Pharmaceutical Treatment Of BPH And Its Effect On Indications For Prostate Surgery

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Benign Prostatic Hyperplasia (BPH) is a pathological description of an aging process that affects a great majority of men. Classically, obstructive and irritative symptoms such as frequency, nocturia and weak urinary stream are described as "prostatism". Microscopically, BPH can be described as hyperplasia of stromal and epithilial cellular element which can macroscopically present as a gross adenomatous enlargement of the prostate gland. Thus, treatment of BPH is aimed at alleviating symptoms of prostatism and associated morbidities of prostatic obstruction.

Historically, the decision to intervene in the disease was based on the severity of symptoms as perceived by the patient or until the obstruction posed an increased risk to the patient's health. Today, driven by the impact of social and financial factors influencing payment of therapeutic procedures for BPH, a variety of alternative therapies to treat BPH have evolved. These have included both medical therapy and the advent minimally invasive options. This review will focus on the medical therapies, however, it is important to understand the risk factors and natural history of BPH to appreciate the potential role that these therapies will have.

Natural History and Etiology of BPH

BPH is both a scientific and medical enigma because it has been difficult to relate its pathogenesis to its clinical presentation. Autopsy studies (Berry et al, 1984) and the Baltimore Longitudinal Study of Aging (Guess et al, 1990) have demonstrated that most men above the age of 65 will have both clinical and pathological evidence of BPH. Unfortunately, true estimates of its prevalence in males around the world has been hampered by a lack of a precise clinical definition of BPH. This lack of a precise definition has made studies examining surgery rates and results, geographical data, racial differences, environmental factors and diet associations in different studies difficult to compare (Barry, 1990).

Additionally, the etiology of BPH remains debated. Common theories have included the role of androgens, specifically dihydrotestosterone (Coffey, 1986); a re-induction of embryonic cells (Cunha, 1973); growth factors (Griffiths et al,1991); and, most recently, a disturbance of prostate apoptic process or programmed cell death leading to size increased secondary to a decreased rate of cell death (Montironi, 1993). What remains most clear today is that there is still much to learn about BPH.

Despite the lack of a precise definition, studies available that describe the natural history of BPH such as those of Clarke (1937) , Birkhoff (1976) and Ball (1981) provide qualitative conclusions. Although these studies were small and with undefined selection criterias, one can see that BPH is not necessarily an unrelenting process and that factors predicting progression are largely undefined. In their studies, symptomatology seems to be the most important parameter to not only assess but to compare and measure for outcome.

Clinical Assessment of BPH

Thus, the clinical assessment of BPH has generally focused on symptoms until the obstruction produced by the prostate poses a threat to the patients clinical status. Symptoms can be divided into obstructive and irritative categories, and attempts have been made to quantify these symptoms with quantitative symptom indices. Among the various indices utilized are the Boyarsky (Boyarsky,1976), Madesen-Iverson (Madsen,1983) and Maine Medical Assessment Program (Fowler,1988). In providing a platform to develop a rational approach to treating BPH, the AUA develop a standardized symptom indices that is now widely utilized and statistically validated in several studies as a reliable tools for comparison (Barry, 1992). The value of these indices are that it quantifies the severity of baseline symptoms and allows a parameter with which to measure disease progression and response to therapy. These symptom indices are not BPH specific and have so far not been proven to correlate to degrees of obstruction. In fact, comparison of AUA symptom scores in men and women demonstrate surprisingly similarly distribution per matched age group (Huang, 1994). This is not surprising since there have not been any good studies correlating symptom severity to obstruction.

While there are clinical issues that influence management such as impaired bladder emptying, bladder outlet obstruction, infection, urinary retention and hematuria, they are not necessarily BPH specific and studies have not proven a clear relationship to BPH. While there are tools to measure obstruction, such as uroflometry and multichannel video urodynamics, the correlation of functional obstruction to symptoms and symptom improvement is not clear. While these tools are limited in their evaluation of BPH, they do help clarify issues of differential diagnosis in individual cases such as patients with diabetes who may have a non - BPH related voiding dysfunction. No clear correlation has been demonstrated between severity of obstruction and clinical, physiological and pathological progression of end stage BPH.

