"A prospective randomized study comparing the efficacy of tamsulosin and placebo in the management of patients with acute urinary retention secondary to benign prostatic hyperplasia undergoing trial without catheter until definitive therapy"

Submitted for M.Ch degree examination

BRANCH – IV UROLOGY
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CHENNAI – 600010

THE TAMILNADU DR. MGR MEDICAL UNIVERSITY
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CERTIFICATE

This is to certify that the dissertation titled **"A prospective randomized study comparing the efficacy of tamsulosin and placebo in the management of patients with acute urinary retention secondary to benign prostatic hyperplasia undergoing trial without catheter until definitive therapy"** submitted by Dr.V.CHANDRAMOHAN to the Faculty of Urology , The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the requirement for the award of M.Ch Degree in Urology branch is an original bonafide work carried out by him during the academic period August 2011 to August 2014 under direct supervision and guidance.

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DECLARATION

I, **Dr.V.CHANDRAMOHAN** solemnly declare that the dissertation titled **"A prospective randomized study comparing the efficacy of tamsulosin and placebo in the management of patients with acute urinary retention secondary to benign prostatic hyperplasia undergoing trial without catheter until definitive therapy"** is a bonafide work done by me at Govt. Kilpauk Medical College & Hospital and Govt. Royapettah Hospital during August 2012 to February 2014 under the guidance and supervision of PROF.K.THIAGARAJAN M.S., M.Ch.,DNB (Urology) , Professor of Urology. The dissertation is submitted to Tamil Nadu, Dr. M.G.R Medical University, towards partial fulfilment of requirement for the award of M.Ch. Degree (Branch-IV) in Urology three years course.

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ANNEXURE LIST

INTRODUCTION

Acute urinary retention (AUR) is the most common urological emergency in patients with benign prostatic hyperplasia**.**

Acute urinary retention (AUR) is defined as the sudden and complete inability to void urine voluntarily despite the presence of urine in the bladder and the desire to urinate. 10% of men in 61 to 70 years age group and 30% in 71 to 80 years age group would have acute urinary retention in the next five years (Curtis et al 2001). Acute urinary retention is the main indication for 25 to 30% of the patients undergoing prostatic surgery.

The event triggering acute urinary retention is not identified in most cases. It is the natural history of benign prostatic hyperplasia that progresses to spontaneous AUR. Sudden sympathetic stimulation causes an acute rise in the smooth muscle tone resulting in urinary retention. Alpha blockers aid in voiding by relaxing the smooth muscle tone and relieving obstruction (1).Patient quality of life is affected by AUR to the extent that it can be comparable to quality of life impaired by acute renal colic (2). Acute urinary retention is usually managed by immediate catheterisation and emptying the bladder followed by trial without catheter or immediate surgery for benign prostatic hypertrophy. Immediate surgery (within few days after AUR) with urinary catheter in situ is associated with more complications in the post operative period. Patients on

prolonged catheterization without undergoing surgery have to undergo potential morbidity in the form of bacterial colonisation the urinary tract, bacteriuria, fever and urosepsis with involvement of upper urinary tracts.

To date the first line of treatment in these patients is giving trial without catheter (TWOC) with a prior administration of an alpha blocker that should increase the likelihood of success. An initial drained volume of urine less than one litre following catheterisation of AUR, patients with less than 60 to 65 years of age, a precipitated AUR and catheterisation for more than 3 days would increase the chance of successful trial without catheter. Patients undergoing TWOC are later subjected to elective transurethral resection of prostate (TURP) or continue drug therapy in the form of alpha blockers alone or in combination with 5 α reductase inhibitors (5 α RI). 5 α RIs like Dutastride are added to alpha blockers if the gland size is above 30cc to reduce the gland size and risk of AUR (3).

In this study effect of tamsulosin has been evaluated in the temporary management of acute urinary retention by increasing the rate of successful trial without catheter (TWOC) until definitive therapy. Successful TWOC helps patient to undergo elective transurethral resection of prostate (TURP) without an indwelling urinary catheter or may continue medical therapy if he opts for medical therapy over surgery depending on indication.

AIM

To compare the efficacy of tamsulosin and placebo in the immediate management of patients with acute urinary retention secondary to benign prostatic hyperplasia undergoing trial without catheter and assess effect of tamsulosin in the success rate of trial without catheter with respect to prostate size, patient age and post void residual.

REVIEW OF LITERATURE

Acute urinary retention (AUR) is the sudden and complete inability to void despite having adequate urine in the bladder and the desire (urge sensation) to urinate. It is usually be preceded by a history of progressively decreasing force of voided stream. An individual may have complaints of lower abdominal pain. The bladder has to be drained immediately or it can lead to acute renal failure or bladder rupture.

Incidence of AUR in BPH

Incidence of AUR varies from 5 to 25 per thousand person years. It is approximately 0.5 to 2.5% annually for BPH patients. This risk increases with age and with each year of patient living with symptoms of BPH. For a patient in the 50 year age group with mild to moderate BPH symptoms suffering from an episode of acute urinary retention, would have 20% chance of undergoing subsequent AUR, if he lives upto 80 years of age without intervention. If the same patient of 60 years of age lives without intervention, would have 23% of chance of recurrent AUR over another 20 years period. A 70 year old patient having mild to moderate BPH symptom score with an episode of AUR, would

have the 30% chance of suffering from another AUR. The risk of AUR is higher in patients suffering from symptomatic benign prostatic hypertrophy. Risk factors for AUR in men with symptomatic BPH are elevated serum PSA, large prostate volume as measured by transrectal ultrasound (TRUS), Qmax (maximal urinary flow rate) and symptom severity (4).

In patients in 45 to 49 year age group with mild BPH symptoms with IPSS score of 0 to 7, incidence of AUR is from 0.4 per 1000 person-years. In patients in 70 to 83 year age group incidence of AUR is 7.9 per1000 person-years. In Patients with IPSS score 8 to 35, incidence is 3.3 per1000 person-years in 45 to 49 years age group. Incidence in patients of symptomatic score of 8 to 35 in the age group of 70 to 83 years is 11.3/1000 person-years. Patients having clinically diagnosed BPH and a BPH symptom score of 8 or greater had the largest age adjusted incidence of 13.7 per1000 person-years for AUR (5).

In the Olmsted County Study (6), evaluation was done based on age, severity of symptoms, Qmax (maximum urinary flow rate), and prostate size. Study showed incidence rates from 2.6 per 1000 person years for men in their 40s to 9.3 per 1000 person years for patients with BPH in their seventh decade if they had mild symptom score. Study also showed incidence rates from 3.0 per 1000 person years to 34.7 per 1000 person years, respectively, if same age group patients had more than mild symptoms.

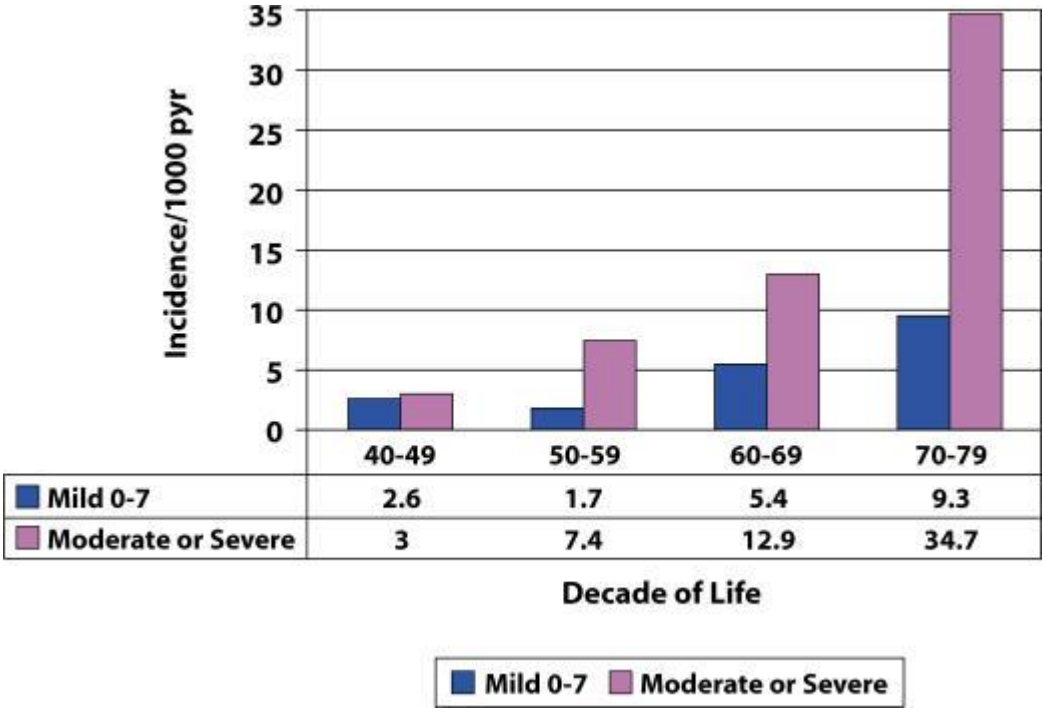

Figure1. AUR incidence rates in Olmsted County Study by age group and symptom severity score. Jacobsen et al data (6).

The relative risk of acute urinary retention is increased with older age, moderate to severe BPH symptom scores (3.2 times), Qmax flow rate less than12 ml per second (3.9 times), and prostate size more than 30 cc as measured by transrectal ultrasound (3.0 times) with comparison as baseline risk of 1.0 times for the corresponding groups.

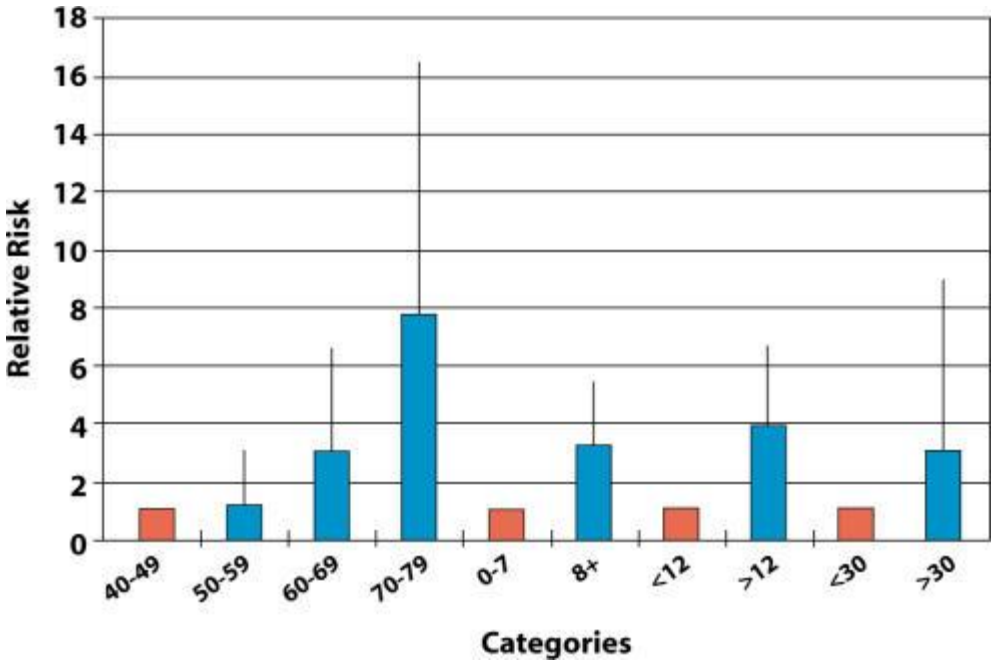

Figure2. Relative risk of AUR in Olmsted County Study in the form of age group from 40 years up to 79 years, symptom severity score of 0 to 7 and more than 8, Qmax of less than 12 and more than 12 ml per second, and TRUS measured prostate size of less than 30cc and more than 30 cc. The red columns represent the baseline relative risk (RR) of 1.0. The vertical lines represent the 95% CI. Data is from Jacobsen et al (6).

