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DIFFERENCE IN HISTOPATOLOGICAL AND VASCULAR INDICES BETWEEN LATERAL LOBE AND INTRAVESICAL PROSTATIC PROTRUSION IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA REFRACTORY TO MEDICAL MANAGEMENT.

Urology

KEYWORDS: Benign prostatic hyperplasia , Lateral lobe , Intravesical prosatatic protrusion , resistive index, histopathological difference.

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ABSTRACT

Introduction and objectives: Benign prostatic hyperplasia (BPH) is the most common neoplasm affecting ageing male population worldwide. Introduction of combination medical therapy has revolutionized in the management of symptomatic benign prostatic hyperplasia. It has been observed that the alpha blockers are relatively ineffective in patient with intravesical prostatic protrusion (IPP). This study is being design to evaluate whether there exist any difference of vascular parameters and histopathology between lateral lobe and IPP.

Methods: All symptomatic BPH patients attending the urology OPD from February 2015 to Oct. 2016 are included in this study who are refractory to medical management and those with complication of bladder outflow obstruction due to BPH with IPP. Patients were evaluated with doopler ultrasound and resected specimens were send separately for histopathological examination with the pathologist blinded regarding the nature and origin of specimen.

Results: 28 patients qualified included in the study. Ultrasonographically estimated average prostatic volume of the patients in our study is 59.68 gm (SD 27.59) ranging from 26 -146 gm, mean invesical prostatic protrusion is 19.11 mm (SD 6.511) ranging from 9-34 mm comprising. Mean intraprostatic resistive index measured by color doppler of lateral lobe is 0.7132 (SD 0.139 and mean SE 0.026) and Intravesical prostatic protrusion mean resistive index is 0.642 with SD 0.117 in our study patients. On T- test we observed a statistically significant difference between resistive index of lateral lobe and intravesical prostatic protrusion (p value 0.045 , 95% CI 0.00156 – 0.13987) . Histopathology of 12 patients showed a difference with hyperplasia predominat of stromal componant in intravesical prostatic protrusion (IPP). In intravesical prostatic protrusion (IPP), stromal hyperplasia with or without chronic inflammatory cells more commonly seen in 11 (39%) patients and in 1 (3%) patient mainly chronic inflammatory changes were observed whereas this finding was absent in lateral lobe specimens. On statistical analysis using Chi-Square test this difference is statistatically significant (p value <5%).

Conclusion: Some degree of cellular abnormality as well as alteration of intraprostatic vascular parameters were observed in our study. However it needs to be confirmed in randomized control study involving large number of population, having symptomatic benign prostatic hyperplasia with intravesical prostatic protrusion who failed medical therapy.

Introduction:

Lower urinary tract symptoms (LUTS) develop due to benign prostatic enlargement causing bladder outlet obstruction [1]. In benign prostatic enlargement prostatic growth does not occur homogeneously and often prostatic protrusion into the bladder occurs, resulting in morphological changes [2]. It has been suggested that a prostatic volume with a high grade protrusion causes more severe voiding dysfunction [3- 5]. It was also reported that along with voiding symptoms, increased intravesical prostatic protrusion (IPP) can affect the storage symptoms due to stimulation of bladder by protrusion [6,7]. Park HY et al suggested that increasing grade of IPP worsens voiding symptoms and in such situation the response to treatment with alpha blockers is not satisfactory (8). Patient with benign prostatic hyperplasia (BPH) causing bothersome lower urinary tract symptoms (LUTS) usually seek medical advice. There are various options in the management of BPH like watchfull waiting, medical therapy, conventional surgical therapy, and minimally invasive therapy. Recently, various lasers like Holmium , KTP, Diod , Thulium, have become an established mode of surgical treatment options for LUTS secondary to BPH. However, transurethral resection of the prostate (TURP) is still considered the gold standard surgical therapy for BPH [9-11]. It has been observed that the alpha blockers are relatively ineffective in patients with intravesical prostatic protrusion [12,13]. This study is being designed to evaluate whether there exists any difference of intraprostatic vascular parameters like resistive index (RI) and histopathological (HPE) findings between lateral lobes and intravesical prostatic protrusion which may influence the outcome of medical management. The findings further corrected with markers of inflammation namely neutrophil to lymphocyte ratio (NLR).

