Introduction: To compare the safety and efficacy of tamsulosin, tadalafil, deflazacort and combination of tamsulosin with tadalafil in lower ureteric orifice negotiation by large size ureteroscope (8/9.8 Fr) prior to intracorporeal lithotripsy.

Patients and methods: In this prospective study, 180 patients presented with ureteric stone of size 8–15 mm were randomly assigned to 5 groups: tamsulosin (group A), tadalafil (group B), deflazacort (group C), combination of tamsulosin with tadalafil (group D) and placebo (group E). After 10 days of drug therapy 168 patients were underwent ureteroscopy and findings like endoscopic configuration of ureteric orifice, need for ureteric dilatation, ureteroscope negotiation, operating time, drug related side effect and procedural complication were noted in each group.

Results: All four groups (A, B, C, D) were significantly better than group E in terms of ureteric orifice appearance (wide) during endoscopy. Negotiation of ureteric orifice was easy in group A (70.59%), B (58.82%) and D (78.13%) as compare to group E (31.43%) which was statistically significant. Group A (32.35%) and D (34.38%) were statistically better with group E (62.86%) in terms of ureteral dilatation. Operative time was less in all four groups as compared to group E. All patients well tolerated the drugs with no serious side effects.

Abbreviations: PDE 5i, phospho diesterase 5 inhibitor; UVJ, ureterovesical junction.

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Conclusion: Both tamsulosin and tamsulosin with tadalafil helps in forward propagation of large size ureteroscope as compared to other groups with less operative time without any significant complications. So, we can conclude that tamsulosin alone can be helpful for lower ureteric orifice negotiation during intracorporeal lithotripsy with minimal side effects.

Introduction

Narrowest part of human ureter is the ureterovesical junction (UVJ) which provides difficulty in spontaneous stone expulsion as well as ureteroscope negotiation [1,2]. Peremans described the microanatomy of UVJ as three different zones namely the intramural and submucosal part of intravesical ureter and the extravesical ureter at ureteral hiatus [3]. Functionally, three different muscle groups with different innervations are present at UVJ namely the detrusor, inner and outer layer of ureter muscle and muscularis mucosae [4]. After the introduction of first rigid ureteroscope in 1980 by Perez Castro and Martinez Pineiro, several modification and miniaturization has been occurred for diagnostic and therapeutic accuracy that minimizing the morbidity but also compromises the visibility [5–7]. UVJ negotiation is an important part during ureteroscopy and many patients (almost 40–60%) may require dilatation of ureteric orifice for negotiation of large size ureteroscope (8/9.8 Fr) [8]. Various maneuvers have been described for UVJ negotiation (cases in which difficulty encountered during traversing the ureteric orifice) but none is free from complications [9].

A number of studies had found the role of α blocker and phosphodiesterase inhibitors (PDE 5i) in ureteric calculus expulsion. Although α-adrenergic receptors are distributed along the entire length of human ureter, highest concentration is present in the lower ureter. PDE 5i acts on nitric oxide/cyclic guanosine monophosphate (cGMP)-signaling pathway that will lead to increased levels of cGMP which is responsible for relaxation of the smooth muscle of ureter [10,11]. Antagonism of these receptors relaxes the ureteric smooth muscle, reduces ureteral spasm and promotes expulsion of calculi [12,13]. Ureteric calculus can lead to inflammatory reaction and mucosal edema and anti-inflammatory drugs like corticosteroid can reduce the inflammatory response thus increases stone expulsion [2,11,14].

Aim of our study was to compare the safety and efficacy of α blocker (tamsulosin), PDE 5i (tadalafil), corticosteroid (deflazacort) and combination of α blocker with PDE 5i (tamsulosin with tadalafil) in lower ureteric orifice negotiation by large size ureteroscope prior to intracorporeal lithotripsy.

Subjects and methods

After taking institutional review board approval (2701/MC/EC/2016), this prospective randomized double blind placebo controlled study was conducted in our department of urology from February 2016 to April 2017. Informed written consent was taken from all the study participants. A total of 206 patients aged 18–60 years with an uncomplicated, single ureteric stone size 8–15 mm, located in either lower or mid ureter (up to upper border of sacrum) were included in this study. Patients either not meeting inclusion criteria or not willing to participate were excluded from this study (these patients were 26 in number). Patients who were ready to accept drugs like alpha blocker (tamsulosin), PDE5i (tadalafil), corticosteroids (deflazacort), combination (tamsulosin with tadalafil) and placebo (multivitamin) prior to surgery were included in this study. Patients with fever, moderate to gross hydronephrosis, presence of symptomatic bacteriuria, multiple or bilateral ureteric stones, stone located at VUJ, patients who passed stone spontaneously, patients with acute or chronic renal insufficiency, solitary kidney or congenital urinary abnormality were excluded. Patient having history of surgical interventions either open or endoscopic urinary tract surgery, diabetes, cardiac disease, bleeding diathesis, peptic ulcer or on concomitant treatment with drugs like alpha blocker, beta-blockers, calcium antagonists or nitrates, immunosuppressant without's, any malignancy, pregnant or lactating females and patient who demand immediate active intervention and not willing to participate were also excluded from this study. So, finally, 180 patients met the inclusion criteria and underwent intracorporeal ureteroscopic lithotripsy.

All patients satisfying inclusion criteria were randomized into five groups by use of sequentially numbered, opaque sealed envelopes (SNOSE) method [15]. Group A, B, C, D and E were given, Tamsulosin (0.4 mg OD), Tadalafil (5 mg OD), Deflazacort (30 mg OD), Tamsulosin (0.4 mg OD) + Tadalafil (5 mg OD) and placebo (multivitamin), respectively only for 10 days prior to surgery. All patients were informed about the side effects of the drugs. History and physical examination were done in all the patients. General characteristics of all patients were recorded like age, gender, side, size and location of calculus, height, weight and BMI. Investigations like serum creatinine, urinalysis with urine culture, ultrasonography, plain X-ray of the kidneys, ureter, and bladder (KUB) and computed tomography (CT) were done in every patient before surgery. The greatest dimension of the stone was taken into consideration as the stone size. Postoperatively, X ray KUB and ultrasonography were done in every patient to know the residual fragment.

Tab diclofenac 50 mg was given in each group for pain relief as and when required. After 10 days of drug intake, patients of each group underwent cystourethroscopy. Ureteric orifice configuration (wide/narrow) was noted and then 0.035 Fr guide wire placed. After this, 8/9.8 Fr wolf ureteroscope was tried to insert into ureteric orifice over guide wire. If ureteroscope was negotiated easily into ureteric orifice without using any maneuver than procedure was considered as complete. If ureteroscope could not be negotiated through ureteric

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