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Preventive Measures and Medical Management of Prostate Enlargement in Diabetic Patients

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Abstract

What are the reasons for the failure of COP 27? For the undersigned they are the same as the failure of the failure of all 26 previous COPs, including the good intentions of the countries that signed the Paris agreements of 2015.

Keywords: Omission; environment; multinationals

Introduction

Benign Prostatic Hyperplasia:

BenignprostatichyperplasiaalsocalledBPHisaconditioninmeninwhichtheprostategland is enlarged and not cancerous. Benign prostatic hyperplasia is also called benign prostatic hypertrophy or benign prostatic obstruction.

The prostate goes through two main growth periods as a man ages. The first occurs early in puberty, when the prostate doubles in size. The second phase of growth begins around age 25 and continues during most of a man's life. Benign prostatic hyperplasia often occurs with the second growth phase.

As the prostate enlarges, the gland presses against and pinches the urethra. The bladder wall becomesthicker.Eventually,thebladdermayweakenandlosetheabilitytoemptycompletely, leaving some urine in the bladder. The narrowing of the urethra and urinary retention.The inability to empty the bladder completely cause many of the problems associated with benign prostatic hyperplasia1

Fig:1 Structure of benign prostate hyperplasia
With type-2 diabetes, the body either doesn't produce enough insulin, oritresists insulin

DIABETES:

Agroupofdiseasesthatresulttoomuch sugarin the blood [Glucose].

TYPE2DIABETES:

Achroniccondition thataffects theway the body processes the blood sugar [Glucose].

Symptomsincludeincreasedthirst,frequenturination,hunger,fatigueandblurredvision2.

Fig;2structureoftype2 diabetes

Diabetes mellitus cause prostate enlargement:

Enlarge prostate size. The autonomic nervous hyperactivity was associated with increased LUTSandprostatesizeinmaleabove38years.IncreasedInsulinconcentrationsecondaryto

Diabetes may have atrophic affect that leads to Diabetes mellitus(DM)is a serious problem in male health.Apositiveassociationexistsbetweenclinicalmarkersofbenignprostatichyperplasia(BPH)and DM. Subnormal serum free testosterone is detected in diabetic men.Clinical observation of larger prostate glands in men with diabetes mellitus type 2 led some investigators to hypothesize that an association between these two conditions exists. In fact, both diseases are very common in men as they age and seem to be sharing similar epidemiologic.
BPH pathogenesis along with the fact that both BPH and diabetes mellitus type 2 (DM-2) are both high prevalent diseases is posing doubts on the association between these two common

Fig:3structureofprostateenlargement.

diseases.Ontheotherhand,eventhoughBPHandDM-2areapparentlydisparateclinicalentities,both diseases seem to besharing similarepidemiologic features, which arepossibly connected to a common pathogenic pathway related to aging and diet. Typically, clinicians treat BPH and type 2 diabetes as entities, although some have suggested that diabetes may be a risk factor for the development and progression of BPH.Vascular damage and atherosclerosis caused by diabetes3

HISTORY:
Theprostatewasfirstformallyidentifiedby Venetiananatomist NiccolòMassainAnatomize libriintroductory(IntroductiontoAnatomy)1536andillustratedbyFlemishanatomistAndreas Vesalius in Tabulae anatomical sex (six anatomical tables) in 1538.Massa described it as a "glandularfleshuponwhichreststheneckofthebladder,"andVesaliusasa"glandularbody".
Thefirsttimeawordsimilarto'prostate'wasusedtodescribetheglandiscreditedtoAndrédu Laurens in 1600, whodescribed it as aterm already in usebyanatomists at thetime.Theterm was at least as early as 1549 however used by French surgeon Amboise Pare.
At the time, Du Laurens was describing what was considered to be a pair of organs (not the single two lobed organ), and the Latin term prostate that was used was a mistranslation of the term for the Ancient Greek word used to describe the seminal vesicles, parastatal; although it hasbeenarguedthatsurgeonsinAncientGreeceandRomemusthaveatleastseenthe prostate as anatomical entity. The term prostate was taken rather than the grammatically correct prostrator(singular)andprostrators(plural)becausethegenderoftheAncientGreektermwas takenasfemalewhenitwasinfactmale.
Thefactthattheprostatewasoneandnottwoorgans was an idea popularized throughout the early 18th century, as was the English language term used to describe the organ, prostate, attributed to William Haselden. A monograph, “Practical observationsonthetreatmentofthediseases oftheprostategland”byEverardHomein1811, was important in the history of the prostate by describing and naming anatomical parts of the prostate, including the median lobe. The idea of the fivelobes of the prostate was popularized followinganatomicalstudiesconductedbyAmericanurologistOswaldOwsleyin1912.John
E. McNeal first proposed the idea of “zones” in 1968; McNeal found that the relatively homogeneous cut surface ofan adult prostatein no way resembled “lobes” and thus led to the description of “zones..

Fig:4comparisonofnormalprostateandenlargedprostate.

STRUCTURE:

Theprostateisaglandofthemalereproductivesystem.Inadults, itisabout the size of a walnutand has an average weight of about 11 grams, usually ranging between 7 and 16 grams. The prostateis located in the pelvis. It sits below the urinary bladderand surrounds the urethra. The part of the urethra passing through it is called the prostatic urethra, which joins with the two ejaculatory ducts. The prostate is covered in a surface called the prostatic capsuleorprostaticfascia.

The internal structure of the prostate has been described using both lobes andzones.Becauseofthevariationindescriptionsanddefinitionsoflobes, the zone classification is used more predominantly.
The prostate has been described as consisting of three or four zones. Zones aremoretypicallyabletobeseenonhistology,orinmedicalimaging,such as ultrasoundorMRI4.

ANATOMYOFTHEPROSTATE:
- Theprostateisawalnut-shapedglandthatispartofthemalereproductivesystem.The mainfunctionoftheprostateistomakeafluidthatgoesintosemen.Prostatefluidis essentialforaman’sfertility.Theglandsurroundnodstheurethraattheneckofthe bladder. The bladder neck is the area where the urethra joins the bladder. The bladder and urethra are parts of the lower urinary tract. The prostate has two or more lobes, or sections,enclosedbyanouterlayeroftissue,anditisinfrontoftherectum,justbelow the bladder. The urethrais the tube that carries urinefrom the bladder to the outside of thebody.Inmen,theurethraalsocarriessemenoutthroughthepenis.
- TheProstateisaglandofthemalereproductivesystem.
- Itislocatedinfrontoftherectumandjustbelowthebladder,theorganthatstoresurine.
- The prostate consists of a base, an apex, an anterior, a posterior and two lateral surfaces.
- Themainpurposeoftheprostateistoproducefluidforsemen,whichtransportssperm during the male orgasm.

Fig:5 Anatomyof prostate

Lobes Of the Prostate:
Theprostate is divided into two lobes
ANTERIORLOBE:
Theanteriorlobeisusedtodescribe theanteriorportionoftheglandlyinginfrontofthe urethra. It is devoid of glandular tissuebeing formed completely of fibromuscular tissue.
MEDIANLOBE:
The medianlobe is a cone shaped portion of the gland situated between the two ejaculatoryducts and the urethra.
LATERALLOBE:
Thelaterallobes(rightandleftlobes)formthemainmassoftheglandandarecontinuous posteriorly. They are separated by the prostatic urethra.
POSTERIORLOBE:
The posteriorlobe is used by some to describe the posteromedialpart of the lateral lobes that can be palpated through the rectum during digital rectal exam (DRE).

ZONESOFTHEPROSTATE
CENTRALZONE:
Itsurroundsthe ejaculatoryducts,comprising approximately25%of normalprostatevolume.

The ducts of the glands from the central zone are obliquely emptying in the prostatic urethra, thus being rather immune to urine reflux.

TRANSITIONALZONE:

It is located centrally and surrounds the urethra, comprising approximately 5-10% ofnormal prostate volume.
The glands of the transitional zone are those that typically undergo benign hyperplasia (BPH).
PERIPHERALZONE:
Makes up the main body of the gland (approximately 65%) and is located posteriorly.
Theductsoftheglandsfromtheperipheralzoneareverticallyemptyingintheprostatic urethra; that may explain the tendency of these glands to permit urine reflux.
Thatalsoexplainsthehighincidenceofacuteandchronicinflammationfoundinthese compartments, a fact that may be linked to the high incidence of prostate carcinoma at the peripheral zone.
The peripheral zone is mainly the area felt against the rectum on DRE, which is of irreplaceable value.

FIBROMUSCULARSTROMA:

Thefibromuscularstroma(orfourthzonefor some) issituated anteriorly inthe gland.
Itmergeswiththetissue oftheurogenital diaphragm.
This part of the gland is actually the result of interaction of the prostate gland budding around the urethra during prostate embryogenesis and the common horseshoe-like muscle precursor of the smooth and striated muscle that will eventually form the internal and external urethra sphincter5.

Fig:6structureofFibromuscular stroma.

