EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY;
CAN ALPHA BLOCKER IMPROVES STONE CLEARANCE?

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ABSTRACT... Objective: To determine the efficacy of Alpha blocker as adjunctive medical therapy , which increases the stone clearance after extracorporeal shock wave lithotripsy (ESWL) to treat renal stones. **Design:** Quasi Experimental study. **Setting:** Department of Urology, Liaquat National Hospital, Karachi. **Period:** September 2010 to March 2011. **Materials & Method:** Ultrasound guided Dornier Alpha Impact lithotripter was used for shock wave lithotripsy. Study was carried out on 60 patients who underwent single session of ESWL for renal calculus. Patients were divided in two groups, Group A (n=30) received conventional treatment and Group B (n=30) received Alpha-1 Blocker in addition to conventional treatment. All patients were evaluated with X-ray and Ultrasound (KUB) after 2 weeks and repeated at the end of month. Failure is defined as unsuccessful expulsion after 4 weeks and patient desire to remove the stone before day 30. **Result:** Out of 60 patients, 45(75%) were males and 15(257%) were females with male to female ratio was 3:1. The average age of the patients was found 36.32 ± 14.8 (Ranging from 15 to 75) years. Complete clearance was achieved in 76.7% of those receiving Alpha-1 Blocker and in 46.7% of controls at 1 month (P = 0.001). This difference was statistically significant. **Conclusions:** The results of my study demonstrate that Alpha-1 Blocker therapy, as an adjunctive medical therapy after ESWL is more effective than lithotripsy alone for the treatment of patients with large renal stones and is equally safe.

Key words: Alpha-blockers, Ureteral stones, Kidney stones , Extracorporeal Shock Wave Lithotripsy.

INTRODUCTION

Renal stone disease is a significant worldwide health problem. This disease affects about 8% to 15% of the population in Europe and North America[1]. Pakistan is located within the geographical distribution of stone disease, which is the commonest urological problem in Pakistan. The mean age group of affected population in Pakistan is 40 years[2].

Surgery has been the most important treatment modality for stone disease and open surgery is still performed especially for large complicated staghorn stones[3].The goal of treatment is to make patients stone free as bacteria retained in stone fragments lead to stone growth[4]. The site (kidney or ureter) and size (dimensions) of the stone are the criteria for the choice of treatment[5]. Recent advances in endoscopic stone management have allowed kidney stones to be treated using minimally invasive techniques, which have increased success rates and decreased treatment-related morbidity. These advances include shock wave lithotripsy (SWL), ureteroscopy (URS), and percutaneous nephrolithotomy (PCNL)[6].

Dornier, a German aircraft corporation, first developed the ESWL technology in conjunction with Chaussay and his co-workers in Munich[7]. Three forms of energy source used most frequently in SWL are electro hydraulic, piezoelectric and electromagnetic sources[8]. The ideal treatment for renal stones of less than 20 mm in diameter is ESWL and it is also a favourable choice for proximal ureteric stones[9].

The rate of spontaneous passage for a stone of 5 mm or smaller in the proximal ureter is estimated to be 29% to 98%, and in the distal ureter, it is 71% to 98%. The most

important factors in predicting the likelihood of spontaneous stone passage are stone location and stone size[10].

Recently medical expulsion therapy (MET) has been investigated as a supplement to observation in an effort to improve spontaneous stone passage rates which can be unpredictable, because ureteral edema and ureteral spasm have been postulated to affect stone passage. These effects have been targeted for pharmacologic intervention[11]. Therefore the primary agents that have been evaluated for MET are calcium channel blockers, steroids, non-steroidal anti-inflammatory drugs (NSAIDs) and á1-adrenergic receptor antagonists. A recent meta-analysis was performed which compared stone passage rates in patients who were given calcium channel blockers or á1-adrenergic receptor antagonists versus controls who did not receive these medications. The analysis demonstrated a 65% greater chance of passing a ureteral stone in patients who received either medication[12].

Our study was focused on the use of á-blocker (Alpha-1 Blocker) in the management of expulsion of stone fragments after getting ESWL treatment for renal calculus.

MATERIALS AND METHODS

This was Quasi Experimental study performed in the Department of Urology, Liaquat National Hospital Karachi from September 2010 to March 2011. This study consisted of sixty patients who were divided in two groups A (n=30) and B (n=30). Non-probability convenience type was used as sampling technique.

Patients with solitary renal stone between 5 mm and 15 mm size located in the renal pelvis or middle or upper calices were included in the study. Those patients having concomitant stones in lower pole of kidney, previous unsuccessful attempts at ESWL, elevated serum creatinine (>2mg/dl), urinary tract infection, hydronephrosis, concomitant treatment with calcium antagonist, urinary congenital anomalies or previous pyelouretral surgery, pregnancy, severe obesity, severe skeletal malformations were excluded from the study. Patients were explained about the research protocol and related implication. The study was conducted after taking informed and written consent from all the patients. Patient's safety and comfort was assured. Stone size assessment was done by X-ray KUB (kidney, ureter and bladder) and ultrasound KUB. After history, examination and investigations, only those who match with the selection criteria underwent single shock wave lithotripsy by an Ultrasound guided Dornier Alpha Impact lithotripter.