The incidence raised from 5.6% to 7.7% in BPH patients with a serum PSA value less than 1.4 ng/mL and mild to severe symptoms, and from 7.8% to 10.2% for those with a serum PSA value more than 1.4 ng/mL over the period of 4 years in PLESS study (7).

ETIOPATHOGENESIS OF AUR IN BPH

Etiopathogenesis of AUR needs to be evaluated in patients presenting with AUR for planning of immediate management and preventing recurrent AUR on long term basis. From the clinical management aspect, precipitated AUR needs to be differentiated from spontaneous AUR. Precipitated AUR is the sudden inability to pass urine following any precipitating event like any non prostatic surgery, temporary urinary catheterization for causes other than AUR, anaesthesia and administration of sympathomimetic or anticholinergic drugs or drugs having these effects, taking antihistaminic drugs. All other acute urinary retentions, without a precipitating factor, are categorised as spontaneous AUR (8). The management of precipitated AUR is different from spontaneous AUR. In case of spontaneous AUR, patient would probably have another episode of AUR in 15% of cases.75% of these patients with spontaneous AUR would have to undergo surgery. In case of a precipitated AUR only 9% would have recurrent episodes of AUR and 26% of these patients would have to undergo surgery in the long term (8).

Acute urinary retention causes are categorised in to three groups; any event that increases the bladder out flow resistance, interference in neuronal pathways supplying the bladder and any event causing bladder over distension

(9). The exact mechanism which precipitates acute urinary retention in patients with benign prostatic hyperplasia has not been fully understood. The following causes may be responsible for precipitation of acute urinary retention in benign prostatic hepertrophy.

Inflammation of the prostate

Prostatic inflammation is thought to be a causative factor in the progression of the disease in BPH, notably the first incident of acute urinary retention. Tuncel *et al* reported a more incidence of inflammation (54.7%) in prostatic tissue in patients with AUR than in patients suffering from lower urinary tract symptoms alone (28.9%). In the MTOPS study, 1197 patients underwent prostate biopsies as base line. Out of 1197 patients, 544 were found to have inflammatory changes of acute nature and 513 had inflammatory changes of chronic in nature. Patients who found to have inflammation in their baseline prostatic biopsies, had bigger prostate gland size and an elevated PSA values (known risk factors for AUR) than those found to have no evidence of inflammation. These patients with prostatic inflammation were more likely to have symptomatic progression or to undergo surgery for BPH. Even in patients within placebo group, all the patients who had acute urinary retention, were found to have inflammation in their baseline prostatic biopsies. All these patients had evidence of inflammatory infiltrates, but these changes could not be

correlated to bacterial or other foreign antigens. Prostate secretory products were recognised by auto reactive T cells in animal models subjected to experimental prostatitis. These findings demonstrated a possible autoimmune reaction leading to chronic inflammation in prostate. These infiltrates consist mostly of chronically activated CD4 T lymphocytes. These activated CD4 T lymphocytes are recruited to the prostate tissue through increased expression of interleukin 15 (IL-15) and gamma interferon (IFN-gamma) which are inflammatory cytokines predominantly secreted by smooth muscle cells and T cells, respectively (10).

Prostatic infarction

Spiro and colleagues demonstrated findings of infarction in 85% of prostate biopsies operated for acute urinary retention. This is in contrast to evidence of prostatic infarction found only 3% in prostatic specimens removed from patients with symptoms of lower urinary tract alone (11). Prostatic infarction could probably be caused by interference of the intra glandular blood supply, any form of injury including iatrogenic and possible infection. The correct mechanism causing prostatic infarction resulting in acute urinary retention has not been established. A new hypothesis is proposed recently that prostatic infarction may lead to swelling and an increase in intraprostatic urethral pressure in areas surrounding the zone of infarction. This may in turn

stimulate efferent α adrenergic nerves which may result in ultimate increase of intraurethral pressure leading to acute urinary retention (12). But another study by Anjum and colleagues has established same findings of prostatic infarction in men without AUR (35 men present with AUR and without AUR 1.9% vs. 3.0% respectively). Hence the causative role of infarction of the prostate in the pathogenesis of acute urinary retention is questionable (13).

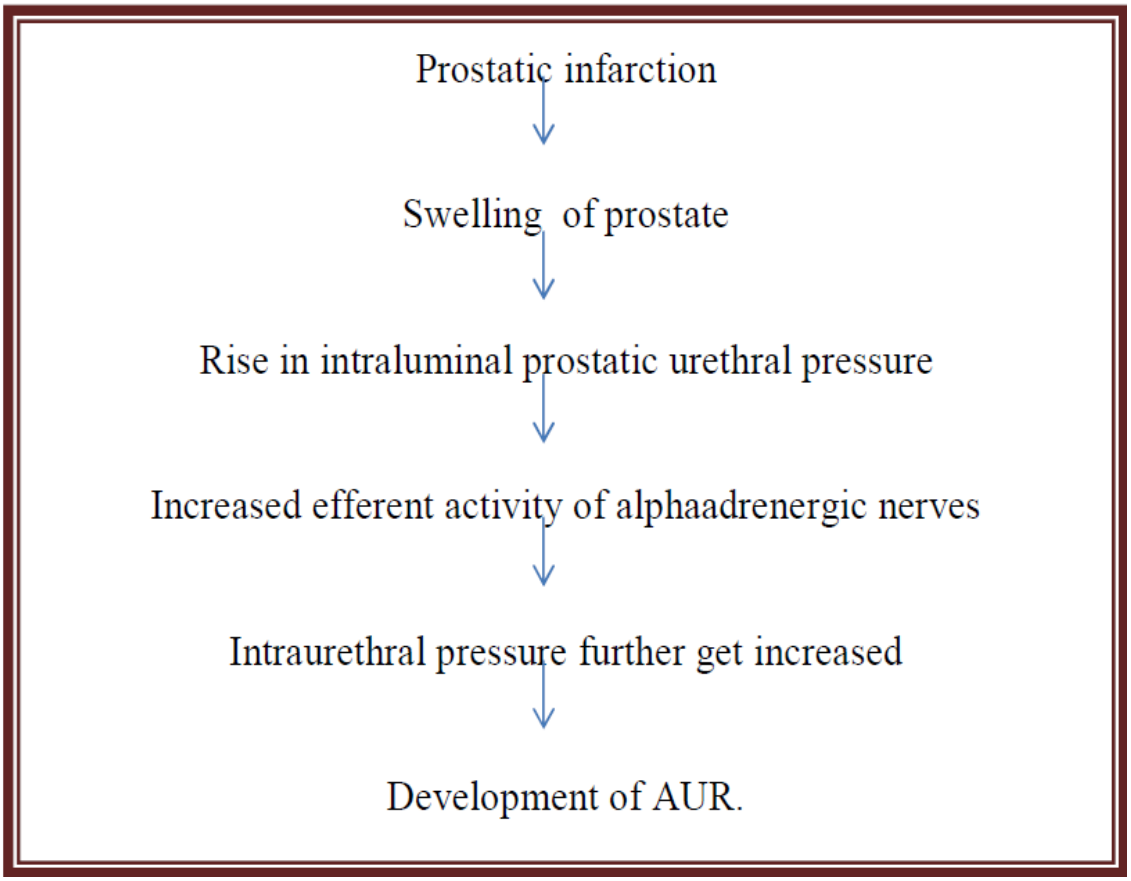

Figure 3, Prostatic infarction role in the AUR development

Stromal cell /Epithelial cell ratio and prevention of recurrent AUR

In a prospective comparative study of pathological prostatic specimens of 35 men who had AUR in initial presentation with evidence of BPH and 35 patients who had presented with only refractory lower urinary tract symptoms, it was found that those presenting with AUR had a predominant (71%) epithelial component than patients with LUTS only having (60%) epithelial component. Differential growth of epithelial component in relation to the stromal component may result in ischemic damage (infarction) by decreasing the vascular supply of prostatic tissue which may precipitate acute urinary retenton. This finding may clarify the effect of 5α reductase inhibitors, which acts by preferably reducing epithelial component, can decrease progression of disease, there by recurrence of AUR on long term treatment.

Role of Constipation in AUR

It is widely considered that constipation can precipitate acute urinary retention. Studies found no valid evidence to prove that this can occur in patients not having feature of bladder outlet obstruction, evidence of a neurological disease or finding of fecal impaction. In the Alfuzosin in Acute Urinary Retention (ALFAUR) study, history about their regular bowel habits

like constipation was carefully elicited from 363 patients presenting with acute urinary retention secondary to BPH. Success of trial without catheter was not altered by the presence of constipation history. Therefore a history of constipation alone without evidence of faecal impaction should not alter the management strategy of patients having acute urinary retention because of BPH. But it may provide an indication of how the patient can be managed in the longer term with respect to the need for surgical intervention and recurrent episodes of AUR.

Urinary tract infection (UTI) and AUR

Urinary tract infection in the male may cause AUR or precipitate AUR in a patient suffering from BPH or other causes that compromise bladder emptying. Stasis caused by poor emptying in a case of bladder outlet obstruction may lead to infection. A complete evaluation of voiding function is needed when a patient presents with retention and evidence of urinary infection. In these cases AUR might be relieved by treatment of UTI along with TWOC though the cause of bladder outlet obstruction needs to be addressed to prevent recurrent AUR due to recurrent UTI.

Role of drugs in AUR

Drugs with Cholinergic antagonist effects by inhibiting detrusor contractility and alpha-adrenergic agonist effects enhancing bladder outlet resistance may precipitate urinary retention. Medications having anticholinergic actions are used for the treatment of depressive disorders, allergic disorders, Parkinson's disease and OAB (over active bladder). α agonists are commonly used for cold remedies. In a study by Athanasoupolos *et al*, it was shown that tolterodine drug could be administered safely in combination with α blocker in patients with established bladder outlet obstruction by urodynamic studies, without causing AUR (14). In their study, Reynard *et al*. have established that use of anticholinergics in men with BPH may lead to a slight rise in the post-void residual (PVR) which would not significantly increase the risk of acute urinary retention (15). Both the agents can be safely given together in the management of BPH, especially in patients who have predominant irritative voiding symptoms with low post void residual urine. When acute urinary retention develops in association with BPH and concomitant use of these drugs, management should follow standard procedure. Trial without catheter would be appropriate once drug causing retention is withdrawn.

Role of Non-steroidal anti-inflammatory drugs (NSAIDS) in AUR

A prospective case control study of BPH patients with more than 45 years of age for evaluating the role of NSAID in AUR in the Netherland population

established that patients using NSAIDs would have a relative risk of 2.02 for developing acute urinary retention than those not taking NSAIDs. Patients who were using NSAIDs at a dose more than the recommended daily dose, had the highest risk for AUR (odds ratio 3.3). Previous history of use of NSAIDs was not associated with increased rate of AUR. NSAIDs have a direct inhibitory effect on prostaglandin synthesis (especially PGE2). Prostaglandins especially PGE2 play an important role in contractile mechanism of the detrusor muscle in the bladder (16).