Geneandproteinexpression:

About 20,000 protein coding genes are expressed in human cells and almost 75% of these genes are expressed in the normal prostate. About 150 of these genes are more specifically expressed in the prostate, with about 20 genes being highly prostate
specific. The corresponding specific proteins are expressed in the glandular and secretory cells of the prostatic gland and have functions that are important for the characteristics of semen, including prostate-specific proteins, such as the prostate specific antigen (PSA), and the Prostatic acid phosphatase6.

Development:

Theventraldivisionofcloacawhichistheterminalpartofhindgut,formstheurogenitalsinus. Duringninthtotenth weekofdevelopment,themesenchymesurroundingtheurogenitalsinus interactwithendodermofproximalpartofurogenitalsinuswhichlaterformsthepro

ximalpart of urethra. As a result of these interactions, the initial outgrowths arise from the lateral aspect of the endodermal tube. The outgrowths form the outer glandular zone of prostate. The subsequentout-growthsarisefromitsdorsalwallwhichformstheinternalglandularzone.The outgrowthsdevelopintofivedistinctgroupsofepithelialbudsbytheendofthe11thweekand arecompletedbythe16thweek.AccordingtotheclassificationgivenbyLowsley,five groups ofepithelialbudsgiverisetofivelobes,namely,themedian,rightandleftlateralandposterior

and anterior lobes (Lowsley 1912). These lobes of prostate gland till are recognized the 20th week of gestation. With an advance in gestational age, only three lobes are recognizable–two lateral lobes and a median lobe. The epithelial buds branch and rebranch ending into complex ductal system that meets the differential mesenchymal cells. The mesenchymal cells develop around the tubules by the 16th week and become denser at the periphery to form the prostatic capsule.
Development of prostate gland (a–e): the endodermal outgrowths from the prostatic urethra into the surrounding mesenchyme form the gland primordium which further proliferate and enlarges.1allantois,2urinarybladder,3ureter,4definitiveurogenitalsinus,5seminalvesicle,
6 pelvic part of urogenital sinus, 7 anorectal canal, 8 ductus deferens, 9 prostate, 10 penile urethra, 11 endodermal tube, 12 glandular outgrowths, (f) prostatic glands, (g) enlarged view of tubuloalveolar glands7.

Fig: 7structureofdevelopment of prostate.

FUNCTIONOFPROSTATE:

Ithelpsproduce semen.
The main function of the prostate is to help produce semen. It makes an alkaline fluid which mixes with sperm during ejaculation to create semen. The alkaline fluid helps to protect the sperm once it reaches a woman's vagina as this is an acidic environment.

Itproducesprostate-specificantigen(PSA).
Theprostateproducesafluidcalledprostate-specificantigen(PSA)whichalsohelpsthesperm byactinglike a glueto attachitto awoman's cervix.The "glue"thendissolvesandthesperm is free to swim into the uterus to find an egg.

The high levels of PSA in a man can also be an indication of prostate cancer. Men over a certainageshouldhavetheirPSAlevelscheckedonayearlybasis.Thisisdonethrough a simple blood test.

Itpumpssperm.

As well as helping to make semen, the prostate gland helps to pump out sperm during intercourse.Thepumpingactionensuresthatthespermcantravelfarenoughintothe uterusto possibly find an egg. This experience helps make sex pleasurable for men.

It'sthe"G-spot."
Theprostateglandisalsoknownasthemale"G-spot"andifstimulatedduringsexcanleadto an intense orgasm for some men.

Itactsasafilter.

Theprostategland acts as afilterforsperm,removing any toxins that would inhibit thesperm from doing its job. It's believed that there is an increase in prostate diseases because there are more toxins in the air we breathe and food we eat, so the prostate has to work harder.

Itcreates erections.
Theprostatenervesplayaroleincreatingandmaintainingerectionsduringsexasthe ytrigger extra blood to the penis to help its well. Many prostate treatments have the potential to disrupt this process and cause issues with erections.

It protects against urinary tract infections.

Prostatesecretionscanhelpprotecttheurethrafromurinarytractinfections(UTIs).

Itcontrolsurine flow.
The prostate controls the flow of urine down the urethra and stops urine from leaving the bladder until a man needs to urinate. It also ensures that no urine is mixed with sperm when a man ejaculates. As the prostate grows, the pressure on the urethra can cause problems with urination.

Itproduces hormones.
Theprostateisresponsiblefortheproductionofthemalehormonesdihydrotestosterone(DHT) whichhappenswhentestosteroneisconvertedtoDHTbythe5-alpha-reductaseenzymeinthe prostate.DHTisresponsibleforthemalesexdriveandasamanagesthisproductionmayslow due to toxins in the prostate and lead to a reduced sex drive.
PROSTATEDYSFUNCTION.

Itmainlycausedby

Malehormonal changesin old men

Aging

Inflammation And

Fibrosis

Atbirth, theprostate hasasystem ofducts embeddedin a stroma

AGECHANGESINTHEPROSTATE:

Atbirth,theprostatehasasystemofductsembeddedinastromathatFormsalargepartofthe gland.Follicles are representedby small endbuds on theducts. Before birth, theepithelium of theducts,seminalcolliculusandprostaticutricledisplayhyperplasiaandsquamous metaplasia, possiblyduetomaternalestrogensinthefoetalblood.Thissubsidesafterbirthandisfollowed by a period of quiescence lasting for 12–14years. At puberty, between the ages of approximately 14 and 18years, the prostate gland enters a maturation phase and more than doublesinsizeduringthistime.Growthisalmostentirelyduetofollicular development,partly from end-buds on ducts, and partly from modification of the ductal branches. Morphogenesis and differentiation of the epithelial cords starts in an intermediate part of the epithelial anlage andproceedstotheurethralandsubcapsularparts ofthegland;thelatteris reachedbytheage of17–18years.Theglandularepitheliumisinitiallymulti-layeredsquamousorcuboidalandis transformed into a pseudostratified epithelium consisting of basal, exocrine secretory (including mucous) and neuroendocrine cells. The mucous cells are temporary and are lost as the gland matures. The remaining exocrine secretory cells produce a number of products, includingacidphosphatase,prostatespecificantigenandβ-microseminoprotein.Growthofthe secretory component is associated with condensation of the stroma, which diminishes relative to the glandular tissue. These changes are probably a response to the secretion of testosterone bythetestis.Duringthethirddecade,theglandularepitheliumgrowsbyirregularmultiplication oftheepithelialinfoldingsintothelumenofthefollicles.Afterthethirddecade,thesizeofthe prostate remains virtually unaltered until 45–50years, when the epithelial folding's tend to disappear,follicularoutlinesbecomemoreregular,andamyloidbodiesincreaseinnumber:all signs of prostatic involution. After 45-50 years, the prostate tends to develop BPH:an age- related condition. If a man lives long enough, then BPH is inevitable, although not always symptomatici8.

Prostate Disease and Ageing:

Around 25 per cent of men aged 55 years and over have a prostate condition. This increasesto50percentbytheageof70years.Earlystagesofprostatediseasemayhave no symptoms.

Man with 50s or 60s, talk to the doctor about whether they need to have their prostate glandcheckedand,ifso,howoften.Iftheyhaveafamilyhistoryofprostatedisease(or particular concerns), talk to the doctor earlier about when prostate checks might be suitable for men.

TYPES OF PROSTATE DISEASES:

Thethreemostcommontypesofprostatediseaseare
Benignprostatic hyperplasia
Prostatitis
Prostatecancer
Althoughthesediseaseshavedifferentcauses,theyhavesimilarsymptoms.Thisisw hy it's important to discuss prostate cancer screening with the doctor as part of yearly
physicalexamination.doctorwilloftenrefertoaurologist(adoctorwhospecializesin diseases of the urinary tract and the male reproductive system) if they have symptoms of any of the following diseases.

PROSTATITIS:

Prostatitisisaninflammationoftheprostate.Thiscanbecausedbyabacte rialinfection. Menofallagescangetprostatitis,andit canoccurinanysizeprostate(enlargedor not).
Symptomsofprostatitis include:
Difficulty urinating
Frequenturination, especiallyat night
Painor burningduring urination
Chillsand feveralong withurinating problems.

PROSTATECANCER:

Prostatecancer,initsearlystages,maynotcauseanysymptoms.Butasitprogresses,s ymptoms often appear.
Symptomsofprostatecancerinclude:
Aneedtourinate frequently,especiallyatnight.
Difficultystarting urination.

Inabilitytourinate.
Weakorinterrupted flowof urine(dribbling).
Painfulorburningurination.
Painfulejaculation.
Blood in urineor semen.
Frequentpainorstiffnessintheback,hips,orupper thighs.

NON-CANCEROUSPROSTATE[BPH]:

BenignprostatichyperplasiaalsocalledBPHisaconditioninmeninwhichtheprostat e gland is enlarged and not cancerous. Benign prostatic hyperplasia is also called benign prostatic hypertrophy or benign prostatic obstruction. The prostate goes through two main growth periods as a man ages.
Age-associatedprostateglandenlargementthatcancauseurinationdifficulty.
Thistypeof prostateenlargement isn't thoughtto beaprecursorto prostatecancer. With this condition, the urinarystream may beweak or stop and start. In somecases, it can lead to infection, bladder stones and reduced kidney function. Treatments include medication that relaxes or shrinks the prostate, surgery and minimally invasive surgery9.