Group A patients were assigned to take conventional treatment and used as control group. Drugs given were Diclofenic Sodium 50 mg as per required by patient, Drotaverine (No Spa) 80mg and Omeprazole 20mg. While Group B were assigned to take Alpha blocker 5mg twice daily in addition to conventional treatment. Treatment was started after ESWL and continued for one month or until alternative treatment was given. Further more all patients were instructed to drink a minimum of 2 litres water daily. Patients were asked for stone expulsion, use of analgesics and episodes of pain in follow up visits.

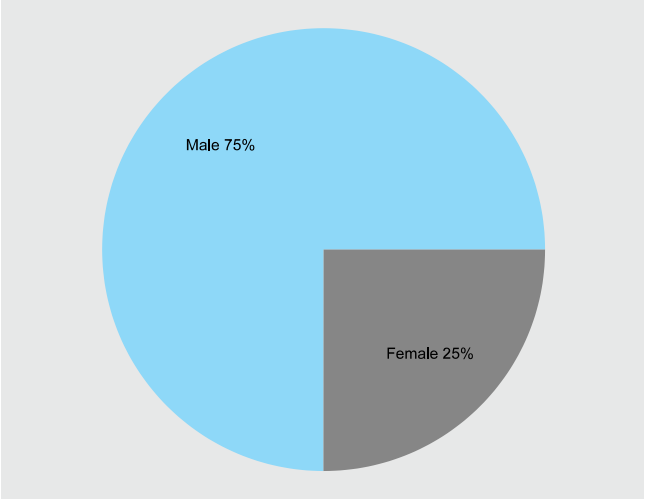
The follow-up protocol includes plain abdominal x-ray or renal Ultrasonography every 2 weeks until complete stone clearance. Success is defined as the absence of residual stones or the presence of insignificant gravel of 3 mm or less in diameter. Failure is defined as unsuccessful expulsion after 4 weeks, uncontrolled pain on conventional therapy, fever and patient desire to remove the stone before day 30.

RESULTS

The study was carried out in 60 patients divided into two groups, Group-A (Control Group) included 30 patients who received conventional treatment and Group-B also included 30 patients treated with conventional treatment with Alpha-1 Blocker 5mg twice daily.

The average age of the patients was 36.32 ± 14.8 (Ranging from 15 to 75) years. Out of 60 patients, there were 45(75%) males and 15(25%) females with male to female ratio of 3:1(Figure 1). Most stones were located in the middle pole. The mean largest diameter of stones was 12.45± 2.7 mm.

Fig-1. Gender distribution



Both treatment groups received single shock wave lithotripsy. A mean of 2860 ± 140 shocks per patient was delivered at mean voltage of 13.7 ± 0.5 KV, with no difference between group A and B (P>0.05).

A statistically significant difference was found in the rate of clinical success after four weeks between those receiving Alpha-1 Blocker, tablet Alpha-1 Blocker HCl (Group B ; 76.7%) and the control group (Group A; 46.7%; P = 0.01, Figure 2). Although the percentage of clinical success seemed to increase at each visit in both groups, we observed that statistically relevant difference was achieved only in group B. Alpha-1 Blocker was statistically superior to conventional treatment both at 02 and 04 weeks in terms of clinical success.

With stone size 11 to 15 mm in diameter, we found a relevant difference in the success rate between the two groups (56.7% in group B and 23.3% in group A; P=0.02). In contrast, among patients with stone 5 to10 mm in diameter, no significant increase occurred in the success rate (20% in group A versus 23.3% in group B; P > 0.05; (Figure 3).

Secondary ESWL or other invasive interventions (URS, lithoclast, and DJS) were necessary in 38.3% (23 patients) of the total cohort. There was no difference in the rates of these interventions for the Alpha-1 Blocker or conventional treatment groups.

Fig-2. Comparison of patients with overall clinical success between groups after 2nd and 4th week