MANAGEMENT OF AUR IN BPH

Most patients with AUR in BPH can be managed with catheterisation. A few cases may require placement of a supra pubic cystostomy in the event of failure of urethral foley insertion. Following catheterisation, after few days, patient is given trial without catheter. Patient may be hospitalised or treated as outpatient. But in patient treatment is required in cases of renal failure, uro-sepsis, patients with severe co-morbid conditions and patients who may not return for regular follow up following catheter placement.

Duration of catheterisation

In their study, Djavan et al evaluated the effect of duration of catheterisation in the management of AUR and found that patients who had

retention volumes more than 1300 ml benefited most from long term indwelling catheters (17). But long term use of indwelling catheters may lead to higher incidences of urinary tract infection.

Complications of prolonged catheterisation

UTI is the most common nosocomial infection (40%). 80% of hospital acquired UTIs are due catheterization. Risk factors for CAUTIs (catheter associated UTI-CAUTI) include patients catheterised for more than 6 days, patients not taking systemic antibiotics, poor catheter care, female population, any active infections in areas other than urinary tract, pre-existing medical conditions, malnutrition, chronic kidney disease, catheter insertion in an unsterile atmosphere or outside operating room, and keeping drainage tubing or urobag placed above the level of the bladder. Risk of development of UTI and bacteriuria in patients with an indwelling urinary catheter is approximately 10% per day and continues to increase with increasing duration of catheter. Even sterile and clean intermittent catheterization has been found to be associated with incidence of bacteriuria ranging from 1% to 3% per catheterization. Patients kept on indwelling urinary catheter for more than 6 days are found to have significantly higher morbidity due to hematuria, urosepsis, lower urinary tract infection, asymptomatic bacteriuria, catheter obstruction, prolongation of hospitalization for adverse events and urinary leakage around the catheter and more hospital stay than in men catheterized for shorter period of time.

Complications of prolonged urethral catheterization include urethral stricture and meatal stenosis, urethral perforation, and allergic reactions (due catheter material) including anaphylaxis. Patients on prolonged indwelling catheters are having increased risk of developing stone formation (46% to 53%), bladder neck stenosis, urethral erosion and stricture and malignant neoplasms (2.3 to 10%).

Trial without catheter (TWOC)

Trial without catheter is given after a short time of 3 or 4 days following catheterisation for AUR. Trial without catheter is successful in 23% to 40% of cases without any drugs helping TWOC. In case of BPH, TWOC allows the patient to remain catheter free until elective surgery planned at a later date. This would effectively reduce the morbidity associated with an indwelling catheter for the patient and reduce the post operative morbidity after surgery due to decreased incidence of catheter associated complications mentioned above.

Immediate surgery for BPH following AUR would increase perioperative complications than elective surgery for same. As bacterial colonization of an indwelling urinary catheter is significantly more after catheterization for more than 6 days (catheter associated UTI-CAUTI). Successful trial without catheter allows patients to undergo elective surgery .To increase the success of TWOC in patients with BPH presenting with AUR alpha blockers are added and

continued to prevent the recurrence of AUR until patient undergoes definitive treatment.

Justification for α blockers use in TWOC and BPH

Acute urinary retention in patients with BPH is due to the result of a sudden stimulation of α 1 - adrenergic receptors present in the bladder. The reason for the use of alpha blockers in BPH is suggested that they act up on the "dynamic" component of bladder outlet obstruction (BOO) by relaxing smooth muscle elements located in the bladder neck, prostatic urethra, prostate and its capsule. This study was done to evaluate and compare the efficacy of tamsulosin as compared to placebo in patients with AUR secondary to BPH.

Miguel Maldonado-Avila etal proved in their prospective randomized study, comparing the efficacy of tamsulosin , alfuzosin and placebo in the management of acute urinary retention secondary to benign prostatic hyperplasia, that TWOC was successful in 28% of patients in the placebo group, 38% of patients in alfuzocin group and 45% of patients in tamsulosin group, after 4 days of catheterisation (18). They also found that tamsulosin was slightly more successful than alfuzocin, though statistically not significant.

In their study S. Alan McNeill et al (19) have evaluated the use of alpha blockers in TWOC in the management of acute urinary retention. They found that a TWOC following an episode of acute urinary retention, is beneficial by the

reducing the number of patients undergoing TURP with an indwelling urinary catheter. By using an alpha-blocker following an episode of AUR, chances of successful TWOC is increased and may delay or reduce the need for subsequent immediate surgical intervention by improving urinary flow rates and decreasing post void residual urine. Alpha-blockers may not prevent BPH progression and reduce the need for surgery following an episode of AUR. They allow an immediate surgical intervention to be planned into an elective procedure by increasing the success rate of a TWOC. This may, in turn, reduce the perioperative morbidity and mortality observed in patients with AUR who undergo TURP with an indwelling catheter.

The Medical Therapy Of Prostatic Symptoms (MTOPS) (20) trial established that α blockers treat symptoms of BPH with a relatively rapid onset of action but they do not prevent disease progression of BPH. To prevent disease progression an α-blocker is combined with a 5α-reductase inhibitor (5 ARI) for a short period (3 to 9 months).This is followed by withdrawal of the α-blocker when 5ARI has established its peak effect and continuation of 5α-reductase inhibitor monotherapy if patient chooses medical therapy over TURP due to various reasons.

The Symptom Management After Reducing Therapy (SMART-1) study (21) evaluated the combined efficacy of dutasteride and tamsulosin. In this study men with BPH were randomized to tamsulosin and dutasteride for a

period of 24 weeks initially. After 24 weeks, 50% of the patients stopped using tamsulosin. 84% of the patients with an initial IPS Score of less than 20, had sustained improvement in BPH symptoms after placed under 5 ARI monotherapy. Therefore, it has been concluded that majority of patients with mild to moderate IPSS symptom score may benefit from an initial short period (3to9 months) of combination therapy of alpha blockers and 5ARIs followed by 5ARI monotherapy.

In all these studies involving various alpha blockers, tamsulosin, alfusozin and silodosin are commonly used for increasing the success rate of TWOC following an AUR. Their effect varies depending on the prostate size, patients age and post void residual. Various studies established the effect of these drugs on increasing the success rate of TWOC from 38% to 70%. Some studies suggest that addition of alpha blockers before TWOC doubles the success rate. This study is done for evaluation of efficacy of tamsulosin in TWOC in relation to age, prostate size and post void residual. After successful TWOC most of these patients underwent definitive therapy in the form of surgery and few of them continued medical therapy due to various reasons.

TAMSULOSIN DRUG PROFILE

Actions

Tamsulosin competitively blocks α_1 adrenoceptors in post synaptic junction with relative selectivity to α1A and α1D subtypes. It causes smooth muscle relaxation in bladder neck, prostate and prostatic urethra. Tamsulosin 0.4-mg/day dose showed a fast onset of action in 4 to 8 hours assessed by Qmax. Half life is 5 to 10 hours. Tamsulosin 0.4 mg increases the Qmax (maximum urinary flow rate). Drug effect on symptoms of BPH is maintained for longer periods. It will not prevent disease progression in BPH patients hence subsequent AUR but it would delay the need for surgery and reduce the incidence of AUR. α 1 blockers can reduce BP by reducing peripheral resistance. This effect is not clinically significant for use as an antihypertensive.

Pharmacokinetics

Absorption

Tamsulosin is absorbed rapidly by the intestines and bioavailability is complete. Recent meal reduces the drug absorption from intestines. Tamsulosin

shows linear kinetics. In the fed state, after a single dose of Tamsulosin 0.4 mg, peak plasma level is attained around 6 hours with steady-state concentrations by the fifth day of once daily dose. There is a considerable variation in plasma levels with each individual irrespective of dosage.

Distribution

99% of ingested tamsulosin is in bound form with plasma proteins. The volume of distribution is very less about 0.2L/kg.

Biotransformation

Tamsulosin has less first pass metabolism effect, as it is slowly metabolized. Most of the ingested tamsulosin is circulating in the blood plasma in an unchanged form. CYP450 enzymes in liver metabolize tamsulosin. Dose reduction is not required in patients with moderate hepatic insufficiency.

Excretion

Majority of the tamsulosin and its metabolic products are excreted in the urine. About 9% of drug is excreted without any change. Following a single dose, elimination half-life of tamsulosin is about 10 hours. Dose reduction is not required in renal insufficiency.

Indications

It is used in the treatment of lower urinary tract symptoms caused by bladder outlet obstruction due to BPH.

Dosage and Administration

Tamsulosin is taken as once daily dosing either in the day or before going to bed.

Contraindications

Hypersensitivity or allergic reactions to tamsulosin.

Patients suffering from orthostatic hypotension or a history of it.

Chronic decompensated liver disease with liver failure.

Adverse effects and safety precautions

Dizziness, and retrograde ejaculation are commonly seen. Postural hypotension, palpitations, asthenia and headache are seen in few cases.

Like other alpha 1 blockers, fall in BP may be seen after treatment with Tamsulosin 0.4mg. Hence patient may have giddiness or syncope. If the patient develops symptoms or signs of orthostatic hypotension (dizziness, weakness), he has to lie down until the disappearance of symptoms.

Use of tamsulosin in patients with severe renal impairment (creatinine clearance of < 10ml/min) is not advisable as effects on these patients have not been studied.

Intra-operative Floppy Iris Syndrome

'Intra-operative Floppy Iris Syndrome' (IFIS) is seen in few patients undergoing cataract surgery while using tamsulosin along with α1 adrenoceptor antagonists. This is characterized by the combination of a flaccid iris that billows in response to intra-operative irrigation currents, progressive intra-operative miosis, inspiteof pre-operative dilation with mydriatic drugs and potential prolapse of the iris toward the phaco-emulsification incisions. The patient's ophthalmologist has to use modifications in their surgical technique, like use of iris hooks, iris dilator rings, or visco-elastic substances. Discontinuation of α1-adrenoceptor antagonist therapy prior to cataract surgery may not be beneficial.

Drug Interactions

Drug interactions have not been seen when Tamsulosin was used concomitantly with atenolol, enalapril, and nifedipine. Simultaneous use of cimetidine causes a rise, and furosemide causes a fall in the plasma levels of tamsulosin, but within the normal range. Hence dose reduction is not required.

No interactions at the level of hepatic metabolism have been seen during *in vitro* studies with liver microsomal fractions (representative of the cytochrome P_{450}-linked drug metabolizing enzyme system), involving amitriptyline, salbutamol, glibenclamide and finasteride. Diclofenac and warfarin may increase the elimination rate of tamsulosin.

Concurrent administration of other α_1-adrenoceptor antagonists could lead to hypotensive effects.

Over dosage

Acute overdose with 5 mg tamsulosin hydrochloride has been reported. Acute hypotension (systolic blood pressure 70 mm Hg), vomiting and diarrhoea were seen, which were treated with fluid replacement.

If acute hypotension occurs after over dosage, cardiovascular support has to be given. Blood pressure and heart rate could become normal by lying down. Volume expanders and vasopressor drugs could be administered. Renal function has to be monitored and general supportive measures needs to be given. Dialysis is not useful as tamsulosin is highly plasma protein bound.

