



Research Article

## EVALUATION OF THE CHANGES IN LEVEL OF 5- $\alpha$ REDUCTASE, TESTOSTERONE & DIHYDROTESTOSTERONE IN PATIENTS OF VATASTHEELA WITH SPECIAL REFERENCE TO BENIGN PROSTATIC HYPERPLASIA UNDERGOING AYURVEDIC MANAGEMENT

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### ABSTRACT

The vitiated *Apanvayu* when takes seat in the space between *guda* (rectum) and *Basti* (urinary bladder), produces firm and elevated stone like growth. This growth in turn produces obstruction to passage of faces, urine and flatus and *Adhmana* (produces distension) and leads to intense pain in suprapubic region.

'kd`uekxZL; cLrs`p ok;qjUrjekfJr%A vCVhykor~ ?kua xzfUFk djksR;pyeqUure~AA fo.ew=kfuyI`x`p r=k/ekua p tk;rsA osnuka p ijk cLrkS okrk"Bhysfr rka fonq%AA ¼lq0m0 59@9&10½ In *Vatavyadhi Nidan*, *Acharya Sushruta* also explained the disease *Vatashitala* as one of *Vatavyadhi*. v"Bhyko)ua xzfUFkew/oZek;ueqUure~A okrk"Bhyk fotkuh;kr~ cfgekxkZojksf/kuhe~AA ¼lq0fu0 1@10½ In *Vatashila* there is a growth in between rectum and urethra which leads to symptoms like sanga etc. therefore the disease BPH correlates closely to *Vatashila*.

BPH is a slow progressive disease and the management of which is achieved by either conservative or surgical methods. Prostatectomy i.e. surgical removal of prostate gland is a golden treatment for BPH but it is associated with many complications like post operative morbidity, impotence, retrograde ejaculation etc. However, following surgery, despite the relief of obstruction, not all patients are relieved of their symptoms. The incidence of voiding dysfunction and associated symptoms after prostatectomy for benign disease has been reported to be 5 to 35% [Emberton *et al* 1996]. Apart from that a cumulative probability for reoperation has been estimated up to 15% within 8-10years. Hence, considering above facts, the conservative methods from both modern and *Ayurveda* point of views are seems to be more feasible.

In *Ayurvedic* classics, several drugs in different dosage forms and combinations have been advocated for treating *Mutrakrichchhra* or *Mutraghat*. After referring several classical texts, following drugs have selected for present study for oral administration. The selected drugs are: - *Varuna* stem bark (*Crataeva nurvala*), *Shigru* stem bark (*Moringa olerifera*) and *Goksuru* fruit (*Tribulus terrestris*) & *Shodhit Shilajit*. These drugs (*Varuna*, *Shigru*, *Goksuru* and *Shilajit*) have been used in combination in the form of *ghansatva* filled in capsules for better compliance. *Basti* therapy has also given by using *Dashmool Kwatha* with *Narayan Tail* (for *Niruha basti*) and *Narayan Tail* (for *Anuvasan Basti*). The case described in this article is treated with the same guideline as described in *Ayurveda* and a satisfactory result were obtained. Though 30 cases are not enough to prove the efficacy, author has tried to share his experience through this article to state that *Ayurvedic* treatment for *Benign Prostatic Hyperplasia* is very effective and enhances the quality of life of patient without creating any side effects or with minimal side effects.

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### INTRODUCTION

*Ayurveda* is a comprehensive scientific system of medicine developed through ancient wisdom, clinical experiences and experimentations.

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Exploration and discrimination of this knowledge throughout the world can be done only by scientific studies on different parameters. Since time immemorial, *Ayurveda* has been showing the ideal way of living, which promises a disease free, happy and long life. *Ayurveda* has a unique speciality in the field of *Shalya Tantra* in which *Acharya Sushruta* explained the most sophisticated principles of surgery as well as conservative management of various diseases.

Prostate is an accessory gland of male reproductive system, the secretion of which adds bulk to the seminal fluid along with other glands, with no known endocrine function and located deep within the confines of male pelvis below the neck of urinary bladder. The peculiarity of the prostate gland is that it enlarges as the age advances and causes the features of Bladder Outlet Obstruction (BOO), where as the most of the glands / organs of the body other than the prostate gland show regression with advancement of age.