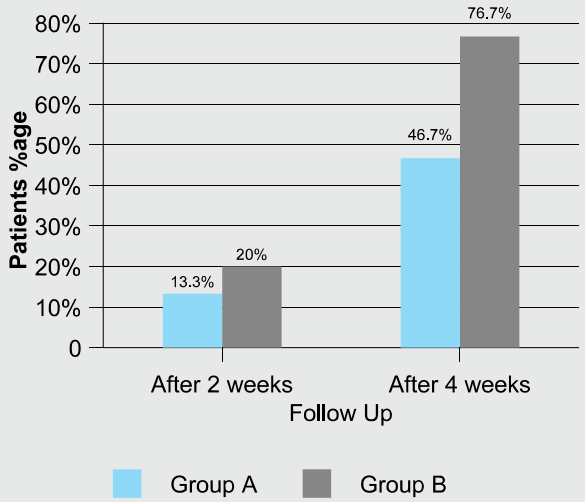
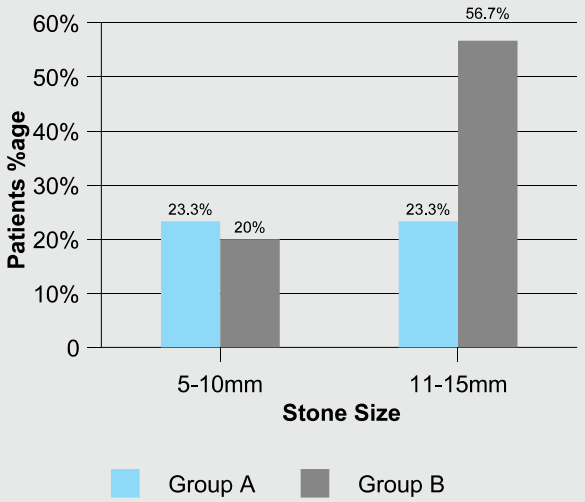


Fig-3. Success rate after 4th week according to stone size



Group A = Control Group *Group B = Alpha-I Blocker*

The mean cumulative doses of Diclofenic in the Alpha-1 Blocker and conventional treatment groups were 485 and 768 mg, respectively, with statistically significant difference between the groups were observed (P=0.002). No difference in side effects was observed among the groups.

DISCUSSION

Stone fragment expulsion after ESWL is probably not dissimilar to spontaneous discharge. Several variables play a fundamental role for the migration process of calculi: stone size, configuration and location, smooth muscle spasm, submucosal edema, intrinsic areas of narrowing within the ureter; ureteral peristalsis and infections[13].

Some investigators have reported the effectiveness of different pharmacologic therapies in increasing ureteral stone expulsion by acting primarily on spasm and ureteral peristalsis. Borghi et al[14] and Porpiglia et al have shown that the association of nifedipine and steroids improved the rate of ureteral stone expulsion and reduced the time for stone passage. Furthermore, alpha1-adrenergic antagonist can cause a decrease in ureteral peristaltic frequency and reducing ureteral spasm[15].

Several studies have been done to demonstrate that lower tract ureteral stones can be treated efficiently with different types of alpha1 blockers with a few incidences of side effects[16,17].

Of the available alpha1 blockers, I chose Alpha-1 Blocker because it is much cheaper, easily available and like Tamsulosin have comparatively less observed cardiac side effects then other alpha1 blockers like Doxazosin or Terazosin. Moreover it is a combined alpha1A and alpha1D – selective adrenergic antagonist and existence of alpha1A and alpha1D adrenoreceptor subtypes have been demonstrated in the smooth muscle cells of the human ureter[18].

In our study Alpha-1 Blocker was used in addition to conventional medical therapy which comprises oral analgesic, antispasmodic, proton pump inhibitor and 2 litres of drinking water.

By analyzing the difference in the stone-free rate of my groups, I observed that 1 month of Alpha-1 Blocker therapy had a favourable impact on the clearance of residual fragments after ESWL. However it is possible that prolongation of Alpha-1 Blocker therapy beyond the follow up period could yield an increased stone-free success rate. This assumption originates from the observation that the stone-free status in the control group-A presented with only a little increment between 2 and 4 weeks, but in the treatment group-B, during the same weeks, we observed a continuous increase in the success rate.

The administration of Alpha-1 Blocker was particularly effective in the presence of large stones. Stratifying patients according to stone size, I was unable to demonstrate relationship between an original stone diameter up to 10mm and the success rate. For stones larger then 10 mm, however, success rate was significantly greater in the Alpha-1 Blocker group then in the control one.

During ESWL, larger stone usually broke in larger fragments that migrate less easily. In this occurrence, Alpha-1 Blocker potentiate the passage of stone fragments either by increasing the intra ureteral flow or by decreasing the peristalsis above the obstruction[16].

Morbidity as measured by pain was significantly lower when ESWL was combined with Alpha-1 Blocker, as shown by significant decrease in analgesic use together with easier home patient management. In this regard colicky pain is related to ureteral spasm and Alpha-1 Blocker could decrease the algogenic stimuli by decreasing the frequency of peristaltic contractions during expulsion[19].

The side effects of Alpha-1 Blocker therapy after ESWL were mild, completely reversible, and did not lead any patient to discontinue the drug. On the basis of these results, we propose a simplified algorithm to manage renal stones after ESWL. Patients with a renal stone of 10 mm or less should be primarily treated with ESWL alone. In contrast, patients with a renal stone larger then 10 mm may benefit from adjunctive therapy.

CONCLUSIONS

Extracorporeal Shock Wave Lithotripsy in association with Alpha-1 Blocker is more effective than lithotripsy alone for the treatment of patients with renal stones and is equally safe. Alpha-1 Blocker is more useful for stones with larger dimension, because the larger the original

diameter of stone, the greater the number of subjects achieving success. Alpha-1 Blocker also decreases the use of analgesic drug after ESWL.

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