Comparative study between tamsulosin and nifedipine in the treatment of lower ureteric stones

THESIS
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Summary and conclusion

The worldwide incidence of urinary stone disease (urolithiasis) is estimated to be about 4% to 15% in the lifetime of the population**.** Ureteral stones account for 20% of urolithiasis**.** Nearly all ureteral stones are supposed to be expelled spontaneously when their diameters are smaller than 4 mm (Gravas et al., 2007). However, the spontaneous expulsion rate of distal ureter stones is about 25% if their sizes are between 4&6 mm and 5% if greater than 6 mm. (Gravas et al., 2007). Extracorporeal shock wave lithotripsy and ureteroscopy represent the current therapeutic options for distal ureterolithiasis. Nevertheless these techniques are not risk-free, are problematic and are quite expensive (Lotan, 2002)**.** On the other hand, a watchful waiting approach can be used in a large number of cases, as demonstrated by several studies that revealed spontaneous passage rates of up to 98% for small distal ureteral stones. (Hubner et al., 1993; Ueno et al., 1977 and Coll et al., 2002). Moreover, even the simple watchful waiting approach can result in complications, such as infection of the urinary tract, hydronephrosis and renal function effects (Ueno et al., 1977). Therefore, use of the watchful waiting approach has been extended by using pharmacological therapy, which can reduce symptoms and facilitate stone expulsion (Borghi et al., 1994 and Cervenakov et al., 2002) .Such a therapy has been identified in what is now referred to as medical expulsive therapy (MET), (Preminger et al., 2007).The primary agents that have been evaluated for MET are calcium channel blockers, steroids, non steroidal anti-inflammatory drugs (NSAIDs), antispasmodics and α1-adrenergic receptor antagonists (Hollingsworth et al., 2007).

Nifedipine is the most studied calcium channel blocker used to treat ureteral spasm and promotes stone passage. Its use in MET for distal ureterolithiasis has been tested in various studies, which have demonstrated its excellent efficacy for inducing stone expulsion and relieving pain. Alpha-1-adrenergic receptor antagonists have been the next agents investigated for their potential to promote stone expulsion and decrease pain. The current classification recognizes the existence of three α1-adrenoceptors (α1A, α1B and α1D), (Malin et al., 1970). The rationale in using α1 antagonists in MET has been that they are capable of decreasing the force of ureteral contraction, decreasing the frequency of peristaltic contractions, and increasing the fluid bolus volume transported down the ureter (Davenport et al., 2006). Tamsulosin has been the most commonly studied α1-blocker in the treatment of ureteral stones. Tamsulosin is a selective α1 antagonist that has equal affinity for α1a and α1d receptors (Richardson et al., 1997).

Several groups have investigated the role of pharmacologic therapy to facilitate spontaneous stone passage. Borghi et al demonstrated the beneficial effect of calcium antagonist (nifedipine) in reducing time to stone passage and improving expulsion rates. Cervenakov et al (2002) in a randomized study registered a significant statistical difference in stone expulsion rate between the group treated with tamsulosin and the control group.

Although, as we previously mentioned, tamsulosin and nifedipine are the most effective and the most commonly studied drugs in MET, direct comparative studies between them are limited in the literature which led us to conduct our comparative study between safety and effectiveness of tamsulosin and nifedipine in the treatment of lower ureteric stones.

Our study was carried out in the outpatient division of urology department –Fayoum University hospital. It included the study of forty patients with lower ureteric stones smaller than 1 cm. The age of the patients ranged between 21 and 75 years comprising 12 females and 28 males. These forty patients were randomly divided into 2 groups; group 1 comprising 20 patients who received tamsulosin 0.4 mg capsules once daily and group 2 comprising again 20 patients who received nifedipine 10 mg capsules three times daily. In both groups, the treatment duration was until stone expulsion or 30 days, whichever comes first.