When large quantities of tamsulosin are involved, gastric lavage may be of useful and activated charcoal and an osmotic laxative, such as sodium sulphate, has to be given to reduce drug absorption.

MATERIALS AND METHODS

Prospective study

Study period – September 2012 to February 2014

Randomised into two groups

Tamsulosin group A / placebo group B

Tamsulosin group; Patients with acute urinary retention after catheterization were given once daily dose of tamsulosin o.4 mg for 4 days.

Placebo group; Patients with acute urinary retention after catheterization were given 4 days of vitamin tablets.

Success criteria for TWOC; Trial without catheter is considered successful if the patient passes urine more than 100 ml with a PVR of less than 200 ml either in USG or actually measured by inserting an IFT.

Inclusion criteria –

- Patients with acute urinary retention due to benign prostatic enlargement

Exclusion criteria –

- AUR due to stricture
- AUR due to carcinoma prostate or carcinoma bladder
- AUR due to hematuria clot retention
- AUR due to neurogenic causes
- AUR in immediate post operative period (any surgery)
- AUR post TURP (due to early or late complications of TURP)
- Any other previous surgery in bladder neck or urethra or prostate
- AUR due to stone disease
- Drug induced AUR
- AUR due to trauma or spinal cord diseases

Patients with acute urinary retention after catheterization are to be given 4 doses of tamsulosin / placebo and given trial without catheter. Trial without catheter is considered successful if the patient passes urine more than 100 ml

with a PVR of less than 200 ml either in USG or actually measured by inserting an IFT.

Follow up

After 4 doses of tamsulosin / placebo, catheter removed and after patient passing urine, actual urine passed is measured and post void is measured using USG or IFT. Patient would be planned for TURP and sent to operation theatre without an indwelling catheter or would be given alpha blockers with or without 5-alpha reductase inhibitors depending on the indication.

Statistical analysis;

Statistical analysis is done using SPSS software.

OBSERVATIONS AND RESULTS ANALYSIS

About 74 patients were selected for the study and randomly allocated in two groups, Group A and Group B, each comprising of 37 patients. Following catheterisation patients in group A were given 4 doses Tamsulosin 0.4 mg in once daily dosing and 8 - 12 hours after the 4^{th} dose, TWOC given. Group B patients were given vitamin tablets for four days and TWOC given same like group A.

Patients selected for both groups were comparable in terms of age group and prostate size.

Age group wise comparison of group A and B

In age group 1 comprising of patients within 51 years to 60 years, there were 18 patients in total (24.3%). In this group there were 7 patients in group A (18.9% within group and 9.5% of total) and 11 patients in group B (29.7% within group and 14.9% of total).

Age group 2 comprises of patients with 61 to 70 years age. In this age group there were 35 patients in total (47.3%). In this age group there were 16

patients in group A (43.2% within group and 21.6% of total) and 19 patients in group B (51.4 % within group and 25.7% of total)

In age group 3 comprising of patients within 71 to 80 years, there were 21 patients (28.4%). In this age group there were 14 patients in group A (37.8% within group and 18.9% of total).

Age group wise both group A an B patients were comparable and statistically no significant difference among both groups.

			GROUP		
			A	B	Total
AGE GROUP Years	1 (51 to 60)	Count	7	11	18
		% within GROUP	18.9%	29.7%	24.3%
		% of Total	9.5%	14.9%	24.3%
	2(61 to 70)	Count	16	19	35
		% within GROUP	43.2%	51.4%	47.3%
		% of Total	21.6%	25.7%	47.3%
	3(71 to 80)	Count	14	7	21
		% within GROUP	37.8%	18.9%	28.4%
		% of Total	18.9%	9.5%	28.4%
	Total	Count	37	37	74
		% within GROUP	100.0%	100.0%	100.0%
		% of Total	50.0%	50.0%	100.0%

Chi-square - 3.479. P= 0.176. This infers that there is no statistical significance exists between the both group with respect to Age distribution.

Chi-square test

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	3.479[a]	2	.176
Likelihood Ratio	3.532	2	.171
N of Valid Cases	74		

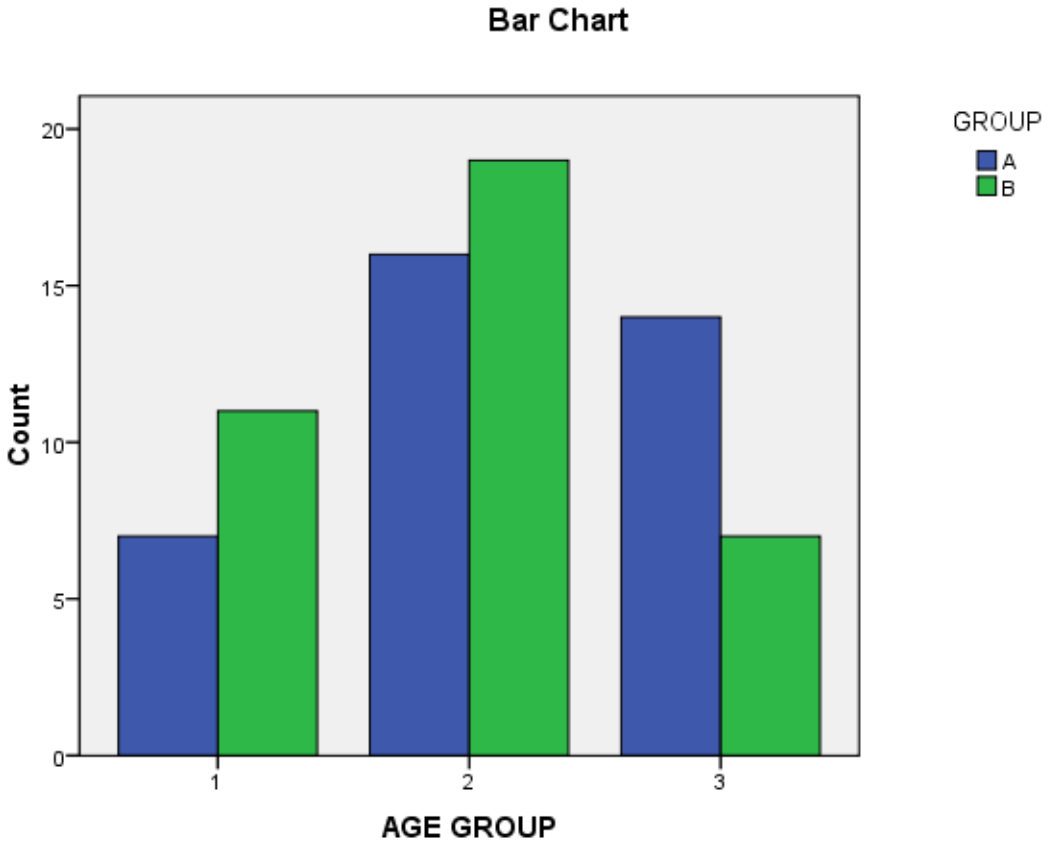

Figure4. Age group wise comparison of group A (blue) and B (green) with group 1 - 51 to 60 years, group 2 – 61 to 70 years, group 3 - 71 to 80 years.

Prostate size wise comparison of group A and group B

Out of the total 74 patients in the study, 22 patients had grade 1 prostate (29.7% of total) and 12 patients were in group A (32.4% within group and 16.2% of total) and 10 patients were in group B (27% within group and 13.5% of total). 38 patients had grade 2 prostate (51.4% of total), out of which 16 were in group A (43.2% within group and 21.6% of total) and 22 were in group B (59.5% within group and 29.7% of total). 14 patients had grade 3 prostate (18.9% of total), out of which 9 were in group A (24.3% within group and 12.2% of total) and 5 were in group B (13.5% within group and 6.8% of total). Both groups were comparable in terms of prostate size as per statistical analysis.

			GROUP		
			A	B	Total
P/R Prostate size Grade	1	Count	12	10	22
		% within GROUP	32.4%	27.0%	29.7%
		% of Total	16.2%	13.5%	29.7%
	2	Count	16	22	38
		% within GROUP	43.2%	59.5%	51.4%
		% of Total	21.6%	29.7%	51.4%
	3	Count	9	5	14
		% within GROUP	24.3%	13.5%	18.9%
		% of Total	12.2%	6.8%	18.9%
	Total	Count	37	37	74
		% within GROUP	100.0%	100.0%	100.0%
		% of Total	50.0%	50.0%	100.0%

Chi square=2.272. P=0.321.

There is no statistical significance exists between both groups with respect to prostate size.

Chi-square test

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	2.272[a]	2	.321
Likelihood Ratio	2.292	2	.318
N of Valid Cases	74		

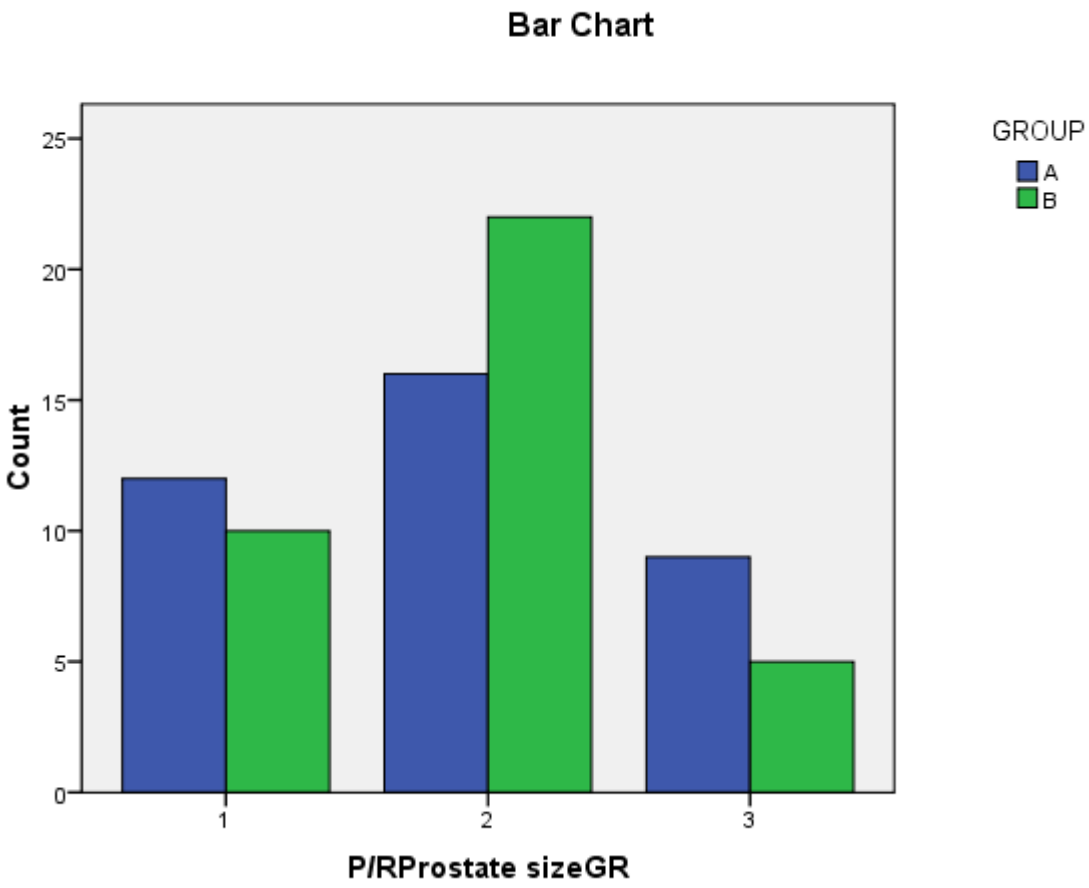

Figure5. Prostate size comparison between Group A (blue) and B (green)

RESULTS OF TWOC

TWOC success comparison between group A and B

			GROUP		
			A	B	Total
TWOC	success	Count	22	12	34
		% within GROUP	59.5%	32.4%	45.9%
		% of Total	29.7%	16.2%	45.9%
	failure	Count	15	25	40
		% within GROUP	40.5%	67.6%	54.1%
		% of Total	20.3%	33.8%	54.1%
	Total	Count	37	37	74
		% within GROUP	100.0%	100.0%	100.0%
		% of Total	50.0%	50.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	5.441[a]	1	.020		
Continuity Correction[b]	4.407	1	.036		
Likelihood Ratio	5.512	1	.019		
Fisher's Exact Test				.035	.018
N of Valid Cases	74				

Chi square= 5.441. P=0.020.