In all *Ayurvedic* texts, various *Mootrarogas* and their management have described. *Vatasthila*, and *Mootragranthi* resembles obstructive uropathy due to enlarged Prostate on the basis of symptomatology. *Vatasthila* is a condition in which the *Apana Vayu* due to vitiation produces mobile, elevated and intensely painful glandular swelling which obstructs the passage of urine and faces. On the basis of this description *Vatasthila* seems to be more closely related with benign Prostatic Hyperplasia.

As per the *Samprapti* (etiopathogenesis) of *Mootraghata*, there is deranged function of *Vata Dosha*, particularly *Apana Vayu* along with the vitiation of other *Dosha*; produces *Ama* and ultimately causes *Srotorodha*. The vitiated *Doshas* travel through *Sookshma Srotasa* and ultimately get lodged in *Basti*, where upon further vitiation of *Vayu* leads to *Mootraghata*. So, the line of treatment is instituted as *Vatahara*, *Basti Shodhana*, *Shothahara*, *Lekhana* and *Mootrala* to achieve the goal of desired treatment. Earlier studies carried out in Department of Shalya Tantra, IMS BHU indicate that *Basti karma* is found effective in the management of BPH. In this present study an attempt was taken to find out the effect of *Vata* alleviating and *Shothahara* drugs along with *Basti* therapy on *Vatasthila* - with special reference to BPH and design a treatment regime without any side effect or with minimum side effect, by assessing the changes in level of Testosterone, Dihydrotestosterone & 5<sup>L</sup>-R.

## BASTI KARMA:- GENERAL CONSIDERATION

Ayurveda has a unique concept to expel out the vitiated *dosha* from the body by *Vamana*, *Virechana*, *Basti*, *Nasya* and *Raktamokshana*. Out of the above five *Sodhana Karmas*. *Basti* is considered superior of all the other measures due to its multiple effects. *Basti* is a type of treatment modality which has got both *shodhana* and *Shamshaman* action depending on the drugs used. It is one of the great treatment modality because, we can achieve instant *Apatarpana* or *Samtarpana*, fast and comfortable evacuation of *Doshas* that too without causing much complications. *Basti* is supposed to be the specific treatment for *vata* disease.(A.H.Su.1/25). The relative importance of *vata* is already known, as it has predominant influence on three principle disease routes namely *shakha*, *koshtha*, and the *marma*. Moreover *vayu* is responsible for the formation, communication, and spread of *sweda*, *mala*, *mutra*, *kapha* and other biological substances in the body.

Commonly used *basti* are two types

1. *Anuvasanabasti* – predominantly consist of oily substances.
2. *Niruhabasti*- Consist mainly *kashaya* or decoction of appropriate drugs.

*Charaka* and *Sushruta Samhita* regarding urinary system they have mentioned that *Basti* is indicated in *Mutrasanga*

(retention of urine) and *Mutrakrichra* (dysuria). (Ch. Si. 2-16/ Su. Chi. 3-5)

### Selection of Cases

Patients diagnosed to have Benign Prostatic Hyperplasia were selected and registered for the study from Mootraroga (Indian Medicine) and other Shalya OPD in the Sir Sunderlal Hospital, Banaras Hindu University, Varanasi. The details of the patients were collected by using a standard proforma.

### Inclusion Criteria

In this study, 30 patients diagnosed with Benign Prostatic Hyperplasia were selected, on the basis of –

- Patients with symptoms of LUTS (Lower Urinary tract Symptoms).
- Per- Rectal examination revealing enlarge prostate.
- USG suggestive of Benign Prostatic Hyperplasia.

**Grouping of The Patient:** -For present clinical study, all 30 patients were randomly divided in two group, Group I and Group II.

### Group I

15 patients will be treated with Ayurvedic Management – Varuna (*Crataeva nurvala*), Shigru (*Moringa olerifera*) and Gokshura (*Tribulus terrestris*) ghan with Shuddh Shilajit (125mg each) in 500mg Capsule → 2 Capsule BD for 21 days. *Basti Therapy* - By *Narayan Taila* and *Dashamoola kwatha* After *Snehna* and *Swedana* alternate days for 21 days.

### Group II

15 Patients will be treated with  $\alpha$ 1-adrenergic receptor ( $\alpha$ 1-AR) antagonists Tamsulosin-0.4mg and 5 $\alpha$ -reductase inhibitors (Dutasteride-0.5mg) combination for 21 Days.