BENIGNPROSTATEHYPERPLASIA:

Benign prostatic hyperplasia (BPH) refers to the non-malignant growth or hyperplasia of prostate tissue and is a common cause of lower urinary tract symptoms in men. Disease prevalence has been shown to increase with advancing age. Indeed, the histological prevalence of BPH at autopsy is as high as 50% to 60% for males in their 60's, increasing to 80% to 90% of those over 70 years of age.
Several definitions exist in the literature when describing BPH. These include bladder outlet obstruction (BOO), lower urinary tract symptoms (LUTS), and benign prostatic enlargement (BPE). BPH describes the histological changes, benign prostatic enlargement(BPE)describestheincreasedsizeofthegland(usuallysecondarytoBP H)
andbladderoutletobstruction(BOO)describestheobstructiontoflow.ThosewithB PE who present with BOO are termed benign prostatic obstruction. Lower urinary tract symptoms(LUTS)simplydescribe urinarysymptomssharedby disorders affectingthe

bladder and prostate (when in reference to men). LUTS can be subdivided into storage and voiding symptoms. These terms have largely replaced those historically termed "prostatism."
Thedevelopmentofbenignprostatichyperplasiaischaracterizedbystromalandepi thelialcellproliferationintheprostatetransitionzone(surroundingtheurethra),thi s leads to compression of the urethra and development of bladder outflow obstruction
(BOO)whichcanresultinclinicalmanifestationsoflowerurinarytractsymptoms (LUTS),urinaryretentionorinfectionsduetoincompletebladderemptying.Long-term, untreateddiseasecanleadtothedevelopmentofchronichigh-pressureretention(a potentially life-threatening emergency) and long-term changes to the bladder detrusor (both overactivity and reduced contractility).
Treatment options for BPH range from watchful waiting, to medical and surgical intervention. Risk factors may be divided into non-modifiable and modifiable, with factorssuch asage,genetics,geographicallocation,andobesity,allshown toinfluence
thedevelopmentofBPH.Itis,therefore,importanttobeabletoidentifythoseatriskof disease progression and those who can be managed more conservatively to reduce associated morbidity and health care burden.

ETIOLOGY:

Theetiology ofBPHis influenced by awidevariety ofrisk factors in addition to direct hormonal effects of testosterone on prostate tissue.

AlthoughtheydonotcauseBPHdirectly,testicularandrogensarerequiredinthedev elopment of BPH with dihydrotestosterone (DHT) interacting directly with prostatic epithelium and stroma. Testosterone produced in the testes is converted to dihydrotestosterone (DHT) by 5alpha-reductase2inprostatestromalcellsand
accountsfor90%oftotalprostaticandrogens. DHT has direct effects on stromal cells in the prostate, paracrine effects in adjacent prostatic cells,andendocrineeffectsinthebloodstream,whichinfluencesbothcellularprolife rationand apoptosis (cell death).
BPH arises as a result of the loss of homeostasis between cellular proliferation and cell death, resultinginanimbalancefavouringcellularproliferation.Thisresultsinincreasednu mbers of epithelial and stromal cells in the periurethral area of the prostate and can be seen histo- pathologically.

MAINCAUSES:

Agingalong withendocrine factors

Idiopathic

Alcoholconsumption

Overactiveofbladder

Inflammation

Obesity

Cancerofprostate

EPIDEMIOLOGY:
DifferencesincasedefinitionsmakeinterpretationofpopulationbasedstudiesregardingBPH difficult. Whereas BPH can refer to histology, benign prostate enlargement, and physiciandiagnosisofBPH,LUTSreferstotheurinarysymptomssharedbydisorders affecting the prostate and bladder.
AgeisasignificantpredictorofbothdevelopmentofBPHandsubsequentLUTS,with50%of men over the age of 50 shown to have evidence of BPH and the association with the development of LUTS shown to increase with age in a linear fashion. This is supported by studies that have demonstrated increases in prostate volume with age (2% to 2.5% increase in size per year). In the US, studies have shown BPH prevalence to be as high as 70% in those between 60 and 69 years of age and more than 80% in those over 70 years. The prevalence of male LUTS alone demonstrated a significant increase with age from 8% (30 to 39yrs) to 35% (60 to 69yrs) in the Boston area community health survey, other US population-based studies have shown 56% of men between 50-79yrs reported symptoms.
At a population-level, the prevalence of BPH increased dramatically between 1998 and 2007 in the US, nearly doubling in the number of cases. These increases are suggested to be attributabletoanagingpopulation,withthoseover80yearsofageprojectedtobearo und19.5 million in 2030 (from 9.3 million in 2003). As populations age, the number of cases can, therefore, be expected to rise.
InternationalstudieshavesuggestedthatWesternpopulationshavesignificantlyhi gherprostate volumes compared to those from southeast Asia. Further studies looking at the correlation of prostate volume with LUTS, however, found that lower prostate volumes did not necessarily correlate with symptoms, with

higher mean IPSS (international prostate symptom scores) observed in a cohort of Indian men compared to western population10.

PATHOPHYSIOLOGY:

Genetics/HereditaryFactors:
GeneticsandhereditaryfactorsimpactawidevarietyofdiseaseprocessesandtheirroleinBPH hasbeenexamined.AhereditaryinfluenceforthedevelopmentofBPHhasbeenshowninthe increased relative risk of 3.3 of disease concordance in monozygotic compared to dizygotic twins and increased incidence risk in siblings with an early onset of BPH disease.
The specific genetic risk factors have ranged from loss of the Y chromosome, to the action of single-nucleotide polymorphisms (SNPs). As the influence of androgens is suspected in prostate cancer and BPH, translational science studies have found a link between androgen metabolism (e.g., 5α-reductase type II gene variants) and BPH incidence. Other SNPs located near genes associated with increased prostate cancer risk (Iroquois homeobox 4 [IRX4], integrin subunit alpha 5 [ITGA5], and regulatory factor X6 [RFX6]) have been linked with more aggressive BPH disease (high IPPS), whilst SNPs linked to metabolic syndromes have correlated with increased prostate volumes. Despite these discoveries, a recent large genomewide association study was unable to identify significant susceptibility loci for BPH development.
Androgens
Whilst ageing is considered essential for BPH development, another factor is the presence of androgens.Theroleofmalesexhormoneshasbeenextensivelyexamined;however,theexact mechanism of action or mechanistic importance is still disputed.
Androgens, especially testosterone derived, play a central role in the normal functional development of the prostate. The main mode of action is via the transcription factor, the androgen receptor (AR), which is predominately located within the luminal epithelial cells, is almost non-existent in basal cells, and present at a lower density in a proportion of human prostatestromalcells.ARexpressionmaybeup-regulatedinBPHcomparedtonormaltissue; however, no consistent evidence has been demonstrated for this.
AkeystepintheARsignallingpathwayistheconversionoftestosteronetodihydrotestosterone (DHT), via the 5α-reductase enzyme, in particular the isozyme type 2. DHTthen bindsto theAR with a10-fold higheraffinity than testosterone.

The importance of androgens in the prostate is demonstrated by the effect of pre-existing deficiency in 5α-reductase. Affected males are found to have significantly smaller prostates than aged-matched controls, and histology from these subjects demonstrated the presence of fibrous connective tissue and smooth muscle, but no epithelial tissue.
So, whilst androgens are required for normal prostate development, their role in BPH pathogenesis is still debated.
Perhapscounter-intuitivelyastheincidenceofBPHincreaseswithage,thelevelsofcirculating testosteroneinserumgenerallydecreases.Paradoxically,hypogonadalpatientswhoaretreated with androgens have no increased risk of BPH development. One answer to this may be that true DHT concentrations are higher in BPH compared to normal tissues, but remain stable during ageing. It is therefore hypothesised that the prostate is insensitive to circulating testosteronelevelvariations,becausetheARinprostatecellsisnormallysaturatedbyrelatively lowandrogenintra-tissueconcentrations.Thus,androgenscanmaintainthegrowthofprostate cellswithinBPH.Additionally,thereis areported 8–10%prevalenceofbasalcellhyperplasia in BPH, which will account for a proportion of the incidence of BPH cases, despite lower circulating androgens.
Due to this perceived importance of androgens (particularly DHT) in BPH, the clinical use of 5α-reductaseinhibitors(5ARIs,e.g.,finasteride)fortreatmenthaslongbeenestablished.
Indeedclinically,improvementsintheIPSS,maximumurinaryflowrate,anddecreased prostatevolumesareseenaftertreatmentwith5ARIs.Thisimprovementdoestakea significant lengthoftimetooccur,~6months,implyingthatperhapsthetruedriver(s)ofthediseaseisnot targeted by this treatment.