Material and method:

All new symptomatic benign prostatic hyperplasia (BPH) patients attending the Urology OPD from February 2015 to Oct. 2016 on 28 who are refractory to medical management for at least 3 months of therapy and those with complication of bladder outflow obstruction due to benign prostatic hyperplasia with intravesical prostatic protrusion during the medical treatment were included in this study. Exclusion criteria included - (i) satisfactorily responders to combination therapy (ii) Untreated urinary tract infection (iii) coexisting prostatitis and prostatic calcification (iv) Any digital rectal examination abnormality (v) Patient with neurovasical dysfunction. All together 28 patients qualified for the study. Patients were evaluated with clinical history including international prostatic symptoms score (IPSS), physical examination and laboratory investigation like Urine culture and sensitivity, Hb%, TC, DLC,ESR, Platelet count, RBS, Blood urea, Serum Creatinine, Sodium, Potassium, Serum PSA, LFT, Neutrophil to lymphocyte ratio (NLR) , Chest x ray, ECG and Trans Abdominal Doppler USG KUB with grading of IPP (Grade I < 5 mm , Grade II 5-10 mm and Grade III > 15 mm) with resistive index (RI) of both lateral lobe and IPP.(Ultra sonography machine used was – Voluson E 8). During the procedure bladder volume was kept at least 150 ml.

During transurethral resection of prostate using monopolar current (schiller, Meditom DT 400P) intravesical prostatic protrusion was resected first and preserved in a container containing formalin separately. Then lateral lobes were resected and preserved in an another separate container.The two container were labeled 1 and 2

and sent for histopathological examination with the pathologist blinded regarding the nature and origin of the specimen (Single pathologist examined all samples ,H & E stain, under high power). All the results were analyzed using SPSS (Paired t test and Chi-squer test).

Results:

We studied a total of 28 patients. All patients underwent transurethral resection of prostate except one patient with 146 gm prostate who underwent open prostatectomy where IPP and lateral lobes were marked and sent for histopathological examination separately. Age of the patients in our study ranges from 40 – 85 years with a mean of 66.79 years (SD -9.51) . In our study mean duration of treatment is 15.94 months (Ranges 3-48 months, SD 12.81) . 26 patients were given trial of voiding without catheter average 2.01 times (SD 0.81) with a ranges of 0-4 times , after 2 weeks of medical therapy . 2 patients were without perurethral catheter whose preoperative IPS Score were 32 and 28 respectively. Average serum creatinine in our study was 1.15 mg/dl (SD – 0.482) ranging from 0.60 -3.04 mg/dl. In our study mean neutrophil to lymphocyte ratio is 3.40 (SD 2.58) . Mean prostate specific antigen (PSA) is 6.08 ng/ml (SD 8.114) , 12 patients PSA was > 4 ng/ml and TRUS guided 12 core biopsy were done in those patients to exclude prostatic carcinoma. During transabdominal ultrasonography bladder volume was kept at least 150 ml. Average prostatic volume of the patients in our study is 59.68 gm (SD 27.59) ranging from 26 -146 gm, bladder wall thickness range from 3.8-7 mm with a mean of 5.57 mm (SD 1.08) and mean invesical prostatic protrusion is 19.11 mm (SD 6.511) ranging from 9-34 mm comprising Grade I : Nil , Grade II : 2 , Grade III : 26 patients . Mean resistive index of lateral lobe is 0.7132 (SD 0.139 and mean SE 0.026) and Intravesical prostatic protrusion mean resistive index is 0.642 with SD 0.117 in our study patients. On T- test we observed a statistically significant difference between resistive index of lateral lobe and intravesical prostatic protrusion (p value 0.045 , 95% CI 0.00156 – 0.13987) . 27 patients underwent tran transurethral resection of prostate (TUR-P) using monopolar current (schiller, Meditom DT 400P) and one had undergone open prostatectomy as prostate volume was 146 grams in that patients.