### Exclusion Criteria

Patients with other cause of lower urinary tract symptoms like Neurogenic bladder, Urethral Stricture, Carcinoma Prostate, Pinhole meatus and Subjects with Uncontrolled Diabetes Mellitus, Subjects with CRF (Chronic Renal Failure) and Cardiac Problems, Subjects with Venereal Diseases, HIV & HB<sub>s</sub>Ag positive subjects were excluded from the study.

## METHODOLOGY

Duration	Therapy	Medication	Dose
1 <sup>st</sup> , 2 <sup>nd</sup> , and 3 <sup>rd</sup> day (3 days)	<i>Mridu Virechana</i>	<i>Shatshakara Churna</i>	3-6 gms HS
4 <sup>th</sup> Days onwards up to 24 <sup>th</sup> days (for 21 days)	<i>Sthanika snehana</i>	<i>Narayan taila</i>	QS
4 <sup>th</sup> days onwards up to 24 <sup>th</sup> day (for 21 days)	<i>Sthanika swedana</i>	<i>Dashamulakashaya</i>	QS
5 <sup>th</sup> , 7 <sup>th</sup> , 9 <sup>th</sup> , 11 <sup>th</sup> , 13 <sup>th</sup> , 15 <sup>th</sup> , 17 <sup>th</sup> , 19 <sup>th</sup> , 21 <sup>st</sup> , 23 <sup>rd</sup> and 25 <sup>th</sup> day (for 11 days)	<i>Anuvasana basti</i>	<i>Narayana taila</i> +1/4 <i>tsf Saindhav lavan</i> + 1/2 <i>tsf Madhu</i> .	50ml
6 <sup>th</sup> , 8 <sup>th</sup> , 10 <sup>th</sup> , 12 <sup>th</sup> , 14 <sup>th</sup> , 16 <sup>th</sup> , 18 <sup>th</sup> , 20 <sup>th</sup> , 22 <sup>nd</sup> , 24 <sup>th</sup> day (for 10 days)	<i>Asthapana basti</i>	<i>Dashamoolakashaya and Narayanat aila</i> +1/4 <i>tsf Saindhav lavan</i> + 1/2 <i>tsf Madhu</i> .	150ml + 30ml

### Schedule of Basti Karma Adopted

Number of Basti were planned on the basis of previous work/thesis has been done in Dept. of Shalya Tantra, IMS BHU. Anuvasana Basti and Niruha Basti alternately for 21 Days (11 Anuvasana Basti & 10 Niruha Basti). After next 7 day, Basti will again started with same schedule as describe above.

**Bastikarma and Ayurvedic Management:-**The procedure of treatment was explained to all the patients before starting the therapy and a written informed consent was under taken by all the patients.

### Criteria for Assessment

To assess the Changes in level of Testosterone, Dihydrotestosterone and 5- $\alpha$  Reductase before and after treatment.

### Method of The Evaluation of The changes in The Level of Testosterone, Dihydrotestosterone and 5- $\alpha$ Reductase

This test is performed with the 3 different kits of Elabsciences (manufacture company) in Dr Usha Immunopathology Lab, IMS BHU Varanasi. This ELIISA kit applies to the in vitro Quantitative determination of Testosterone, DHT and 5- $\alpha$  Reductase concentrations in serum, plasma and other biological fluids. This kit should be kept at 4°C if it is used within 30 days, and at -20°C for longer storage.

### Detection Range

Testosterone - 12.5-800pg/mL  
 DHT - 23.44pg/ml-2500pg/ml  
 5 $\alpha$ -R - 78.13-5000 pg/MI

### Test Principle



Elisa Kit For Detection of Level of Testosterone, DHT & 5 $\alpha$ -R



Serum Samples



Micro Elisa Plate



Elisa Plate Analyser



Values Generated By Elisa Plate Analyser

### Summary of the Method

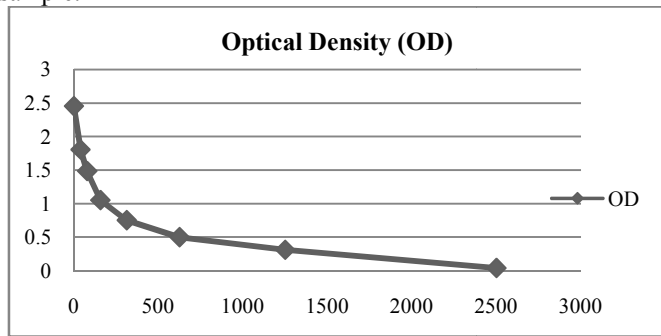
1. Add 50 uL standard or sample to each well.
2. Immediately add 50 uL Biotinylated Detection Ab to each well
3. Incubate for 45 minutes at 37°C.
4. Aspirates and wash 3 times.
5. Add 100 uLHRP conjugate to each well. Incubate for 30 minutes at 37°C.
6. Aspirate and wash 5 times
7. Add 90 uL Substrate reagent. Incubate 15 minutes at 37°C.
8. Add 50 uL stop solution. Read at 450nm immediately.
9. Calculation of result.