Fig:8 Androgens

Oestrogens
Oftenobservedtoworkinoppositiontoandrogens,ithasbeensuggestedthatoestrogenscould be the primary hormone driver behind BPH. This has stemmed from observational animal studies in which oestrogen dosage induced murine prostatic hyperplasia.
Oestrogens, in particular oestradiol, act similarly to androgens, but via their own nuclear hormonereceptors,namelytheoestrogenreceptorα(ERα)andβ(ERβ).Inaddition,thecellular aromatase converts androgens to oestrogens.
In men with metabolic dysfunction, larger adipose tissue volumes can lead to increased aromatase conversion of androgens to oestrogens. This is combined with decreased secretion oftestosterone,alteringthebalancebetweenthetwosexhormones,whichmayaccountforthe increased prostate volumes in this cohort. Additionally, in the ageing male, serum androgen levels decrease, whilst oestrogen levels remain constant or decrease slightly, resulting in an increased oestrogen: androgen ratio. This may be significant in the development of BPH. It couldthereforebethecombinationofhigheroestrogenandandrogenlevelsthatworkstogether in the pathogenesis of BPH.

One reason for this might be the cellular locations of different oestrogen receptors and their perceived actions. The ERα has been shown to be predominately located within prostatic stromaltissue,whilsttheERβismainlylocatedwithintheprostaticbasalepithelialcells.Thus, ERα can not only cause stromal cell proliferation, but also has a paracrine influence on the adjacent epithelial cells. However, decreased levels of ERα have been detected in BPH.

The evidence therefore remains contradictory. Whilst ERβ has a pro-apoptotic effect, ERβ knockout mice develop BPH during ageing, and in humancells, activation of ERβ, via an agonist, causes apoptosis within BPH tissues. Why then does the action of the two different receptors not cancel each other out? This may be explained by the higher level of the enzyme aromatase located within stromal cells, implying that ERα may nevertheless be the dominant receptor leading to the hyperplasia.
However, all attempts to block the influence of ERα or aromatase have failed to yield conclusive clinical results in BPH.

Insulin
A role for insulin has been proposed in BPH, as epidemiological studies have shown an increasedincidenceofBPHinpatientswithdiabetes.Hyperinsulinemiaandinsulinresistance are both considered independent risk factors for the disease.
Insulin'seffectwithintheprostateismediatedviaIGF-1,whosereceptorhasbeenfoundtobe expressedathigherlevelswithinthestromaofBPHcases.IGF-1actstoincreaseproliferation of stromal cells in BPH, whilst also having a paracrine effect on the neighbouring epithelial cells. Indeed, increased levels of insulin and IGF-1 increased the risk of presenting with BPH compared to controls, and even could be used to predict prostate size, where larger prostates expressed the highest levels of insulin and IGF-1.
Thetargeting of insulin/IGF-1 may thereforehave a potential therapeutic benefit for BPH and theuseofmetforminhasbeenshowntoinhibittheproliferationofBPHcellsbydisruptingthe IGF-1 axis, namely inhibiting IGF-1 receptor expression and the phosphorylation of insulin receptor substrate 1 (IRS-1), a substrate of the IGF-1 receptor. Further studies on the effectiveness of this drug on BPH tissue and patients would be needed to clinically evaluate this as a treatment strategy.

GrowthFactors/Inflammation:
Changes in thesex hormonebalanceareimportant in BPH,but it mayprovidethemechanism ofmaintainingthehyperplasticprocessratherthanbeingtheinitiating/causativefactor.Thisis whycurrentopiniondeemstheprocessofinflammation(indeedchronicinflammation)andthe role of growth factors as key to the understanding of BPH.

TheARandGrowthFactors:
Growth factors are chemicals that cause cells to act in a number of ways, mainly either to proliferateortoundergoapoptosis.Theyincludekeratinocytegrowthfactor(KGF),epidermal growth factor (EGF), fibroblast growth factor (FGF) and IGF, all of which promote proliferation; whereas TGF-1 treatment results in apoptosis.
Within the prostate, growth factors are normally released by the stromal cells and maintain prostate cellular homeostasis through autocrine and paracrine pathways, as seen in the very earliest stages of human prostate development, where stromal factors determine cell fate (see below).AnalterationinthebalanceofcellularhomeostasisisatthecoreofBPHdevelopment. Activation of the AR leads to the increase in growth factors responsible for proliferation. For example, in BPH fibroblasts expressing AR, FGF-2 and FGF-7 are overexpressed. TGF-β1 induces the differentiation of fibroblasts into

myofibroblasts in the stroma and regulates the epithelial cells' response to IGF-1 (above) mediated by the stromal–epithelial cell axis, resulting in the hyperplasia linked to BPH.
This complexity underpins the difficulty in determining the causes of BPH. However, the increased levels of growth factors do contribute to BPH, but what causes the increase in the levels of these molecules? Current thought is that inflammation plays a key role, particularly asarecentstudyhasshownthatpro-inflammatorymacrophagesinducedanincreaseinstromal proliferation in BPH tissue via AR signalling pathways. Xu et al. also found that AR located within stromal cells of the TZ of the prostate had an increased ability to recruit inflammatory macrophages compared to elsewhere within the prostate, potentially explaining why BPH is mostly seen with this zone.

RoleofChronicInflammation:
An inflammatory process is thought to be the link between the initial cause and the growth factor-led hyperplasia and gland remodelling seen in BPH.
Thesuggestionforthislinkcamefromthestudyof>8000menwhohadBPH/LUTSand were entered into the Reduction by Dutasteride of prostate Cancer Events (REDUCE) trial. Within this population, 77.6% had chronic inflammation in their prostate biopsy at initial trial entry.
Thenormalprostatecontainsmultiplecellsimportantformaintainingimmunity,ast heprostate can be exposed to many pathogens from the urinary tract. In non-BPH tissue, T lymphocytes represent the majority of these cells (>90%), with mostly cluster of differentiation (CD)8 T cells (the predominant type) located within the peri glandular region, whilst CD4 T cells are present in the stroma. In samples of BPH tissue, a reversal of this ratio is seen, with a higher proportion of CD4 cells seen, along with CD3 T cells, demonstrating a picture of chronic inflammation.
Theinitialstimulusfortheinflammatoryprocessisstillunknown;however,severalh avebeen proposed. They include: bacterial (Escherichia coli) or viral (human papillomavirus, herpes simplex) infections, hormone changes, dietary factors, autoimmune responses, and urinary reflux into the prostate collecting ducts.
The initial stimulus causes the activated T cells in particular to release cytokines and interleukins (ILs) responsible for cell damage, such as an increase in expression of IL-15 in stromal cells, IL-17 from Tcells, interferon-γ in basal and stromal cells, and IL-8 in epithelial cells.IL-8isthoughttobekeyasitinducestheexpressionofFGF-2,whichhasbeenshownto be a potent growth factor for both stromal and epithelial cells.
Thisprocessoflymphocyteactivation,cytokinereleaseandgrowthfactor-inducedhyperplasia actsasaself-perpetuatingcycle,leadingtochronicinflammationandaprogressiveincreasein prostate volume.

Roleofchronicinflammation

SYMPTOMSOFBPH:

Urinaryfrequency—urinationeightormoretimesaday.
Urinaryurgency—theinabilitytodelayurination.
Troublestartingaurine stream.
Aweakoraninterruptedurine stream.

Dribblingattheendofurination.
Nocturia—frequenturinationduringperiodsofsleep.
Urinaryretention.
Urinaryincontinence—theaccidentallossofurine.
Painafterejaculationor during urination.
Urinethathas anunusual colouror smell11.

RISKFACTORS:
Non-modifiableandmodifiableriskfactorsalsocontributetothedevelopmentofBPH.The se have been shown to include metabolic syndrome, obesity, hypertension, and genetic factors.

Metabolic syndrome refers to conditions that include hypertension, glucose intolerance/insulin resistance, and dyslipidaemia. Meta-analysis has demonstrated thosewithmetabolicsyndromeandobesityhavesignificantlyhigherprostatevolum es. Further studies looking at men with elevated levels of glycosylated haemoglobin (Hba1c)havedemonstratedanincreasedriskofLUTS.Limitationsofthesestudiesar e thattherewerenosubsequentsignificantdifferencesinIPSS,andtheeffectofdiabete s on LUTS has been shown to be multifactorial in nature. Further studies are therefore required to establish causation in these individuals.

Obesityhasbeenshowntobeassociatedwithincreasedriskof BPHinobservational studies.Theexactcauseisunclearbutislikelymultifactorialinnatureasobesitymake s up one aspect of the metabolic syndrome. Proposed mechanisms include increased levels of systemic inflammation and increased levels of estrogens.
Genetic predisposition to BPH has been demonstrated in cohort studies, firstdegree relatives in one study demonstrated a four-fold increase in the risk of BPH compared to control. These findings have demonstrated consistency in twin studies lookingatthediseaseseverityofBPH,withhigherratesofLUTSseeninmonozygotic twins.
COMPLICATIONS:

Thecomplicationsofbenignprostatichyperplasia may include

- Acuteurinaryretention
- Chronic,orlonglasting,urinaryretention
- Blood in the urine
- Urinarytractinfections (UTIs)
- Bladderdamage
- Kidneydamage

- Bladderstones
- Mostmenwithbenignprostatic hyperplasiadonotdevelopthesecomplications.

However,kidneydamageinparticularcanbeaseriousheal thth reatwhenit occurs.