There exists a statistical significance exists between both groups with respect to Trial Without catheter. Among the failure patients (N=40), 37.5% (N=15) patients are in Group A. This indicates that the Group A significantly differ from Group B with respect to Trial without Catheter.

From the below table , There is 3.056 times odds(risk) for Group B comparative to Group A with respect to failure of trial without catheter.

Risk Estimate

		95% Confidence Interval	
	Value	Lower	Upper
Odds Ratio for TWOC (0 / 1)	3.056	1.180	7.909

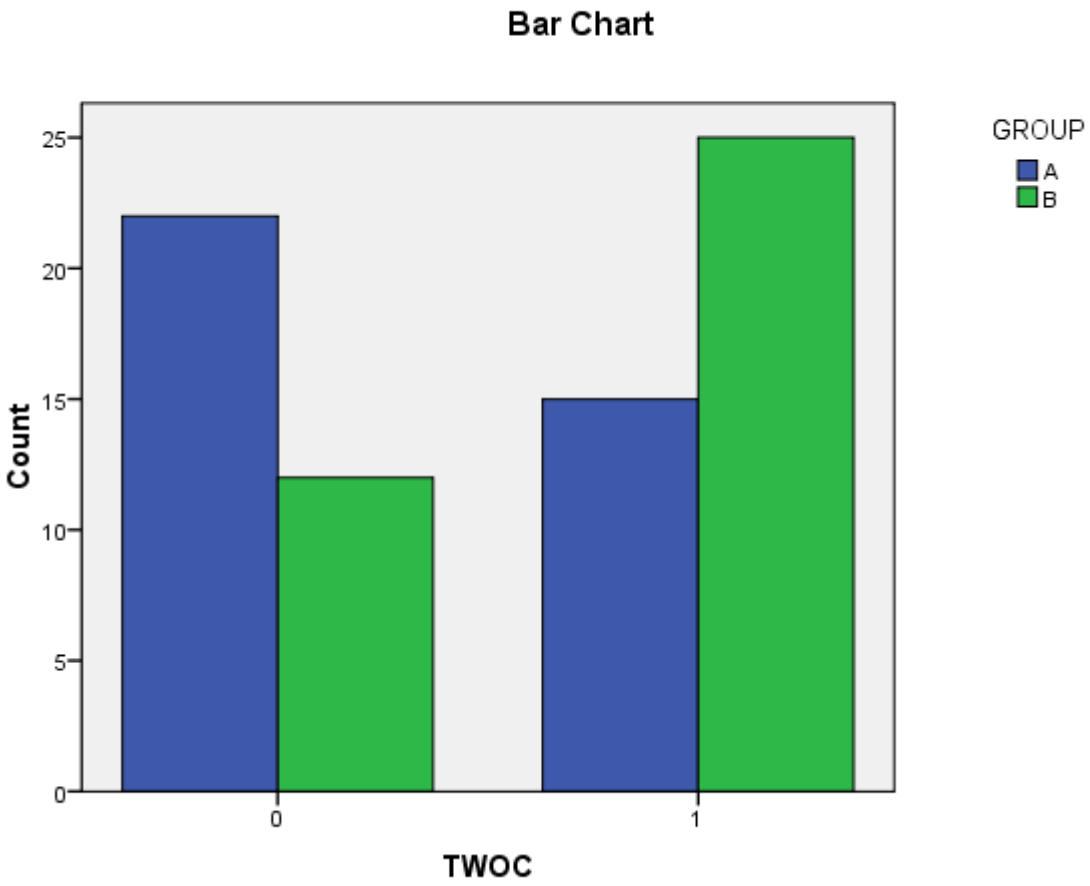

Figure6. TWOC success (0) and failure (1) in group A (blue) and B (green)

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean	Probability value P<0.05 – significant.
AGE YRS	Group A	37	68.08	7.327	1.205	.129
	Group B	37	65.46	7.351	1.208	
Urine drained ML	Group A	37	667.30	155.325	25.535	.404
	Group B	37	711.08	276.825	45.510	
USG Prostate CC	Group A	37	44.19	14.757	2.426	.293
	Group B	37	40.78	12.800	2.104	
Urine passed TWOC ML	Group A	37	185.95	72.589	11.934	.111
	Group B	37	161.35	57.647	9.477	
PVR after TWOC ML	Group A	37	163.51	103.929	17.086	.032
	Group B	37	212.97	90.488	14.876	

Above table shows the following data

1. Average age in group A is 68.06 and in group B is 65.46 with standard deviation of 7.3 years each.

2. Average urine drained after catheterisation for AUR in group A is 667.3 ml with standard deviation of 155.3 ml and in group B is 711.08 with standard deviation of 276.8 ml

3. Average prostate size by USG of the patients taken for study in group A is 44.19cc with standard deviation of 14.76cc and in group B is 40.78 cc with standard deviation of 12.8cc

4. Average urine passed in TWOC in group A is 185.95ml with standard deviation of 72.59ml and in group B is 161.35ml with standard deviation of 57.65ml

5. Average PVR after TWOC in group A is 163.51ml with standard deviation of 103.93 and in group B 212.97ml with standard deviation of 90.49ml.

   The statistical significance (P=0.032) exists only in PVR after TWOC between both the groups.

Analysis of group A results

AGE GROUP and TWOC in group A

Crosstab

			TWOC		
			success	failure	Total
AGE GROUP years	1(51-60)	Count	6	1	7
		% within TWOC	27.3%	6.7%	18.9%
		% of Total	16.2%	2.7%	18.9%
	2(61-70)	Count	10	6	16
		% within TWOC	45.5%	40.0%	43.2%
		% of Total	27.0%	16.2%	43.2%
	3(71-80)	Count	6	8	14
		% within TWOC	27.3%	53.3%	37.8%
		% of Total	16.2%	21.6%	37.8%
	Total	Count	22	15	37
		% within TWOC	100.0%	100.0%	100.0%
		% of Total	59.5%	40.5%	100.0%

In group A, total success rate of TWOC is 59.5% and failure rate is 40.5%.

Age group wise analysis in group A shows the following

1. Age group 1 (between 51 to 60 years) 6 out of 7 patients had successful TWOC (85.7%).

2. Age group 2 (between 61 to 70 years) 10 out of 16 patients had successful TWOC (62.5%).

3. Age group 3 (between 71 to 80 years) only 6 out of 14 patients had successful TWOC (42.9%) and failure (57.1%) is more (8 out of 14) in this age group.

Chi-square= 3.664. P= 0.160. Not significant. Age is not a factor for TWOC success in group A.

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	3.664[a]	2	.160
Likelihood Ratio	3.927	2	.140
Linear-by-Linear Association	3.554	1	.059
N of Valid Cases	37		

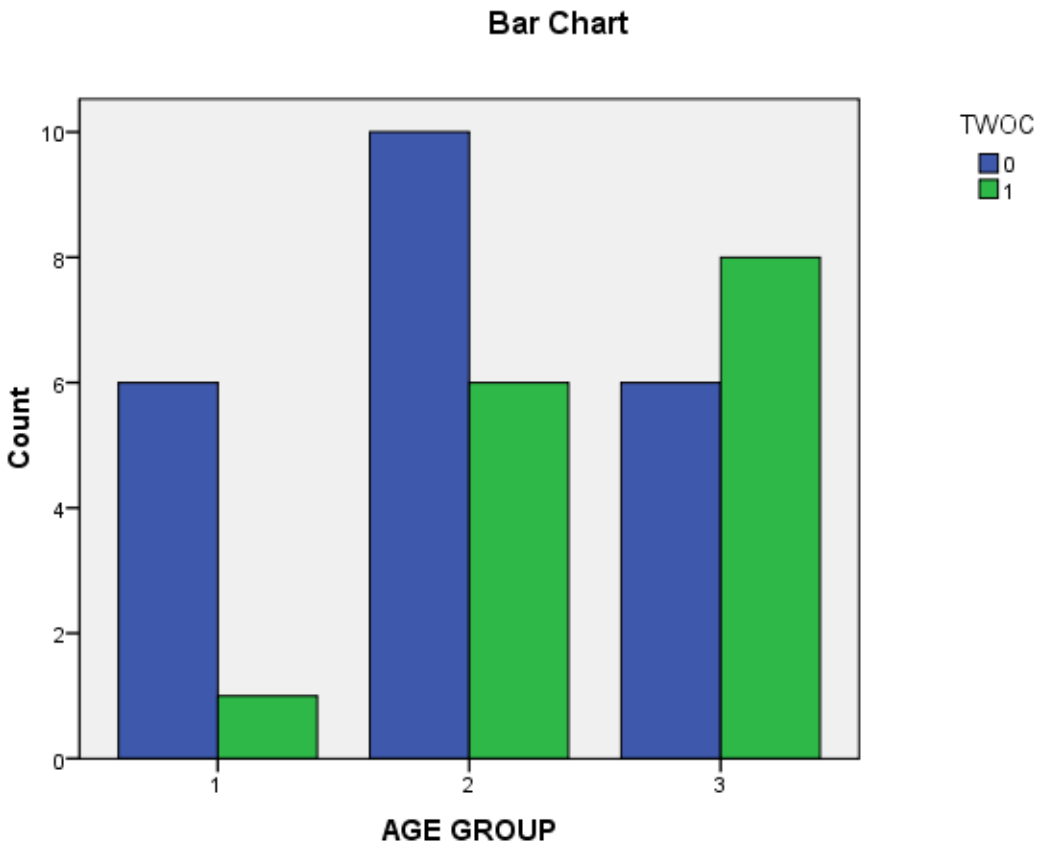

Figure7. Age group wise comparison of TWOC success (blue) and failure (green) in group A patients

Per rectal Prostate size Grade and TWOC in group A

Crosstab

			TWOC		
			success	failure	Total
P/RProstate sizeGR	1	Count	11	1	12
		% within TWOC	50.0%	6.7%	32.4%
		% of Total	29.7%	2.7%	32.4%
	2	Count	9	7	16
		% within TWOC	40.9%	46.7%	43.2%
		% of Total	24.3%	18.9%	43.2%
	3	Count	2	7	9
		% within TWOC	9.1%	46.7%	24.3%
		% of Total	5.4%	18.9%	24.3%
	Total	Count	22	15	37
		% within TWOC	100.0%	100.0%	100.0%
		% of Total	59.5%	40.5%	100.0%

The above results show that in group A

1. In patients with grade 1 prostate, 11 out of 12 had successful TWOC (91.66%).
2. In patients with grade 2 prostate 9 out of 16 had successful TWOC (56.25%).
3. In patients with grade 3 prostate only 2 out of 9 had successful TWOC (22.22%) ie TWOC failure (77.78%) is more in these patients.