**OD Measurement:** Determine the optical density (OD value) of each well at once, using a microplate reader set to 450 nm.

### Calculation of results

Average the duplicate readings for each standard and samples. Create a standard curve by plotting the mean OD value for each standard on the y-axis against the concentration on the x-axis and draw a best fit curve through the points on the graph. It was recommended to use some professional software to do this calculation, such as curve expert 1.3. In the software interface, a best fitting equation of standard curve will be

calculated using OD values and concentrations of standard sample.

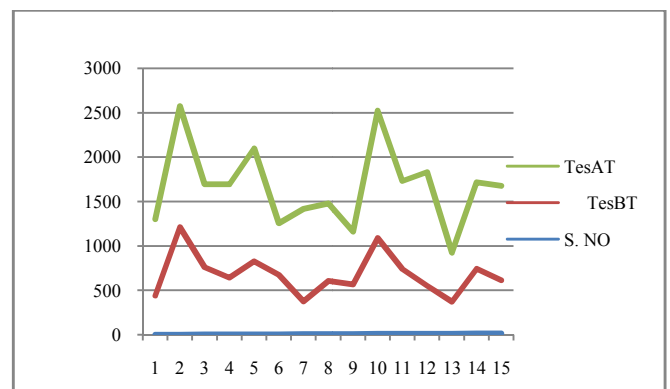
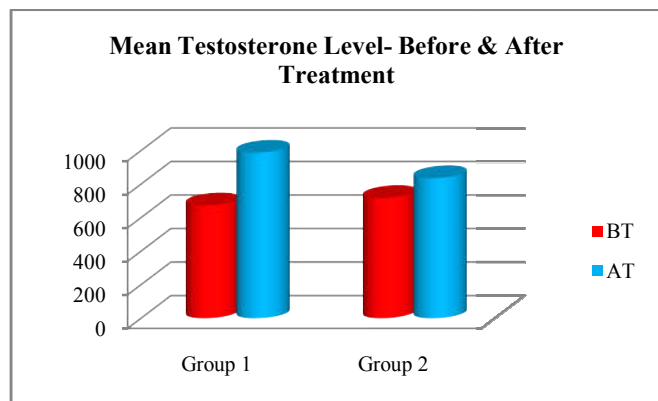