DIAGNOSIS:

Ahealthcareproviderdiagnosesbenignprostatichyperplasiabasedon

Apersonaland familymedicalhistory
Aphysicalexam
Medicaltests

PersonalandFamilyMedicalHistory

Takingapersonalandfamilymedicalhistoryisoneofthefirstthingsahealthcareprov idermaydo to help diagnose benign prostatic hyperplasia. A health care provider may ask a man

- whenthesymptomsbeganandhowoftentheyoccur
- whetherhehasahistoryofrecurrentUTIs
- whatmedicationshetakes,bothprescriptionandoverthecounter
- howmuchliquidhetypicallydrinkseachday
- whetherheconsumescaffeineandalcoholabouthisgeneralmedicalhistory,includ inganysignificant illnesses or surgeries
- Whatsymtomsarepresent

PhysicalExam

A physical exam may help diagnose benign prostatic hyperplasia. During a physical exam, a health care provider most often examines a patient's body, which can include checking for
dischargefrom the urethra

enlargedortenderlymphnodesinthegroin
aswollen ortender scrotum
tapsonspecificareasofthepatient'sbody

Performsadigitalrectalexam:

Adigitalrectalexam,or rectal exam,is aphysical examoftheprostate.Toperformtheexam, the health care provider asks the man to bend over a table or lie on his side while holding his knees close to his chest. The health care provider slides a gloved, lubricated finger into the rectum and feels the part of the prostate that lies next to the rectum. The man may feel slight, brief discomfort during the rectal exam. A health care provider most often performs a rectal examduringanofficevisit,andmendonotrequireanaesthesia.Theexamhelpsthehe althcare provider see if the prostate is enlarged or tender or has any abnormalities that require more testing.

Many health care providers perform a rectal exam as part of a routine physical exam for men age 40 or older, whether or not they have urinary problems.

Fig:9structuredigital rectum.

MedicalTests:

A health care provider may refer men to a urologist a doctor who specializes in urinary problems and the male reproductive system though the health care provider most often diagnosesbenignprostatichyperplasiaonthebasisofsymptomsandadigitalrectalexam.A

urologist uses medical tests to help diagnose lower urinary tract problems related to benign prostatic hyperplasia and recommend treatment. Medical tests may include

Urinalysis.
Aprostate-specificantigen(PSA)blood test.
Urodynamictests.
Cystoscopy.
Transrectalultrasound.
Biopsy.

Urinalysis.

Urinalysis involves testing a urine sample. The patient collects a urine sample in a special containerinahealthcareprovider'sofficeoracommercialfacility.Ahealthcareprovidertests the sample during an office visit or sends it to a lab for analysis. For the test, a nurse or technician places a strip of chemically treated paper, called a dipstick, into the urine. Patches on the dipstick change colour to indicate signs of infection in urine.

PSAbloodtest.

AhealthcareprovidermaydrawbloodforaPSAtestduringanofficevisitorinacommercial facility and send the sample to a lab for analysis. Prostate cells create a protein called PSA. Men who have prostate cancer may have a higher amount of PSA in their blood. However, a high PSA level does not necessarily indicate prostate cancer. In fact, benign prostatic hyperplasia,prostateinfections,inflammation,aging,andnormalfluctuationsoften causehigh
PSAlevels. Much remains unknown about howto interpret a PSAblood test, thetest'sability to discriminate between cancer and prostate conditions such as benign prostatic hyperplasia, and the best course of action to take if the PSA level is high.
Urodynamictests.

Urodynamictestsincludeavarietyofproceduresthatlookathowwellthebladderandurethra
storeandreleaseurine.Ahealthcareproviderperformsurodynamictestsduringanofficevisit
orinanoutpatientcenterorahospital.Someurodynamictestsdonotrequireanesthesia;others

mayrequirelocalanesthesia.Mosturodynamictestsfocusonthebladder'sabilitytoholdurine and empty steadily and completely and may include the following:
- uroflowmetry,whichmeasureshowrapidlythebladderreleasesurine
- postvoidresidualmeasurement,whichevaluateshowmuchurineremainsinthebladder after urination
- reducedurinefloworresidualurineinthebladder,whichoftensuggestsurineblockage duetobenignprostatichyperplasia

Cystoscopy.

Cystoscopy is a procedure that uses a tubelike instrument, called a cystoscope, to look inside theurethraandbladder.Aurologistinsertsthecystoscopethroughtheopeningatthetipofthe
penisandintothelowerurinarytract.Aurologistperformscystoscopyduringanofficevisitor in an outpatient center or a hospital. The urologist will give the patient local anesthesia; however,insomecases,thepatientmayrequiresedationandregionalorgeneralanesthesia.A urologist may use cystoscopy to look for blockage or stones in the urinary tract.
Transrectalultrasound.

Transrectal ultrasound uses a device, called a transducer, that bounces safe, painless sound waves off organs to create an image of their structure. The health care provider can move the transducer to different angles to make it possible to examine different organs. A specially trained technician performs the procedure in a health care provider's office, an outpatient centre, or a hospital, and a radiologist a doctor who specializes in medical imaging interprets the images; the patient does not require anesthesia. Urologists most often use transrectal ultrasound to examine the prostate. In a transrectal ultrasound, the technician inserts a transducerslightlylargerthanapenintotheman'srectum,nexttotheprostate.Theultrasound image shows the size of the prostate and any abnormalities, such as tumours.
Transrectalultrasoundcannotreliablydiagnoseprostatecancer.
Biopsy:

Biopsyisaprocedurethatinvolvestakingasmallpieceofprostatetissueforexaminationwith a microscope. A urologist performs the biopsy in an outpatient centre or a hospital. The urologistwillgivethepatientlightsedationandlocalanaesthetic;however, insomecases,the

patient will require general anaesthesia. The urologist uses imaging techniques such as ultrasound, a computerized tomography scan, or magnetic resonance imaging to guide the biopsyneedleintotheprostate.Apathologist adoctorwhospecializesinexaminingtissuesto diagnose diseases examines the prostate tissue in a lab. The test can show whether prostate cancer is present12.

Fig.10 Biopsy

ThelinkbetweenBPHand diabetes:

More and more evidence is showing that diabetes significantly increases the risk of benign prostatic hyperplasia. It also increases the risk of lower urinary tract symptoms in general. Hyperglycaemia and insulin resistance increase risk as well. People with type 2 diabetes were found to have larger prostate glands.
5a-DHThasaroleinthephysiologicalfunctionofthebetacellsinthepancreas.nasterideand dutasteride are often used in the treatment of benign prostatic hyperplasia. They inhibit enzymes called 5a-reductases.
Thisisinanefforttoreducethebiosynthesisof5a-DHT.Thiscancauseaformoftissuespecific androgendeficiency,butcancontributetovariouspathophysiologicalconditions.Thisincludes insulin resistance and type 2 diabetes.

Some other theories of why patients with diabetes are at higher risk of developing benign prostatic hyperplasia include the following:

Increasedsympathetictone
Insulinand related factorsstimulatingprostate growth
Alterationsinsexsteroid hormone expression
Inductionofsystemic inflammation

Oxidativestress

Experts also say that metabolic disturbances such as prediabetes and metabolic syndrome (which involves diabetes and heart disease and a higher risk of myocardial infarction) could play a role in the development of benign prostatic hyperplasia.
The insulin-like growth factor (IGF) axis and IGF binding proteins. Researchers have found that higher expression levels of IGF binding proteins predict higher prostate volume13.

ENLARGEDPROSTATEAFFECTTHEBLOODSUGAR:

Upon multiple adjusted linear regression analysis, prostate size correlated with elevated PSA ($P < 0.001$) and increased fasting glucose levels ($P = 0.023$). In non-DM BPH patients with normal testosterone levels, fasting glucose level is an independent risk factor for prostate hyperplasia14.

COMPLICATIONS:

Urinaryretention,

UTI[UrinaryTractInfections],
Haematuria,
Renal failure,
Residualurine,
Cardiovasculardisease.

RISKFACTORS:

Age40 years and oldermales,
Diabetesmellitus(Type 2diabetes)
Erectiledysfunction,
FamilyhistoryofBPH.
Hyperthyroidism
Decreasedsperm count

TREATMENT/MANAGEMENT:

Men with benign prostate hyperplasia may present acutely with urinary retention or may be seen in the clinic or primary care setting. Management of male urinary retention is covered in a separate topic.
In those with LUTS, treatment options range from watchful weight in to medical and surgical interventionanddependonthedegreeof"bother"ordiseaseburdentothepatient(as assessed by IPSS).

SURGICALMANAGEMENT

Transurethralresectionoftheprostate(TURP):Thisisthemostcommontreatment for BPH. During this procedure, your urologist will insert a rigid instrument called a resectoscopeintotheurethra.Thisiswhyitiscalledtransurethral.Insertingthescop ethisway means no cutting intotheprostate.Theywillthenusethecharged resectoscopetoremovethe excess tissue that is blocking the urine from leaving the bladder.
Youmaybeputtosleepwithgeneralanesthesia.Localanesthesiaforthelowerpartoft hebody may be used for this procedure. The average in hospital stay for TURP is 1 to 2 days.