Chi-square = 10.409. P value = 0.005. There exists a statistical significant between success and failure patients with respect to prostate size grade.

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	10.409[a]	2	.005
Likelihood Ratio	11.612	2	.003
Linear-by-Linear Association	10.126	1	.001
N of Valid Cases	37		

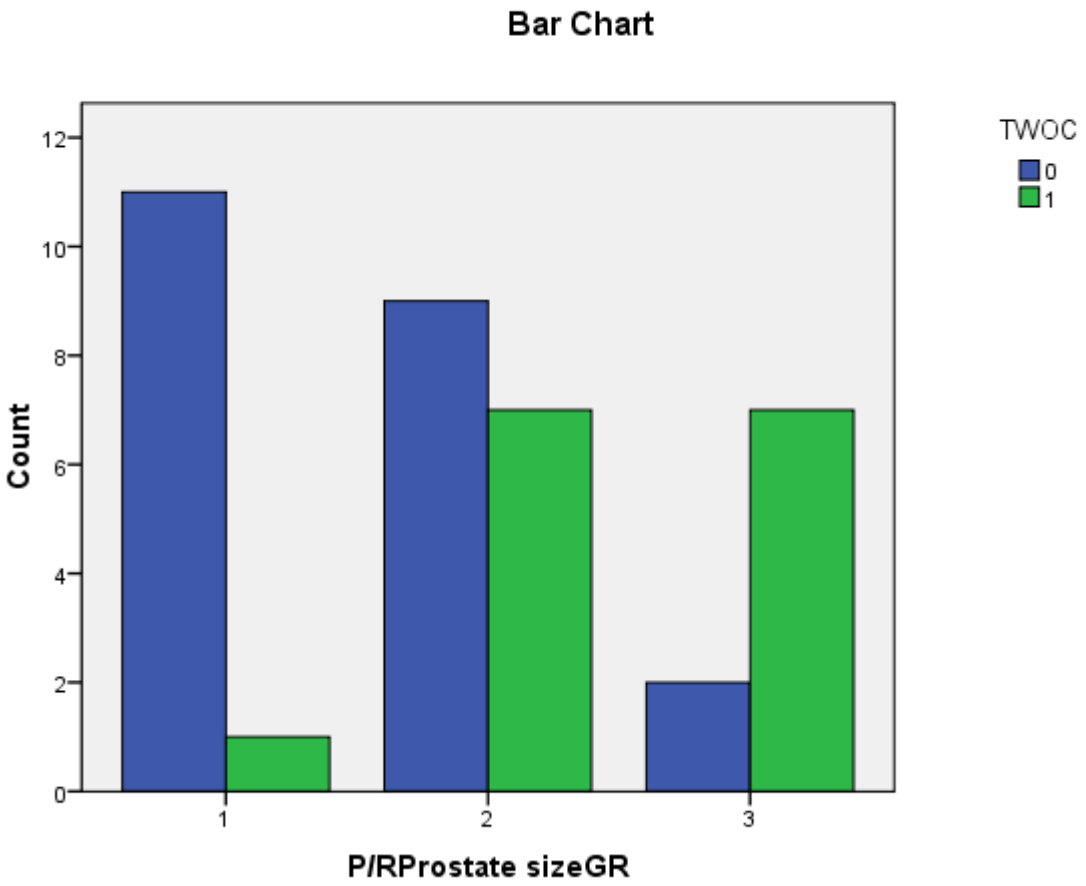

Figure8. Prostate size (grade) wise TWOC success (blue) and failure (green) in group A

Group A Statistics

	TWOC	N	Mean	Std. Deviation	Std. Error Mean	Probability value P<0.05 significant
AGE YRS	Failure	15	71.00	6.414	1.656	.044
	Success	22	66.09	7.374	1.572	
Urine drained ML	Failure	15	673.33	144.996	37.438	.848
	Success	22	663.18	165.224	35.226	
USG Prostate CC	Failure	15	53.07	11.139	2.876	.001
	Success	22	38.14	13.998	2.984	
Urine passed TWOC ML	Failure	15	120.00	42.762	11.041	.000
	Success	22	230.91	50.888	10.849	
PVR after TWOC ML	Failure	15	277.33	37.315	9.635	.000
	Success	22	85.91	45.004	9.595	

From above, The Mean of Age, USG prostate size, Urine passed TWOC & PVR after TWOC are statistically significant between TWOC success and failure.

Analysis of group B results

AGE GROUP and TWOC in group B

Crosstab

			TWOC		
			Success	Failure	Total
AGE GROUP	1(51-60)	Count	3	8	11
		% within TWOC	25.0%	32.0%	29.7%
		% of Total	8.1%	21.6%	29.7%
	2(61-70)	Count	6	13	19
		% within TWOC	50.0%	52.0%	51.4%
		% of Total	16.2%	35.1%	51.4%
	3(71-80)	Count	3	4	7
		% within TWOC	25.0%	16.0%	18.9%
		% of Total	8.1%	10.8%	18.9%
	Total	Count	12	25	37
		% within TWOC	100.0%	100.0%	100.0%
		% of Total	32.4%	67.6%	100.0%

The above results show that success rate of TWOC in group B is 32.4% and TWOC success is uniformly less across all age groups in group B.

Chi- square= 0.487. P= 0.784, Not significant.

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.487[a]	2	.784
Likelihood Ratio	.476	2	.788
Linear-by-Linear Association	.425	1	.514
N of Valid Cases	37		

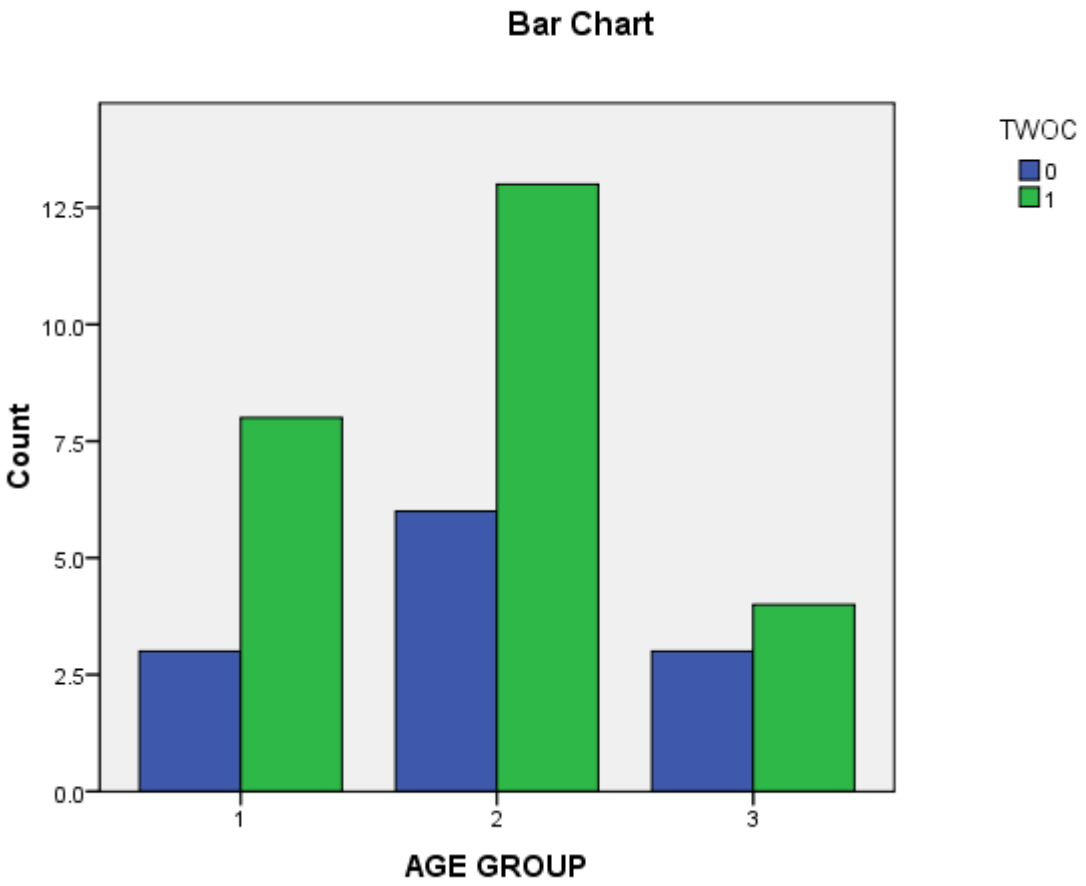

Figure9. Age group wise comparison of TWOC success (blue) and failure (green) in group B patients

Per Rectal Prostate size grade and TWOC in group B

Crosstab

			TWOC		
			Success	Failure	Total
P/RProstate sizeGR	1	Count	6	4	10
		% within TWOC	50.0%	16.0%	27.0%
		% of Total	16.2%	10.8%	27.0%
	2	Count	6	16	22
		% within TWOC	50.0%	64.0%	59.5%
		% of Total	16.2%	43.2%	59.5%
	3	Count	0	5	5
		% within TWOC	.0%	20.0%	13.5%
		% of Total	.0%	13.5%	13.5%
	Total	Count	12	25	37
		% within TWOC	100.0%	100.0%	100.0%
		% of Total	32.4%	67.6%	100.0%

Above results show that in group B patients, TWOC is more successful in patients with grade 1 prostate (6 out of 10). TWOC failure rate is more in patients with grade 2 prostate (16 out of 22) and most in grade 3 prostate (0 out of 5).

Chi square= 6.135 P=0.047. There exists a statistical significant between success and failure patients with respect to prostate size grade.