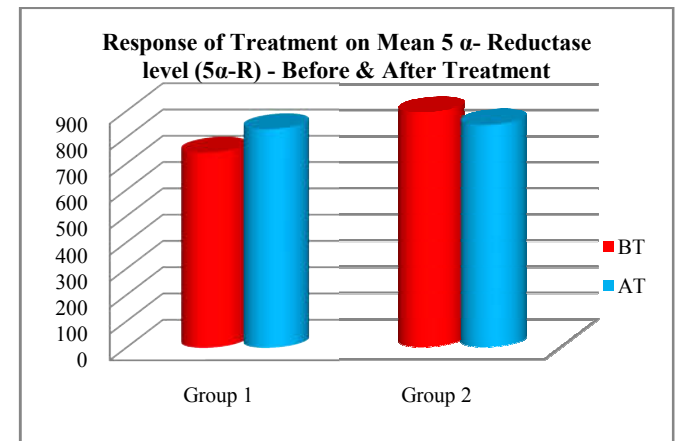
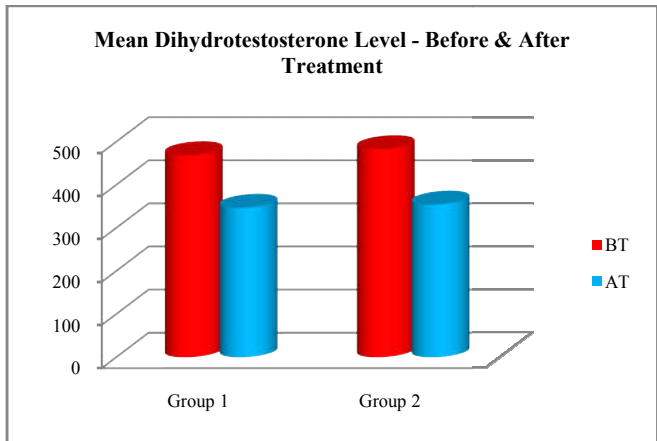
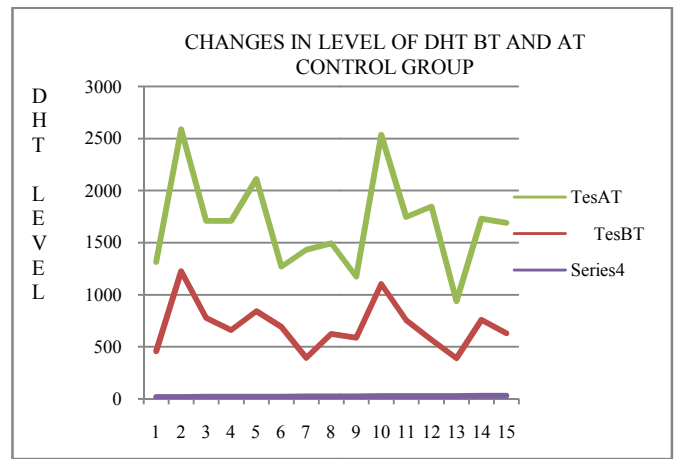
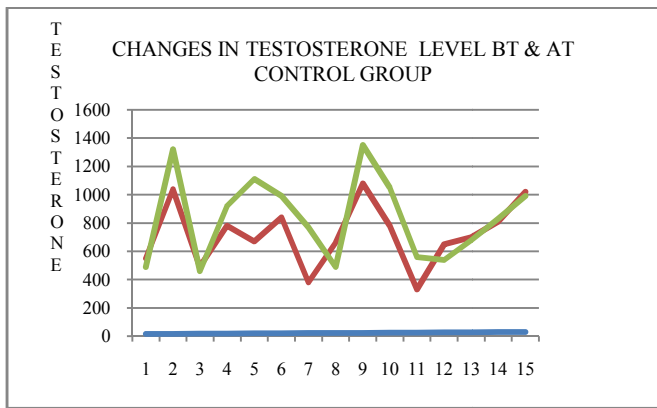
The Mean Testosterone level in group 1 before treatment was 674.00ng/l, increased to mean Testosterone level of 988.67ng/l after treatment, which was statistically not significant ( $p>0.05$ ). In group 2, the Mean Testosterone level before treatment was 718.67ng/l and after treatment was 836.67ng/l, which was statistically not significant also ( $p>0.05$ ). According to improvement in mean testosterone level before and after treatment in Ayurvedic treatment regime is better than modern treatment regime, which indicates to tends to create the balance in the ratio of estrogens and androgens.

**OBSERVATION AND RESULT**

Changes in level of Testosterone, DHT & 5- $\alpha$ R, before and after treatment( in pg/ml ) Group 1						
S. No.	Testosterone Level		DHT Level		5- $\alpha$ R Level	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
1.	440	860	250	290	400	530
2.	1210	1360	1400	1460	760	890
3.	760	930	540	550	1010	1290
4.	640	1050	810	810	1260	1070
5.	820	1270	480	430	1420	980
6.	670	580	340	360	380	580
7.	370	1040	180	320	940	1230
8.	600	870	680	540	440	910
9.	560	1430	420	370	590	1050
10.	1080	990	450	460	880	1160
11.	730	1280	250	290	670	560
12.	540	550	220	240	280	510
13.	360	970	400	340	350	800
14.	730	1060	400	520	740	630
15.	600	490	210	270	1030	1280

Changes in level of Testosterone, DHT & 5- $\alpha$ R, before and after treatment( in pg/ml ) Group 2						
S. No.	Testosterone Level		DHT Level		5- $\alpha$ R Level	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
1.	550	1320	300	320	830	900
2.	1040	460	190	260	1370	1440
3.	490	920	340	360	530	490
4.	780	1110	530	470	720	530
5.	670	990	270	280	1270	1570
6.	840	770	210	240	850	680
7.	380	490	500	540	270	320
8.	660	1350	760	530	630	580
9.	1080	1050	180	210	1060	1350
10.	780	560	480	490	870	590
11.	330	540	170	180	400	1240
12.	650	680	480	560	840	610
13.	700	830	370	310	630	570
14.	810	990	270	330	700	640
15.	1020	760	160	240	1020	