Transurethralincisionoftheprostate(TUIP): ThisisasimilarproceduretoTURP. InsteadofprostatetissuebeingremovedthebladderneckandprostatearecuttorelaxThe bladder opening, allowing urine to flow more freely. TUIP is most successful on men with smaller prostates.

Simple prostatectomy: This method is asurgical procedurein which an incision is made throughtheabdomenorperformedlaparoscopically.Theinnerportionoftheprostat eglandis removed, leaving the outer segment intact.

MEDICALMANAGEMENT:

MEDICALMANAGEMENTOFBPHACCORDINGTOBLADDERCC LEVELS.

Asmall prostatehas avolumeof 30ml to40ml andaweight of20g to 70g.
Amedium prostatehas a value of40mlto 80mland aweightof 20g to 125g.
Alargeprostatehas avolume of40ml to100ml and aweight of 40g to 125g.
Anormalsized prostateisaround 25g.
Anenlarged prostatemay growwell overthreetimesthenormalsize[over 80grams].

Prostate<30 g:Alpha–adrenoceptor blockers.

Prostate>30 g5 Alpha– reductaseinhibitors ±Alpha –adrenoceptor blockers.

MEDICATIONS:
CLASS DRUGS DAILYDOSE
5ALPHAREDUCTASEINHIBITORS FINASTERIDE DUTASTERIDE 5MG 0.5MG
MINERALOCORTICOID RECEPTORSANTAGONIST[MRAs] TOLERODINE FESOTERODINE 1-2MGBID 4-8MG
PHOSPHODIESTERASE[PDEs]

INHIBITORS TADALAFIL 5MG
COMBINATIONPRODUCTS DUTASTERIDE- TAMSULOSIN 0.5/0.4MG

TABLE 1: MEDICATIONS

Medications:
Ahealthcareproviderorurologistmayprescribemedicationsthatstopthegrowthof orshrink the prostate or reduce symptoms associated with benign prostatic hyperplasia:

- alphablockers
- phosphodiesterase-5inhibitors
- 5-alphareductaseinhibitors
- combinationmedications

Alpha blockers:

Thesemedicationsrelaxthesmoothmusclesoftheprostateandbladdernecktoimpr oveurine flow and reduce bladder blockage:

- Terazosin
- Doxazosin
- Tamsulosin
- Alfuzosin
- Silodosin

Phosphodiesterase-5inhibitors:

Urologists prescribe these medications mainly for erectile dysfunction. Tadalafil (Cialis) belongs to this class of medications and can reduce lower urinary tract symptoms by relaxing smooth muscles in the lower urinary tract. Researchers are working to determine the role of erectile dysfunction drugs in the long-term treatment of benign prostatic hyperplasia.

5-Alphareductaseinhibitors:

These medications block the production of DHT, which accumulates in the prostate and may cause prostate growth:

- finasteride
- dutasteride

Thesemedicationscanpreventprogressionofprostategrowthoractuallyshrinkthe prostatein some men. Finasteride and dutasteride act more slowly than alpha blockers and are useful for only moderately enlarged prostates.
Combinationmedications:

Several studies, such as the Medical Therapy of Prostatic Symptoms (MTOPS) study, have shown that combining two classes of medications, instead of using just one, can more effectively improve symptoms, urinary flow, and quality of life. The combinations include

finasterideand doxazosin
dutasteride and tamsulosin (Jalyn), a combination of both medications that is available in a single tablet
alphablockers andantimuscarinics

A urologist may prescribe a combination of alpha blockers and antimuscarinics for patients with overactive bladder symptoms. Overactive bladder is a condition in which the bladder muscles contract uncontrollably and cause urinary frequency, urinary urgency, and urinary incontinence. Antimuscarinics are a class of medications that relax the bladder muscles.

PREVENTIVEMEASURESANDMEDICALMANAGEMENTOFPROSTATE ENLARGEMENT IN DIABETIC PATIENTS

PharmacologicTreatmentOptionsForBPH:
CLASS MOA DRUG DAILY DOSE (ORAL) ADVERSEFFECTS
Alpha- Blockers Relax tension in the prostatesmoothmuscle by targeting alpha receptors Alfuzosin Doxazosin Tamsulosin Terazosin Silodosin 10mg 1-8mg 0.4-0.8mg

1-10mg 8mg Erectiledysfunction, Dizziness, Infection, Hypotension
5 ARIS Block the growth of prostatecellbytargeting the 5alphareductase

Enzymeanddecreasing concentration of DHT Dutasteride Finasteride 0.5mg 5mg Erectile dysfunction, Abnormalejaculation
MRAs Decrease bladder SmoothmuscleCell concentration Byinhibitingmuscarinic receptor Tolterodine Fesoterodine 1-

2mg 4-8mg Dry mouth

PREVENTIVEMEASURESANDMEDICALMANAGEMENTOFPROSTATE ENLARGEMENT IN DIABETIC PATIENTS

PDE5

Inhibitors Decrease detrusor, prostate, and urethra smoothmuscletonevia increaseofintracellular cGMP Tadalafil 5mg Back pain,

Headache,flushing, nausea

Combination product Combined MOA from 5ARIandalphablocker Dutasteride+ Tamsulosin 0.5/0.4mg Seemonotherapyagentsabove

TABLE2:PHARMACOLOGICALTREATMENTLIFE LIFE-STYLE MODIFICATIONS:

Eatingmorefibretohelpprevent constipation,whichcan worsensymptomsof BPH.
AvoidingmedicationsthatcanmakeBPHsymptomsworse,suchasantihistaminesa nd decongestants. Reaching and maintaining a healthy weight.
Adoptingahealthful,low-fatdietandlimiting spicy foods.
Avoid alcohol, caffeine, and nicotine (all bladder irritants) Avoid drinking fluids after your evening meal.
Trytourinate atleast every3 hours.
Doublevoid(afterurinating,waitandtrytourinateagaintomakesureyourbladder is really empty).
Obesity,
Lackofphysicalactivity,
Dyslipidemia,
Diabetes mellitus,
Higherblood pressure,
Aheart-unhealthy diet,

and other factors that increase the risk for cardiovascular disease also appear to be associated with increased risk for BPH.
Reducingliquidconsumptionfor2hoursgoingtothetoiletbeforesleep,longjourney s, or other occasions when urinating may be difficult.
Doing exercises to strengthen the pelvic floor muscles. Working with a physician to train the bladder to hold more urine for longer. Reaching and maintaining a healthy weight.
Adoptingahealthful,low-fatdietandlimitingspicy foods15.

LITERATUREREVIEW.

PeterEClarket.,al.2013 on Association between physicalactivity,lower urinarytract symptoms (LUTS) and prostate volume have concluded that in this cross-sectional analysis,leisure-timeandhome-timePAwasinverselyassociatedwithLUTSseverity.The associationbetweenPAandLUTSseveritywasstrongerforirritativesymptomsanda mong obesemen,andwasnotmediatedthroughchangesinprostatesize.Ourresultsindicat ethe need for further detailed investigation of PA and LUTS16.

F. Comphaire et., al. 2014 on Preventing diseases of the prostate in the elderly using hormones and nutriceuticals have concluded a strategy to prevent prostate cancer that aims at providing men with partial androgen deficiency correct testosterone substitution withasustainedreleasebuccalbio-adhesivetablet.Inaddition,foodsupplementationwith extracts of Serenoa repens and a combination of the antioxidants selenium, (cis)-lycopene and natural vitamin E, together with fish oil rich in long-chain polyunsaturated essential fatty acids of the omega-3 group seems warranted. Clearly, a holistic approach including careful clinical and biological monitoring of the aging man and his prostate remains mandatory17.

N Caretta et.,al.2015 on Hypovitaminosis D is associated with lower urinary tract symptoms and benign prostate hyperplasia in type 2 diabetes have concluded that 25OH-Vitamin D levels were inversely correlated with both IPSS (R = -0.333; p = 0.006) and prostate volume (R = -0.311; p = 0.011). At multivariate analysis, hypovitaminosis D remained an independent predictor of both IPSS and prostate volume. In conclusion, we showed,forthefirsttime,anassociationbetween25-OH-vitaminDdeficiency,LUTS,and BPH in T2DM men18.

Zhen Chen et., al.2015 on Effect of obesity and hyperglycaemia on benign prostatic hyperplasiainelderlypatientswithnewlydiagnosedtype2diabeteshaveconcludet hat Aging, obesity, high glucose level, and insulin resistance increase the risk of BPH progression in elderly patients with newly diagnosed type 2 diabetes. Managing body weight and lowering the level of glycosylated haemoglobin may slow the progression of BPH in people with type 2 diabetes19.

KevinTMcVaryet.,al.2016onErectiledysfunctionandlowerurinarytractsymptoms secondarytoBPHhaveconcludedthatLUTSandsexualdysfunctionarehighlyprevalent in aging men. Both conditions are also significant contributors to overall quality of life. New data has emerged to indicate potential links in epidemiological, physiologic, pathophysiologic and treatment aspects of these two entities20.