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	6.135[a]	2	.047
Likelihood Ratio	7.384	2	.025
Linear-by-Linear Association	5.942	1	.015
N of Valid Cases	37		

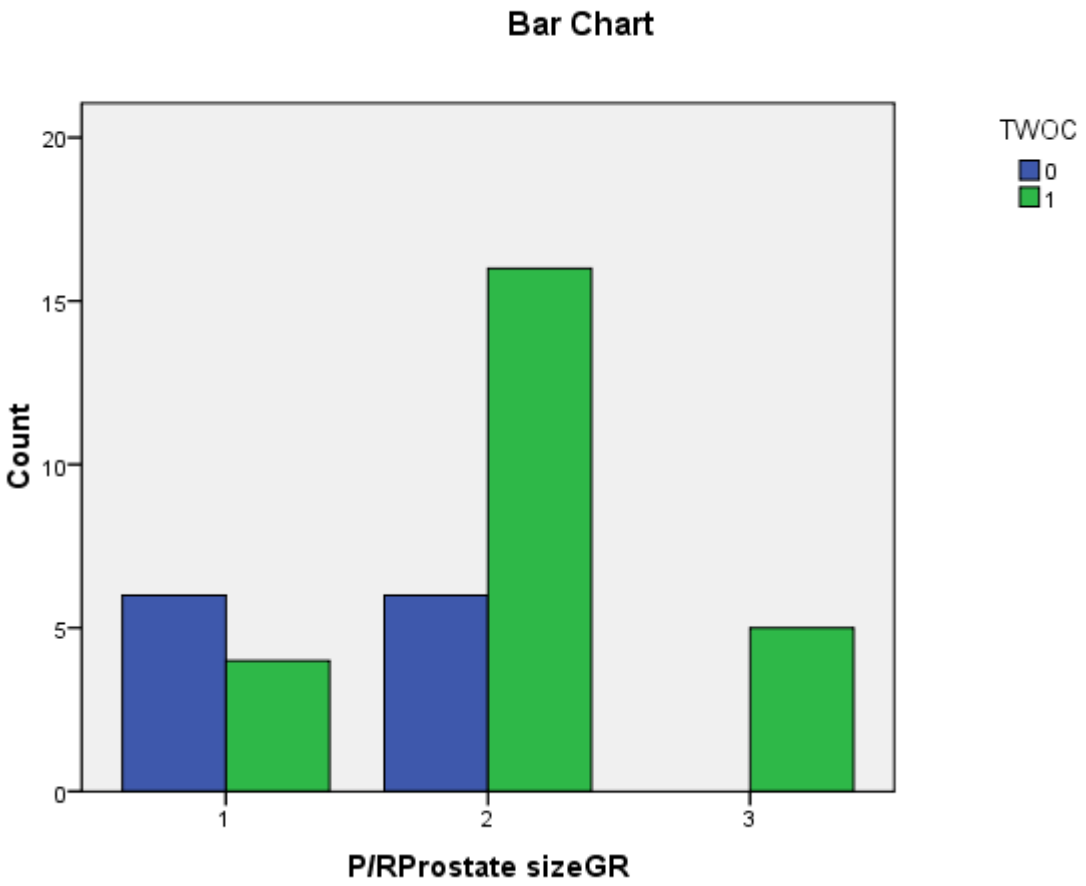

Figure10. Prostate size (grade) wise TWOC success (blue) and failure (green) in group B.

Group B statistics

	TWOC	N	Mean	Std. Deviation	Std. Error Mean	Probability value P<0.05 significant.
AGE YRS	Failure	25	65.08	6.103	1.221	.657
	Success	12	66.25	9.725	2.807	
Urine drained ML	Failure	25	697.20	172.446	34.489	.666
	Success	12	740.00	429.609	124.017	
USG Prostate CC	Failure	25	43.84	13.437	2.687	.034
	Success	12	34.42	8.764	2.530	
Urine passed TWOC ML	Failure	25	137.20	43.159	8.632	.000
	Success	12	211.67	52.194	15.067	
PVR after TWOC ML	Failure	25	269.60	35.995	7.199	.000
	Success	12	95.00	38.730	11.180	

The Mean level of USG Prostate size, Urine Passed TWOC and PVR after TWOC statistically significant between the TWOC success and failure patients in Group B .

DISCUSSION

Management of acute urinary retention (AUR) in patients with benign prostatic hyperplasia (BPH) is trial without a catheter (TWOC). After successful TWOC, as subsequent risk of AUR is high, patient may undergo TURP immediately or electively at a later date. In patients without undergoing any treatment recurrence of AUR is 70% within 1 week of first episode (22). In the past, AUR was an immediate indication for surgery constituting about 25% to 30 % of TURPs (23).

For deciding management, spontaneous AUR needs to be differentiated from precipitated AUR. *Precipitated* AUR is the inability to urinate following a trigger cause. These triggering events may be surgery, insertion of indwelling urinary catheter, anaesthesia, or usage of drugs with sympathomimetic or anticholinergic effects, antihistamines. AUR without a trigger factor are categorised as *spontaneous.* Following an episode of spontaneous AUR, 15% of patients had recurrent AUR, and 75% of these patients underwent surgery. Following an episode of precipitated AUR, only 9% recurrent AUR, and 26% underwent surgery (4) .

Patients undergoing TURP immediately following AUR had significantly higher rates of complications like re-catheterization (13.8%), septicaemia (1.1%) and shock (0.3%) (24).They also had more UTIs, lower tract

symptoms and higher medical expenses. Hence the morbidity like catheter associated urinary tract infection (CAUTI) increased by the presence of an indwelling urinary catheter (25), a trial without catheter is given to patient. When TWOC is successful, patient may undergo surgery electively without catheter associated morbidity. Alpha blockers like tamsulosin increase the TWOC success rate.

Though alpha blockers increase the success rate of trial without catheter, they would not prevent progression of the disease. Patients with significant symptoms of frequency, urgency, voiding symptoms and a prostate size of more than 30 cc on transrectal ultrasound or a PSA level more than 1.5 ng/ml are at high risk of progression of disease (26). For preventing progression of the disease 5 alpha reductase inhibitors (5ARI) are added to alpha blockers. If after taking combination therapy for 3 months there are persistent symptoms of frequency and urgency, antimuscarinics may be added to treat symptoms of over active bladder (26). After a period of time when 5 ARIs have maximal effect (9 months), alpha blockers can be withdrawn and patient may be monitored clinically (26). If patient is symptomatically better, anticholinergics dose reduction or discontinuation may be attempted and patient may be continued on 5ARI monotherapy (26). If the patient still has frequency, urgency or other voiding symptoms as well as erectile dysfunction, then addition of a daily PDE5 inhibitor may be considered (26).

If medical therapy is not tolerated or does not improve symptoms, surgery is considered. According to AUA guidelines surgery is recommended in patients who complain recurrent gross hematuria of prostatic origin, recurrent UTIs, renal dysfuntion secondary to BPH, vesical stones, LUTS refractory to other therapies and refractory or recurrent urinary retention.

Hence alpha blockers are used to increase the TWOC success rate and continued to keep the patient catheter free until he undergoes surgery. Patient may continue alpha blockers in combination with 5ARIs or anticholinergics depending on indications or his option for medical therapy.

In Lucas et al study (27), success rate of TWOC has been increased to 52% and recurrence of AUR significantly reduced by administration of alpha blocker tamsulosin, when compared with success rate of placebo 34%. In our study success rate of tamsulosin group is 59.5% when compared with that of placebo group 32.4%. Patients in placebo group had 3 times more risk for failure of trial without catheter.

In another study by Madhu.S.Agarwal etal (28) in india, following AUR in BPH, TWOC success rate is 70% in patients given tamsulosin, when same is compared with placebo 36%. This success rate with tamsulosin is high when compared with our study (59.5%).

In their study by Hua etal (29), the success rate of TWOC with tamsulosin following an AUR is 61% when compared with control group 28%. But in their study efficacy of treatment was not influenced by volume of prostate. In our study size of the prostate significantly influenced the success rate of trial without catheter both in tamsulosin and placebo group.

In our study there is statistically significant difference in TWOC success in patients given tamsulosin with respect to prostate size. In patients with grade 1 prostate, 11 out of 12 had successful TWOC (91.66%).In patients with grade 2 prostate 9 out of 16 had successful TWOC (56.25%). In patients with grade 3 prostate only 2 out of 9 had successful TWOC (22.22%) ie TWOC failure (77.78%) is more in these patients. (P value = 0.005). In MTOPS study (20) also, it was established that efficacy of alpha blockers were less effective in men with large prostate.

In their study (30), Fitzpatrik etal found that age more than 70 years, prostate size more than 50 cc, severe lower urinary tract symptoms, drained volume at catheterization more than 1000 mL and spontaneous AUR favoured TWOC failure whereas catheterization for more than 3 days and α 1 blockade before TWOC increased success of TWOC. In our study, in patients given tamsulosin, TWOC success rate in 51 to 60 years group is (85.7%) more when compared with same (42.9%) in 71 to 80 years age group but it is not statistically significant. But prostate size influenced the TWOC success in both

tamsulosin and placebo group and that is statistically significant. Patients with grade 3 prostate, TWOC failure is more in both tamsulosin and placebo group, when compared with grade 1 prostate. These patients had higher TWOC success when given tamsulosin (22.22% versus 0%). In our study tamsulosin showed higher success rate of TWOC in patients with larger prostate like grade 2 and grade 3 prostates. TWOC success rate in placebo group is significantly less in these patients. Hence use of tamsulosin in patients presenting with AUR and large prostate increases TWOC success rate.

In our study average post void residual urine after TWOC in patients treated with tamsulosin, is 163.51ml (standard deviation of 103.93) and in placebo group post void residual urine is 212.97ml (standard deviation of 90.49ml). This is statistically significant observation. Hence this study demonstrated prior administration of tamsulosin significantly reduces post void residual urine in trial without catheter.

CONCLUSION

1. Tamsulosin increases the success rate of trial without catheter in patients with acute urinary retention. There are 3.056 times odds (risk) for placebo group comparative to tamsulosin group with respect to failure of trial without catheter.

2. Prostate size has statistically significant influence on trial without catheter. Patients with larger prostate have more chances of failure in trial without catheter in both groups. But tamsulosin increases success rate of trial without catheter in patients with larger prostate.

3. Post void residual urine is significantly reduced by addition of tamsulosin in patients with acute urinary retention undergoing trial without catheter.

4. Tamsulosin increases the success rate of TWOC in older age group patients with AUR due to BPH compared with placebo. But this is not statistically significant in our study.

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PROFORMA

A prospective randomized study comparing the efficacy of tamsulosin and placebo in the management of acute urinary retention secondary to benign prostatic hyperplasia until definitive therapy

Patient Name: KMC/GRH Date

Age: Sex: IP No:

Complaints

History

Strain to void Duration-

AUR duration

Quantity of urine drained after catheterisation

Fever - Present / Absent

Hematuria / Calculuria / Dysuria / Pyuria

LUTS

Obstructive Voiding symptoms

Hesitancy Intermittency Incomplete emptying Straining Postvoid dribbling

Irritative voiding symptoms

Urgency

Frequency day night nocturia

Urge incontinence Incontinence type

Treatment History: Drugs

Surgery details

Catheterisation

Past H/O DM HT TB COPD

Any significant details

General Examination

fever Pallor obesity HT WT

P/A

External Genitalia- Penis

Scrotum

Testis R

L

Per Rectum –

Sphincter tone

Prostate size

Catheterisation details;

Urine drained;

Urine quantity passed after TWOC;

Post void residual after TWOC;

USG;

MASTERCHART-1 GROUP A TAMSULOSIN TWOC SUCCESS CASES

	NAME	AGE YRS	AGE GROUP	KMC/GRH	IP/OP NO	Urine drained ML	P/RProstate sizeGR	USG Prostate CC	Urine passed TWOC ML	PVR after TWOC ML
1	MANI	65	2	GRH	IP10854	550	3	56	200	150
2	MANICKAM	65	2	KMC	IP1324402	1000	2	66	180	140
3	BENUGOMES	65	2	GRH	IP14313	650	3	68	150	160
4	KANNAN	50	1	KMC	IP1322765	500	1	20	200	40
5	ANTHONYSAMY	54	1	GRH	IP11760	650	1	22	250	50
6	MOHANAN	58	1	KMC	IP1306432	700	1	32	300	100
7	MOHAMMED	60	1	KMC	IP1304250	650	2	40	300	150
8	SUBRAMANI	60	1	GRH	IP21817	650	1	30	200	50
9	PERUMAL	60	1	GRH	IP23179	600	1	28	200	100
10	EKAMBARAM	65	2	KMC	IP1302594	500	1	25	300	50
11	ABDULLAH	65	2	GRH	OP5631/13	500	1	28	200	70
12	PONNUSAMY	65	2	GRH	IP854	540	1	28	200	30
13	KARTHIKEYAN	66	2	GRH	IP1266	650	1	20	250	30
14	VENKATESAN	66	2	KMC	IP132634	800	2	38	150	100
15	RAMASAMY	68	2	GRH	IP114528	800	1	30	250	100
16	CHINNAPAIYAN	70	2	GRH	IP13307	600	2	38	200	70
17	NATARAJ	72	3	KMC	IP1331368	700	2	42	300	80
18	ABDUL SATTAR	75	3	KMC	OP1174/12	1000	1	48	300	30
19	SUNDARAMOORTHI	75	3	GRH	IP110083	500	2	47	300	150
20	KUMARASAMY	75	3	GRH	IP9922	450	2	40	250	80
21	LOGANATHAN	77	3	GRH	IP9689	600	2	36	200	130
22	BALAKRISHNAN	78	3	KMC	IP27006	1000	2	57	200	30