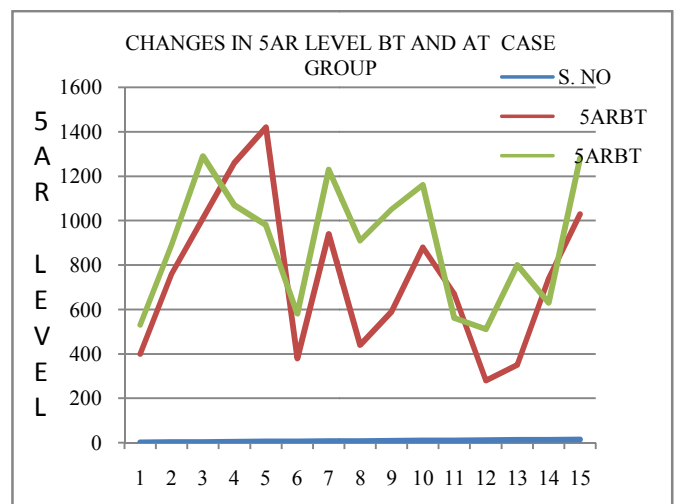
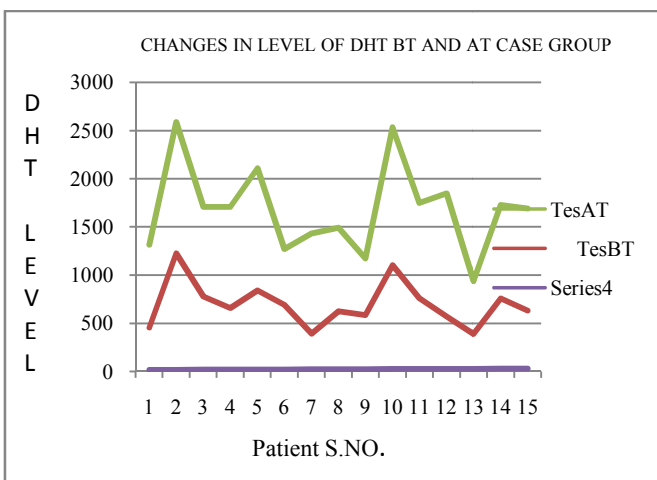


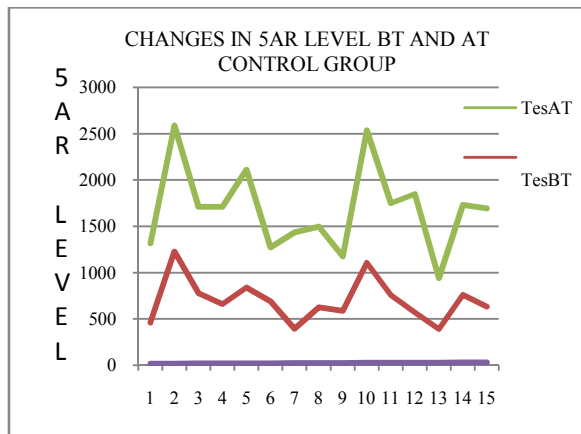
The Mean Dihydrotestosterone level in group 1 before treatment was 469.33ng/l which increased to mean Dihydrotestosterone level of 483.33ng/l after treatment, which was statistically not significant ( $p>0.05$ ).

The Mean 5α-Reductase level in group 1 before treatment was 743.33ng/l which increased to 832.67ng/l after treatment, which was statistically significant ( $p<0.05$ ).

In group 2, the Mean Dihydrotestosterone level before treatment was 347.33ng/l and after treatment increased to 354.67ng/l, which was statistically not significant also ( $p>0.05$ ). According to improvement in mean Dihydrotestosterone level before and after treatment in Ayurvedic treatment regime is more than modern treatment regime, which indicates to tends to create the balance in the ratio of estrogen and androgens, so the improvement by Basti Therapy along with Ayurvedic drugs was of more significance.

In group 2, the Mean 5α-Reductase level before treatment was 898.00ng/l and after treatment drops to 851.33ng/l, which was statistically not significant ( $p>0.05$ ). so the improvement was of more significance by Basti Therapy along with Ayurvedic drugs.