Claus G Roehrborn et., al.2016 on Erectile dysfunction and lower urinary tract symptoms associated with benign prostatic hyperplasia (LUTS/BPH) combined responders to tadalafil after 12 weeks of treatment have concluded novel measure of combined response is useful in differentiating patients with clinically relevant symptom improvementforbothEDandLUTS/BPHaftertreatmentwithtadalafil5mgoncedail yvs placebo.Thiscombinedrespondermeasuremaybeusefulinfutureassessmentoftre atment benefitsacrosspatientgroupsaftervarioustypesoftreatmentintervention(e.g.,sur gicalvs pharmacotherapy vs non-pharmacological intervention)21.

Raymond C Rosen et., al.2016 on Update on the relationship between sexual dysfunction and lower urinary tract symptoms/benign prostatic hyperplasia have concluded that LUTS/BPH is an independent risk factor for sexual dysfunction in aging men. Further studies are needed to define the mechanism(s) underlying the link between LUTS/BPH and male sexual dysfunction. Additional studies of combination therapy for LUTS/BPH, sexual dysfunction, and other age-associated comorbidities are needed to establish new approaches to the optimal management of these conditions in aging men22.

XiaobingQuet., al.2017 on Prostatevolumecorrelates with diabetesin elderlybenign prostatic hyperplasia patients have concluded our study demonstrates that PV is closely correlatedwithdiabetesanddiabeteshasadirecteffectontheoccurrenceanddevelo pment of BPH23.

Sae Woong Kim et.,al.2017 on Results of a Randomized, Double-Blinded, ActiveControlled Efficacy and Safety of a Fixed-Dose Combination Therapy of Tamsulosin and Tadalafil for Patients With Lower Urinary Tract Symptoms and Erectile Dysfunction Trial have concluded he FDC 0.4/5 mg therapy was safe, well tolerated,andefficacious,indicatingthatcombinationtherapycouldprovideclinical benefitsforpatientswithBPH-associatedLUTScomplaintsandamelioratethecomorbidity of ED. Kim SW, Park NC, Lee SW, et al. Efficacy and Safety of a Fixed-Dose Combination Therapy of Tamsulosin and Tadalafil for Patients With Lower Urinary Tract Symptoms and Erectile Dysfunction: Results of a Randomized, Double-Blinded, Active-Controlled Trial24.

Cameron W Johnson et., al.2018 on Metformin inhibits the proliferation of benign prostatic epithelial cells have concluded that Our study demonstrates that metformin inhibits the proliferation of benign prostatic epithelial cells by suppressing the expression ofIGF-1RandIGF-1secretioninstromalcells.MetforminlowerstheG2/Mcellpopulation and simultaneously increases the G0/G1 population. Findings here might have significant clinical implications in management of BPH patients treated with metformin25.

M Rourpret et., al.2018 on Erectile dysfunction and diabetes: a review of the current evidence-based medicine and a synthesis of the main available therapies have concludedthattheaetiologyofdiabeticEDismultifactorial.Endothelialdysfunctioni sthe linkbetweendiabetes-inducedEDandcoronaryarterydisease.Aglobalapproachisneeded for the successful management of diabetic ED26.

Niketa sieunarine et., al.2019 on Investigating the link between benign prostatic hypertrophy, BMI and type 2 diabetes mellitus have concluded that his study did not show any significant differences in the mean values of PSA levels between diabetics and non-diabetics, between the 3 different groupings based on BMI ranges27.

John G Ryan et., al.2019 on Erectile dysfunction and its association with metabolic syndromeandendothelialfunctionamongpatientswithtype2diabetesmellitus

have concluded that Primary care physicians ought to establish trusting relationships with their patients,providingopportunitiesforthemtoprobesuchsensitiveissuesassexualactivities, as a means of addressing the possibility of ED. When making the new diagnosis of sexual dysfunction in the absence of metabolic disease or CVD, physicians ought to consider the riskforT2DMandCVD.Associationsbetweenmetabolicdisease,heartdisease,andsexual dysfunctionfurthersuggestthatallpatientswhoareobeseandhavedyslipidaemia,T2DM, and/or depression should be further screened for ED28.

Jonathan C levy et., al.2020 on Erectile dysfunction in diabetes mellitus that have concludedtheAetiology ofdiabeticEDis multifactorial although therelativesignificance of these factors arenot clear. A holistic approach is needed in the management of diabetic ED29.

Won ki Lee et., al.2020 on Postmicturition Dribble Is Associated with Erectile Dysfunction in Middle-Aged and Older Men with Lower Urinary Tract Symptoms have concluded that PMD was significantly correlated with ED and reinforced the relationship between LUTS and ED in middle-aged and older men. PMD might be an important component of the association between LUTS and ED30.

Michael B chancellor et., al.2021 on Type 2 diabetes but not metabolic syndrome is associated with an increased risk of lower urinary tract symptoms and erectile dysfunction in men aged <45 years have concluded that Men with T2DM and aged <45 years had more LUTS but a similar bladder emptying function than the controls. ED was highly prevalent and was associated with the severity of LUTS. Metabolic syndrome did not aggravate the severity of LUTS, emptying function or ED in the early stage of DM31.

PasqualeAnneseet.,al.2021onPreservingejaculatoryfunctioninyoungpatientswith lower urinary tract symptoms: medium- to long-term follow-up of prostatic urethral liftatasinglecentrehaveconcludedthatUroliftcanimproveurinarydisorderssecondary to BPH, preserving EjF and EF. It is a safe and easy method, reproducible, and with low incidenceofcomplications.Carefulselectionofpatientsismandatory.Themainreasonfor dissatisfaction is the higher expectation of better BPH symptoms relief although patients with high bladder neck and/or prostate volume >45 cm3 were aware of the possible failure32.

Longyun Liu et., al.2022 on Comparison of characteristics between Chinese diabetes mellitus-induced erectile dysfunction populations and non-diabetes mellitus-induced erectile dysfunction populations: A cross-sectional study have concluded that the aetiology, demographic parameters, degree of premature ejaculation, and related biochemical tests were significantly different between the DMED and non-DMED populations33.

Chunlin wang ea., tl.2022 on A Modified Procedure to Diagnose Erectile Dysfunction Using the International Index of Erectile Function (IIEF-6) Combined with the PrematureEjaculationDiagnosisTool(PEDT)viaanInternetSurveyhaveconcluded thatstablishingtheprevalenceofEDbyusing acombinationoftheIIEF-6 andPEDTwas more reliable than using the IIEF-5 alone. Further validation of the modified procedure, especiallyregardingtheeffectsofageontheresults,infuturestudiesisrequired.WangC, Zhang H, Liu Z, et al. A Modified Procedure to Diagnose Erectile Dysfunction Using the InternationalIndexofErectileFunction(IIEF-6)CombinedwiththePrematureEjaculation Diagnosis Tool (PEDT) via an Internet Survey34.

AIMANDOBJECTIVES.

AIM:

Tostudythepreventivemeasuresandmedicalmanagementofprostateenlargementin diabetic patients.

OBJECTIVES:

Tofindthepreventivemeasuresofprostateenlargementindiabetic patients.
Tofindthecomplicationsand riskfactors ofprostate enlargement.
Tofindthemedicalmanagementofprostateenlargementindiabetic patients.

PLANOFSTUDY
PHASE1:[OCTOBER–NOVEMBER 2022]

Identificationofstudyobjectivethroughliterature survey.
Procurementof consentfromhospitalauthorities.
Designofstandarddataentry form.

PHASE2:[DECEMBER2022–JANUARY2023]

Data collection.

PHASE3:[FEBRUARY-MARCH2023]

Data Analysis.

PHASE4:[APRIL-2023]

ReportSubmission.

METHODOLOGY

STUDYSITE:

Thepresent studywas conductedat VijayaHospital .(Pogathota,Nellore)

STUDYDESIGN:

Thestudy design is basedon the prospectivestudy.

STUDYPERIOD:

ThisstudywasconductedoveraperiodofsixmonthsfromOCTOBER-2022to APRIL-2023.

INCLUSIONCRITERIA:

- Theparticipants arethemaleinpatients in urology department.
- Themalepatientswhoareaccepted toparticipateareparticipated inthis study.
- Themen ofage40yearsold people areincluded in thisstudy.

EXCLUSIONCRITERIA:

- Themaleinpatients who arerefused toparticipateareexcludedfrom the study.
- Thefemaleinpatientsin urologydepartment areexcluded fromthe study.

STUDYINSTRUMENT:
Thesuitabledataentryformwaspreparedtoconductthestudy. The different part of the data entry forms are:

PART 1:

Demographicdata:relatedtopatientsage,gender andhabitsofpatientswas collected.

PART 2:

ComplaintsofthepatientsSymptomsofBPHthatleadtoadmissioninthehospitalwas collected.
PART 3:

The various diagnostic tests [ECG,2D ECHO, urine culture, kidney ureter and bladder scan (KUB)] and treatment done to the patients.
PART 4:

Thepostoperativemonitoringdata[painscale,urineoutputdata,senseofreliefscale]of the patient was collected.

INFORMED CONSENT:

Study protocol was approved by Hospital committee. The nature and purpose of study was explained, and their concern was sought.

Thestudysubject wasinterviewedwithappropriatepre-prepareddataentryform.They were provided information about the study and its objectives. The assurance of confidentially datawasgivenandthosewhomettheinclusioncriteriawereinvitedtoparticipateint hestudy.