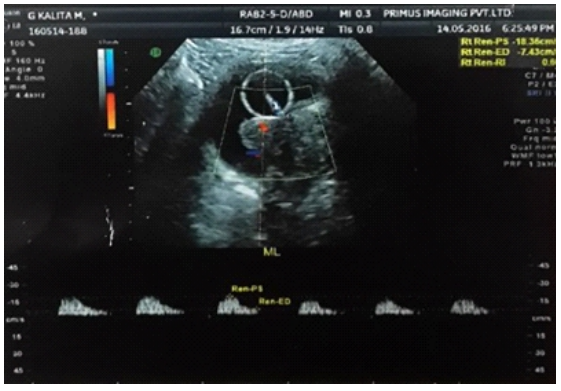

Figure 1: Transabdominal Doppler ultrasonograpy image showing intravesical prostatic protrusion in saggital view.

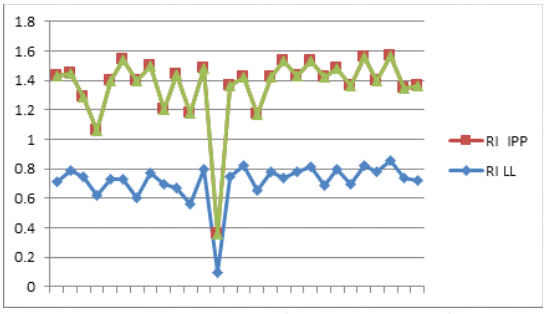

Figure 2 : Line chart showing RI (Both LL and IPP)difference in various patient.

All patients histopathological (HPE) reports were analyzed (Figure 3 and 4). No difference in HPE was found in 16 (57%) patients whereas HPE of 12 (43%) patients showed a difference with hyperplasia predominat of stromal componant in IVPP. Lateral lobes contains glandular hyperplasia with or without chronic inflammatory cells in all patient whereas such isolated glandular hyperplasia present in only 16 (57%) patients of IPP group. In IPP stromal hyperplasia with or without chronic inflammatory cells more commonly seen in 11(39%) patients and in 1 (3%) patient mainly chronic inflammatory changes were observed whereas this finding was absent in lateral lobe specimens. On statistical analysis using Chi-Square test this difference is statistatically significant (p value <5%).

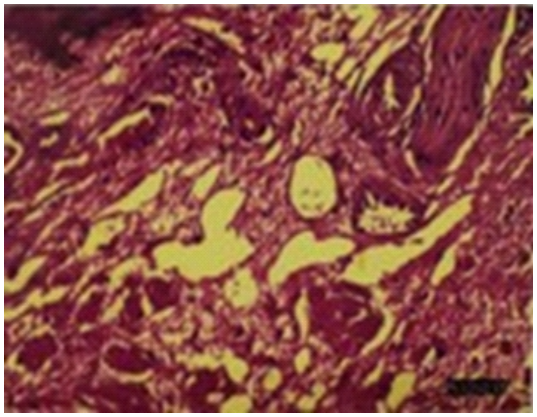

Figure 3 : Histopathological (H & E) image of lateral lobe.

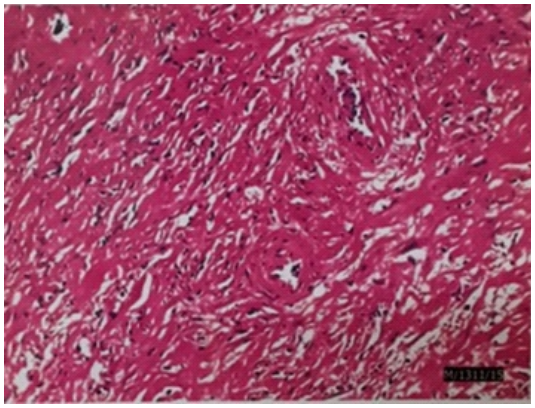

Figure 4 : Histopathological (H & E) images of intravesical prostatic protrusion.

In our study we found that there is positive correlation(correlation coefficient 0.122) between prostatic voume and bladder wall thickness which is not statistically significant (p value 0.537). Intravesical prostatic protrusion and bladder wall thickness are positively correlated (correlation coefficient 0.522) which is statistically significant (p value 0.004). In our study we have also observed negative correlation (correlation coefficient -0.074) between intravesical prostatic protrusion and neutrophil to lymphocyte ratio which is statistically not significant (p value 0.707). Prostatic volume and prostate specific antigen are positively correlated (correlation coefficient 0.355) but statistically not significant (p value 0.064)in our study.