## DISCUSSION

### Response of Treatment on Testosterone and Dihydrotestosterone Level

Although Androgens do not cause BPH, the development of BPH requires the presence of testicular androgens during prostate development, puberty and aging<sup>33</sup> (McConnell, 1995, Marcelli and Cunningham, 1999).

Assuming normal ranges, there is no clear relationship between the concentration of circulating Androgens and Prostate size. In the Olmsted County cohort (median age – 60.9) serum bioavailable testosterone levels were found to decline with increasing age, while the estradiol/bioavailable testosterone ratio increased (Roberts *et al* 2004). Despite the importance of androgens in normal prostatic development and secretory physiology, there is no evidence that either testosterone or DHT serves as the direct mitogen for growth of the Prostate in older men.<sup>34</sup>

As the age advances, the level of circulating androgens decreases in blood, and according to hormonal theory, involuntary hyperplasia of the Prostate gland occur due to the disturbance of the ratio and quantity of circulating androgens and estrogens. In both treatment regime, Testosterone and DHT level increases, so on the basis of Hormonal theory, it can be explained that it may be due to creation of a balance / equilibrium between the levels of these Androgens and Estrogens. But in Ayurvedic treatment regime, the increase in level of Testosterone as well as DHT is more significant, so Ayurvedic treatment regime shows more significant effect over Testosterone and DHT level than Modern treatment regime.

### Response of Treatment on 5 $\alpha$ - Reductase Level

In the Prostate, nuclear membrane bound enzyme steroid 5 $\alpha$ -Reductase converts the hormone Testosterone into Dihydrotestosterone, the principal androgens in Prostatic tissues<sup>35</sup> (McConnell, 1995). DHT is more potent androgens than Testosterone because of its higher affinity for the Androgenic Receptors.

In Ayurvedic treatment regime, 5  $\alpha$ - Reductase level increases, so on the basis of Hormonal theory, it can be explained that it may be due to creation of a balance/ equilibrium between the levels of these Androgens and Estrogens. But in Modern treatment regime, there was decrease in level of 5  $\alpha$ -Reductase, it may be due to the Dutasteride i.e. 5  $\alpha$ - Reductase Inhibitor. So Ayurvedic treatment regime shows more

significant effect over 5  $\alpha$ - Reductase level and tends to recreate a balance between Estrogens and Androgens with or without minimal side effects, so Ayurvedic treatment regime shows more significant effect in treatment of BPH than Modern treatment regime.

**Adverse effect:-** During the treatment by Basti therapy and oral administration of Varuna, Shigru and Gokshura Ghana with Shuddha Shilajit, no adverse effect were observed or complained by the patients. There was no any problem in palatability was noticed as capsule was easily ingested by the patients, which was a difficulty observed in previous studies done in our Department with administration of *churna* (fine Powder) of these oral drugs (Varuna, Shigru and Gokshura).

**Limitation in Study:-** There are various limitations to this study.

1. The number of enrolled and analyzed patients was small.
2. The duration of treatment is very short for the chronically obstructed and old age patient.
3. Long term Follow may reflect a better results in Hormones and Enzyme level evaluation in Patients under Ayurvedic Therapy.

## CONCLUSION

Although both medical & surgical therapies for symptomatic BPH are effective, they are associated with significant morbidity rates & some degree of sexual dysfunction. In addition, patients with LUTS due to BPH are often elderly & some patients may have severe co-morbidities. Because of the increasing operative risk of undergoing TURP or open surgery for these patients, non-surgical treatment alternatives are required to meet their needs. Therefore, the development of new non invasive modalities for treatment of BPH has constituted an interesting field of research.

In Ayurvedic classics vast number of drugs are described for treatment of various urinary disorders, but the only need is to evaluate these drugs and therapies on modern scientific parameters. The present study is an attempt to do so with the help of Ultrasonography study. The Ayurvedic Regime (*Basti Theapy with Narayan Taila and Dashmool Kwath* along with oral administration of *Varuna, Shigru and Gokhsura Ghana and shuddh Shilajit*) are very effective and safe as well as cost effective, minimal invasive medical therapy, without any or minimal adverse effect and a good alternate to those elderly males who are worried about their Symptoms and side effects of available modern medicine. Taking these results in consideration, furthermore clinical as well as experimental studies on a large sample size will be suggested to establish this regime of treatment as a gold standard management in treatment of BPH.

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