Those who agreed to participate in the study signed a pre-informed consent and were interviewed, their diagnostic investigations were collected from the respective sheets.

STATISTICAL ANALYSIS:

ThecollecteddatawasanalysedbyusingSPSS21software.analysiswasdonebyusing number and percentage for nominal data [such as gender, marital status, percentage].

RESULTS

1.PREVALENCEOF BPHIN OURSTUDY AREA.

MONTH	TOTAL NUMBEROF CASES.	NO.OFBPHWITHTYPE2 DIABETES CASES PER MONTH [N=84]
October	200	15
November	240	16
December	110	9
January	140	10
February	250	22
March	170	12

TABLE:3

Figure:11Prevalenceofbph.

1.INCIDENCEOFBPHINMENOFDIFFERENTAGEGROUPS.

Tableno:4

AGEGROUP	NO.OFCASES [N=84]
40-49	6
50-59	12
60-69	24
70-79	20
80-89	22

c

COMPLICATIONSOFBPH.

Tableno:5

COMPLICATIONS	NO.OF CASES
UrinaryRetention	65
UrgencyofUrine	17
UrinaryTract Infections	15
Burning Micturition	05
Nocturia	10
Dribblingofurine	08
Troublingtostarturine	40
Reducedflow	55
Leakageofurine	13
PainfulUrination	12

Fig: 13COMPLICATIONOFBPH

ALPHA ADRENOCEPTOR BLOCKERS[Prostate<30g]. 5-ALPHA REDUCTASEINHIBITORS [Prostate>30g].

Doxazosin
Dutasteride
Prazosin Finasteride
Terazosin COMBINATIONPRODUCTS.
Tamsulosin Dutasteride+ Tamsulosin.
AlfuzosinER Finasteride+ Tamsulosin
Silodosin Siladosin+Dutasteride
Phenoxybenzamine

TABLE: 6

PROSTATESIZE	VOLUME	WEIGHT
Normal	25ml	25g
Small	30-40ml	20-70g
PROSTATESIZE	VOLUME	WEIGHT
Medium	40-80ml	20-125g
Large	40-100ml	40-125g
Enlarged	>100ml	>125g

Fig:14Prostatesizecomparedwithbladdercclevels

HUMANPROSTATEWEIGHTTHATHASCOMPAREDWITH AGE:

TABLE: 7

WEIGHTOFPROSTATE[IN GRAMS]	AGEOFTHEINDIVIDUALS[IN YEARS]
28.2g	40-49years
30.8g	50-59years
35g	60-70years
46.2g	75years

FIG:15Humanprostatesizehas comparedwithage individuals

BPHMEDICATIONSBASEDONAGEGROUP[AnALPHA–BLOCKERS SUBTYPE].

TABLE:8

DRUG	AGE 50-59	AGE 60-69	AGE 70-79	AGE 80-89	% OF RETENTION INCC
Terazosin	31%	31%	34%	41%	50cc
Tamsulosin	43%	42%	37%	36%	51cc-60cc
Alfuzosin	8%	6%	6%	4%	61cc-80cc
Doxazosin	18%	21%	23%	19%	81cc-100cc

PREVENTIVE MANAGEMENT OF BENIGN PROSTATE HYPERPLASIABASEDONBLADDERCCLEVELS.[ALSOINCLUDES SINGLE DRUGS AND COMBINATION OF DRUGS.
TABLE: 9

NO.OF CASES [TOTAL CASES COLLECTED =84]	DRUGSUSED	BLADDER CAPACITY[<100CC]
40 Cases	Siladosin	20-50cc
20 Cases	Tamulosin	50-60cc
24 Cases	Dutasteride+Tamulosin	60-70cc

FIGURE:16

FIGURE:17

AFTERTREATMENT:

FIGURE: 18

IDENTIFICATIONOFBPHIN(TYPE2DIABETES)BYKUBDIAGNOSTIC TESTS COMPARED WITH BMI CLASSES.

TABLE:10

KUB[KIDNEY,BLADDER, URETER] TEST[Totalno. ofcases 84]	BMI[BODYMASSINDEX]
21 cases	Normal
41 cases	Overweight
22 cases	Obese

45 KUBTESTVS BMI
40
35
30
25
20
15
10
5
0 Normal Overweight Obese

Fig:19KUBTestVsBMI

BMIRANGES:

NORMAL	OVERWEIGHT	OBESE
18.5-24.9	25-29.9	30-34.9

BODYMASSINDEXINPICTURISEDDIAGRAM:

STATUSOFDIABETESMELLITUSINBPHPATIENTSDURING TREATMENT:

Fig:20Diabetesmellitusinbph patients

NO.OFPATIENTSHAVINGUTIASSOCIATEDWITHBPH.

Fig:21UTIAssociatedwithbph

NOOFPATIENTSSTAYINGATHOSPITAL:

NO.OFPATIENTSWITH UTI	NO.OFPATIENTS HOSPITALIZED
11	0

1. DISCUSSION

ThestudyentitledPreventiveMeasuresandMedicalManagementofProstateEnlargementin Diabetic Patients: - A prospective study was carried out for a period of six months in a 300 bedded hospital in the department of urology. The study was carried out during the period of October 2022-April 2023, a total number of 84 patients who met the inclusion criteria was enrolled in the study.
TheprevalenceofbenignprostatehyperplasiacasesinVijayahospitalwasnoted,15casesout total 200 cases in a month of October and 16 cases out of total 240 cases in a month of November,9 cases out of total 110 cases in a month of December, 10 cases out of total 140 cases in a month of January, 22 cases out of total 250 cases in a month of February, 22 cases out of total 170 cases in a month of March (TABLE :1).
The age distribution was analysed, and the results revealed that 6 of the patients were in the groupof40-49years,12ofthepatientswereintheagegroupof50-59years,24ofthepatients were in the age of 60-69 years,20 of the patients were in the age group of 70-79, 22 of the patients were in the age of 80-89 years (TABLE:2).
The various symptomatic complications caused by benign prostate hyperplasia that leads to further examination and finalise the diagnosis of the patients were analysed and the results revealed that from 65 patients were complained of urinary retention , 17 of the patients were complained the urgency to urinate, 15 of the patients were complained the urinary tract infections ,5 of the patients were complained the burning micturition , 10 of the patients were complained the nocturia , 8 of the patients were complained about dribbling of the urine,40 of the patients were complained about problem in starting to urinate, 55 of the patients were complained of reduced flow of while urinating,13 of the patients were complained about leakage of urine and 12 of the patients were complained of pain during urination.
Benignprostatehyperplasiamedicationbasedonagegroups.ThedrugTerazosingiventothe agegroupof50-59itshowsto(31%)effectivenessandtotheagegroup60-69itshows(31%) effectiveness and given to the age group of 70-79 it shows (34%) and given to the age group of80-89itshows(41%)effectivenesstothepatientsbasedon50ccbladderretention.Thedrug Tamsulosingiventotheagegroupof50-59itshowsto(43%)effectivenessandtotheagegroup of70-79itshows(37%)andgiventoagegroupof80-89itshows(36%)effectivenesstothe patients based on 51cc-60cc bladder retention. The drug Alfuzosin given to the age group of 50-59 it shows to (8%)effectiveness and given to the age group of 60-69 it shows (6%)effectivenessandgiventotheagegroupof70-79itshows(6%)andgiventotheagegroup of80-89 it shows (4%)effectiveness to thepatients based on 61cc-80cc bladderretention. The drug Doxazosin given to the age group of 50-59 it shows to (18%) effectiveness and given to the age group of 60-69 it shows (21%) effectiveness and given to the age group of 70-79 it shows (23%)and given to the age group of 80-89 it shows (19%)effectiveness to the patients based on 81cc-100cc bladder retention.
Preventive management of Benign prostate hyperplasia based on bladder cc levels. [Also includes single drugs and combination of the drugs]. Out of 84 collected cases in the Vijaya hospital the drug Siladosin were given to the 40 cases of the patients in bladder cc levels of 20cc-50cc, the drug tamsulosin were given to the 20 cases of the patients in bladder cc levels of50cc-60cc,thedrugdutasteride+tamsulosinweregiventothe24casesofthepatientsinthe bladder cc levels of 60cc-70cc.
Before treatment vs after treatment: In the before treatments 37 patients' cases were collected in the range of 50cc bladder capacity,31 patients' cases were collected in the range of 51cc– 70cc bladder capacity, 16 patient cases were collected in the range of 71cc-100cc bladder capacity out of total 84 cases. In the after treatment 37 patients' cases were collected in the range of 50cc bladder capacity, 29 patients' cases were collected in the range of 51cc – 70cc bladdercapacity,18patients'caseswerecollectedintherangeof71cc-100ccbladdercapacity out of 84 cases.
Identification of BPH in[type 2 diabetes] by KUB (kidney ureter and bladder) diagnostic test compared with BMI (Body Mass Index). we have collected 21 cases in the range of normal patientsbasedonBMIcalculations,alsocollected41casesintherangeofoverweightpatients basedonBMIcalculations,alsocollected22casesintherangeofobesepatientsbasedonBMI calculations.