All patients were fully evaluated by history taking and thorough clinical examination with special emphasis on loin pain, fever and irritative symptoms and were investigated by laboratory investigations as serum creatinine and urine analysis and also radiological investigations as P.U.T, abdominal pelvic u/s, I.V.P. and spiral C.T.abdomen and pelvis if needed. All patients were allowed to use symptomatic therapy with injections of 75 mg diclofenac (on demand) and were required to drink a minimum of 2 l of water daily. The follow up was limited to 4 weeks. Patients who failed to expel the stone within 4 weeks underwent ureteroscopy. All patients were examined weekly using x-ray of the kidneys, ureters and bladder and ultrasonography. Side effects of the expulsive therapy were also recorded during follow up visits if present.

Comparing the two groups, regarding stone expulsion rate, medical therapy with tamsulosin [group 1] demonstrated positive results in 85% of patients, whereas nifedipine [group 2] demonstrated positive results in 40% of patients. These figures demonstrate statistically significant difference [p value = 0.003]. Our results differs from that of Porpiglia and his colleagues in 2004 who reported that there is no significant statistical difference between tamsulosin and nifedipine in stone

expulsion rate. However, in more recent study, Dellabella and colleagues (2005) compared tamsulosin, nifedipine, and phloroglucinol, a spasmolytic agent, in 210 patients who were randomly divided into 3 groups and the percentage of stones passed was significantly greater in the group receiving tamsulosin when compared with both the group receiving nifedipine and the group receiving phloroglucinol.

Thus, our results confirms the results obtained by Dellabella and associates and may be due to the higher density of α1 receptors in the lower part of the ureter and the more selectivity of tamsulosin on α1-a and α1-d receptors thus inhibiting basal smooth muscle tone and obstruction induced hyper peristaltic uncoordinated frequency whilst maintaining tonic propulsive contractions allowing distal migration of the stone (Malin et al., 1970).

As far as expulsion time was concerned, mean time to expulsion was 8.7 days in group 1, whereas mean time to expulsion in group 2 was 19.1 days .A statistical significant difference exists between the two groups [p value 0.001].Thus, our results demonstrate that tamsulosin reduced expulsion times significantly in respect to nifedipine and confirms the positive results obtained in reducing stone passage times by others[Ukhal et al.,1999; Cervenakov et al., 2002 and Dellabella et al., 2003).Adding also the fact that the percentage of expulsion rate was significantly greater in tamsulosin group, we hypothesize that tamsulosin is superior and more effective for treatment of distal ureteric stones than nifedipine.

As regards episodes of renal colic, average number of colic was 0.9 in group 1 compared to 1.8 in group 2. The difference among them is statistically insignificant. Our results differs from the results obtained by Porpiglia and colleagues (2004) and Dellabella and colleagues (2005)

who stated that tamsulosin is superior than nifedipine for relieving the pain associated with ureteric colic. Dellabela supposed a double action of tamsulosin on the control of pain associated with ureteral colic, that is a first action on smooth muscles, preventing spasm, and a second action on C-fibers or sympathetic postganglionic neurons, which also blocks pain conduction to the central nervous system (Dellabella et al., 2005).

However, in our study, three patients required hospitalization due to severe persistent pain and fever associated with ureteric colic in the nifedipine group compared to one patient only in the tamsulosin group. This lower incidence of hospitalization in the tamsulosin group may be explained by the double action theory of Dellabella. Further evaluation using larger groups will provide an opportunity to confirm these finding.

Minor therapy related side effects were observed in three patients in group 1 [decreased lipido, abnormal ejaculation, mild headache] and also three patients in group 2[mild dizziness, headache] however, they were tolerable and infrequent and patients were able to complete the study.

With regard to safety, both tamsulosin and nifedipine were well tolerated by the patients. Patients who were not stone-free after one month follow up were successfully treated with ureteroscopy .These data demonstrate that neither watchful waiting nor medical therapy seems to negatively affect the success rate of stone removal.