Discussion:

Theoretically, if voiding symptoms are the main symptoms in BPH, an alpha-1 receptor antagonist is considered to be a treatment of first choice and combination of alpha -1 blocker while dutesteride is addrd to it , usually for voluminous prostates. However, all patients couldn't be treated satisfactorily with medical therapy alone. There are several causes of unsatisfactory medical treatment in LUTS due to BPH. Among them, IPP has been identified as one of the causes for

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unsatisfactory response to medical management. IPP is caused by invegination of the lateral lobes and the median lobe and the protrusions of these enlarged lobes causes voiding symptoms [14]. IPP is a useful predictor for successful voiding trial after acute urinary retention [15]. However, most such reports focused on the length of IPP and its correlation to voiding symptoms. IPP is significantly correlated with greater obstructive symptoms, increased prostate volume, transitional zone index , increased post void residual urine and decreased maximum flow rate (Qmax) in uroflometry [16]. Lee JM et al observed that in patient with BPH with IPP, there is no significant reduction in the quality of life (QoL) score after 8 weeks of medication [6]. Yu Mi Seo showed that Alfuzosin may be less effective in improving symptom scores, post void residual (PVR), and Qmax in the treatment of LUTS due to BPH in the presence of IPP [17]. Hee Young Park et al. in their study observed that Tamsulosin is more effective in improving patient symptom scores and Qmax in patients with mild IPP than in those with moderate or severe IPP[13]. Considering the uniformity in vascular flow, It is presumed that resistive index is same in all parts of normal prostates. Various studies have shown that at bladder volume >100 ml, measuring of IPP , prostatic volume , resistive index are equivalent both in transabdominal and transrectal ultrasonography [18,19]. Kojima et al. demonstrated that the RI value of patients with normal prostatic volume was significantly lower than BPH ($P < 0.0001$) [20]. In BPH, the blood flow between the peripheral zone and transitional zone of the prostate are pressed leading to marked rise of RI of the capsular arteries [21]. However, this increase in resistive index in BPH may not always be due to an increased transitional zone index (TZI ,TZI=TZ volume/TPV) and presumed circle area ratio (PCAR) and some other causes like advanced arteriosclerosis occurring with increasing age, was proposed to be the predominat cause for raise in RI [22,23] . Moreover, the exact mechanism leading to elevated RI in BPH is still unclear [24]. Hayami et al.observed that RI is a reliable indicator for predicting the ratio of glandular lumen to stromal elements in patient with BPH. These values are useful indicator for predicting the therapeutic response to treatment options [25]. Turgut et al. performed power dopler ultrasonogaphy and resistive index evaluation to differentiate prostate cancer from BPH. Though results were statistically insignificant ($P > 0.05$) they have reported that the mean RI for cancer cases was slightly lower than the mean RI value for benign conditions. [26]. Osama Abdelwahab et al. observed that there was a significant difference in RI of both left and right capsular arteries between the obstructed and non obstructed groups ($P < 0.001$). This increased in RI is significantly correlated with obstructive patterns of flow rates . They concluded that there was a significant statistical value between RI of both right and left capsular arteries and urethral arteries when correlated to IPSS, uroflowmetry results and prostate volume although there was not significant difference in mean RI among the individual arteries [27]. In preliminary reports of our study among 28 patients, we found that in patients with BPH having IPP who are refractory to at least 3 months medical treatment with alpha 1 a blocker and dutasteride, were associated with statistically significant difference of resistive index and histopathologial findings between lateral lobe and IVPP.

Conclusion:

Benign prostatic hyperplasia is the most common neoplasm affecting ageing male population worldwide. Although surgical modality is the primary form of treatment of let introduction of alpha blocker and 5 alpha reductase inhibitor has revolutionized in the management of symptomatic benign prostatic hyperplasia. It has been observed that the alpha blockers are relatively ineffective in patient with intravesical prostatic protrusion. Some degree of cellular abnormality as well as alteration of intraprostatic vascular parameters were observed in our study. However it needs to be confirmed in randomized control study involving large number of population, having symptomatic benign prostatic hyperplasia with intravesical prostatic protrusion who failed medical therapy.

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