MASTER CHART -2 GROUP A TAMSULOSIN TWOC FAILURE CASES

	NAME	AGE YRS	AGE GROUP	KMC/GRH	IP/OP NO	Urine drained ML	P/RProstate sizeGR	USG Prostate CC	Urine passed TWOC ML	PVR after TWOC ML
1	DURAIRAJ	60	1	GRH	IP114304	500	1	36	80	350
2	GANESAN	61	2	KMC	IP1304074	900	3	62	120	240
3	KARUPPAIAH	63	2	GRH	IP112586	600	2	58	100	300
4	SUBRAMANI	65	2	GRH	IP432	800	3	70	200	250
5	MURUGAPILLAI	70	2	GRH	IP114063	700	2	42	100	300
6	MUNIYANDI	70	2	KMC	IP1330740	550	2	39	100	280
7	KANNAIH	70	2	KMC	IP1324365	800	3	65	120	300
8	JOHNSON	71	3	GRH	IP21272	700	2	50	100	240
9	KRISHANAN	73	3	KMC	IP1387871	800	3	60	100	350
10	MOHAMMED BUHARI	74	3	GRH	IP24484	800	3	60	100	270
11	RAMASAMY	75	3	GRH	IP25184	500	2	42	100	240
12	EKAMBARAM	76	3	GRH	IP12304	700	2	40	80	290
13	JANAKIRAMAN	77	3	GRH	IP111552	450	2	48	200	250
14	RAJ	80	3	GRH	OP108/14	500	3	60	100	250
15	CHITHIRAI	80	3	KMC	IP1304241	800	3	64	200	250

MASTER CHART-3 GROUP B PLACEBO TWOC SUCCESS CASES

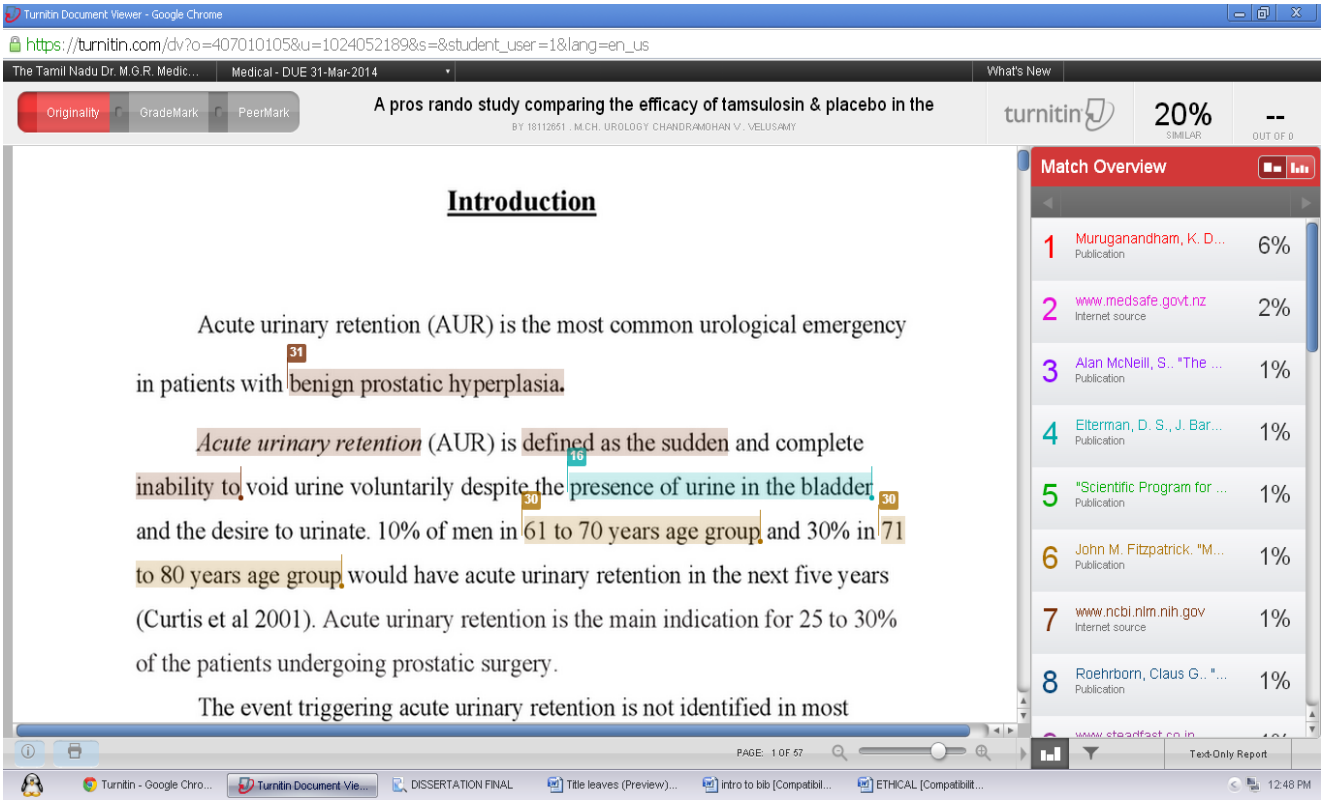
	NAME	AGE YRS	AGE GROUP	KMC/GRH	IP/OP NO	Urine drained ML	P/RProstate sizeGR	USG Prostate CC	Urine passed TWOC ML	PVR after TWOC ML
1	MUNIYAPPAN	49	1	GRH	OP20704/13	600	1	20	150	50
2	PANCHAVARNAM	55	1	GRH	IP9675	500	1	26	200	100
3	CHINNAKANNAN	60	1	KMC	IP1304245	600	2	48	250	100
4	SUBRAMANI	61	2	KMC	IP28289	2000	2	30	200	70
5	RAMU	65	2	KMC	IP1302245	700	1	28	200	70
6	NALLU	65	2	GRH	IP12289	580	1	28	250	100
7	BALAN	65	2	KMC	IP1325920	600	2	45	100	200
8	FRANCIS	69	2	GRH	IP114580	850	2	39	300	100
9	PERUMAL	70	2	GRH	IP110091	400	1	30	250	100
10	RENGANATHAN	75	3	KMC	IP1330592	450	2	38	200	100
11	KANNAN	76	3	GRH	IP111989	1000	1	36	200	50
12	ANNAMALAI	85	3	GRH	IP25086	600	2	45	240	100

MASTER CHART-4 GROUP B PLACEBO TWOC FAILURE CASES

	NAME	AGE YRS	AGE GROUP	KMC/GRH	IP/OP NO	Urine drained ML	P/RProstate sizeGR	USG Prostate CC	Urine passed TWOC ML	PVR after TWOC ML
1	KUMAR	55	1	KMC	IP1304710	1000	2	45	200	350
2	MOHAMMED	55	1	KMC	IP1307530	500	2	40	100	250
3	BEEMLAL	55	1	KMC	OP162/14	400	1	26	80	250
4	CHANDRAN	58	1	GRH	IP13788	500	1	26	100	250
5	VEERAMUTHU	59	1	GRH	IP24732	600	1	26	100	300
6	RADHAKRISHNAN	60	1	GRH	IP114289	550	2	45	100	300
7	POONGAVANAM	60	1	GRH	IP12073	500	1	28	170	220
8	ARUMUGAM	60	1	KMC	IP1323339	650	2	34	160	280
9	EASURAJAN	63	2	GRH	IP110591	800	3	68	200	300
10	ABDUL AZEEZ	63	2	GRH	IP427	1000	2	38	100	300
11	THAMARAO	65	2	GRH	IP725	600	2	40	200	250
12	DEVARAJAN	65	2	KMC	IP1330756	700	2	44	100	220
13	VEERAN	65	2	GRH	IP22086	700	2	40	150	250
14	RAHUMAN	65	2	GRH	IP565	780	2	58	100	250
15	GANESAN	68	2	GRH	IP8445	800	2	40	200	230
16	VENKATESAN	68	2	GRH	IP10377	600	3	62	100	270
17	THANGAVEL	70	2	GRH	IP114062	1000	2	40	200	250
18	MUTHUKRISHNAN	70	2	KMC	IP1306101	1000	2	38	150	250
19	MANI	70	2	KMC	IP1324095	700	3	58	100	250
20	GANESAN	70	2	GRH	IP21234	800	3	58	100	300
21	YASEEN	70	2	GRH	IP1105	600	2	40	120	280
22	RAMAIAH	72	3	GRH	IP112584	700	3	80	200	360
23	VARADHARAJAN	72	3	GRH	IP23514	750	2	38	100	280
24	MASTHANRAO	73	3	GRH	IP10839	500	2	44	150	230
25	RAMANUJAM	76	3	KMC	IP1320923	700	2	40	150	270

ABBREVIATIONS

AUR	Acute Urinary Retention
TWOC	Trial With Out Catheter
TURP	Trans Urethral Resection of Prostate
BPH	Benign Prostatic Hypertrophy
5αRI/5ARI	5 alpha Reductase Inhibitors
TRUS	Trans Rectal Ultra Sound
PSA	Prostate Specific Antigen
Q max	Maximal urinary flow rate
IPPS	International Prostate Symptom Score
AUA	American Urology Association
LUTS	Lower Urinary Tract Symptoms
UTI	Urinary Tract Infection
CAUTI	Catheter Associated Urinary Tract Infection
OAB	Over active Bladder
NSAIDS	Non-Steroidal Anti-Inflammatory Drugs
BOO	Bladder Outlet Obstruction
BP	Blood Pressure
PVR	Post Void Residual urine
USG	Ultra SonoGram
IFT	Infant Feeding Tube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Introduction
Acute urinary retention (AUR) is the most common urological emergency in patients with benign prostatic hyperplasia.
Acute urinary retention (AUR) is defined as the sudden and complete inability to void urine voluntarily despite the presence of urine in the bladder and the desire to urinate. 10% of men in 61 to 70 years age group and 30% in 71 to 80 years age group would have acute urinary retention in the next five years (Curtis et al 2001). Acute urinary retention is the main indication for 25 to 30% of the patients undergoing prostatic surgery.
The event triggering acute urinary retention is not identified in most
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CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "A Prospective randomized study comparing the efficacy of tamsulosin and placebo in the management of acute urinary retention secondary to benign prostatic hyperplasia until definitive therapy"- For Dissertation purpose submitted by Dr.V.Chandramohan, M.Ch Genito Urinary Surgery, PG Student, KMC, Chennai-10.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

GOVT. KILPAUK MEDICAL COLLEGE
14 SEP 2012
Kilpauk, Chennai-10.

CHAIRMAN, 14/9/12
Ethical Committee
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