While no study has clearly demonstrated a correlation between prostate size, degree of obstruction ,and symptom severity with the presently available technology, it can be agreed that symptoms do get better following treatment aimed to decrease obstruction. Thus, in evaluating BPH, the history focuses on symptom severity and its impact on lifestyle or what is now termed ìbotherî. Today, this has evolved into the AUA symptom score and the AUA-BPH guidelines, a set of guideline constructed by a panel reviewing all the available literature and data on BPH (McConnel, 1994).

As described by the guidelines, symptoms are not BPH specific and it is important to consider and exclude diagnoses such as diabetes, neurologic diseases, prostate cancer, bladder cancer and urethral strictures. In addition, medication effects from anticholinergic, antihistamines and alpha adrenergic agonist need also to be considered as agents that affect bladder emptying and storage. The physical exam focuses mostly on the digital rectal exam mainly to exclude other diagnosis such as cancer and prostatitis. One should also examine for a suprapubic mass in order to evaluate retention. Of the many laboratory test available, a urine analysis and serum creatinine serves as a good initial screens to evaluate for diabetes, hematuria, infection and renal insufficiency. An optional test that evaluates for prostate cancer is a serum prostate specific antigen (PSA). Additional diagnostic studies that may be employed are upper tract imaging, cystoscopy, urodynamic studies, and transrectal ultrasonography. These studies are more pertinent when the initial laboratory studies are abnormal or as a guide for treatment selection.

In what has become a point of controversy for many is the indication for intervention and what kind of intervention to use. There are absolute indications for treatment which include: urinary retention, recurrent urinary tract infections, renal insufficiency from prostatic obstruction and refractory gross hematuria. However, relative indications such as symptoms affecting one's quality of life are left to the discretion of both the patient and physician.

Recently, the advent of medical therapies for BPH have added a new dimension to symptom treatment. The major two classes of medical therapy involve either hormonal manipulation of BPH or and alpha adrenoreceptor blockade. These medication have provided is an intermediate treatment for patient symptoms not severe enough to warrant surgery.

HORMONAL THERAPY

Introduction

Hormonal therapy for BPH is not a new approach. It is well known that the two factors which contribute to the development of BPH are aging and androgens. Thus, the suppression of androgens has been a concept that has been studied for over a century (Kirby, 1994). White (1895) and Cabot (1896) reported greater than 80% of patients with BPH had improved symptoms

after castration. In addition, BPH is unreported in males castrated early in life and is rarely seen in men under 40 (Lepor, 1989). Pathologic studies on men and animals have demonstrated androgens suppression to be associated with prostate shrinkage (Peters, 1987; Brendler, 1983).

With the advent of antiandrogen pharmaceutical therapies, studies on animals and men with BPH began. Pierson in 1946 utilized stilboestrol with moderate amelioration of symptoms in his small series of patients. Kaufman and Goodwin (1959) utilized testosterone propionate and diethystilboesterol with improvement in symptoms, uroflow and size in many cases. Progestational agents that inhibit LH release and block androgen receptors had also been used. Geller in 1965 used hydroxyprogesterone with some improvement. Donkervoort (1975) and Geller (1979) reported using megestrol acetate in the 1970s. LHRH analogues and other steroidal androgen receptor blockers have also been utilized such as cyproterone acetate by Scott and Wade (1969) and, naferelin acetate by Peters and Walsh (1987) and buserelin by Bosch (1989). In these studies, an approximate 25% reduction in gland size were noted with some clinical improvement. While improvement was noted in most series, adverse side effects such as decreased libido and impotence have kept these drugs from BPH treatments.

Another potent antiandrogen utilized is flutamide. Caine (1975) reported urodynamic improvements in a small double blind placebo controlled study. In a multicenter study, Stone and associates (1989) reported a 23% reduction in prostate size and maximum uroflow increased from 9ml/sec to 10.1 ml/sec after 3 months along with symptom improvement. What is interesting with flutamide are its side effects. Gynaecomastia. breast tenderness and gastrointestinal symptoms affected half the patient population. However, unlike the other discuss androgen suppression agents, there was minimal loss of potency and libido. Unlike the other antiandrogens, flutamide has less progestational actions and causes an effect resulting in an increasing level of serum testosterone with time. Overall, the search for a antiandrogen ìpillî has demonstrated drug with only modest clinical improvements but with hormonal and hypogonadal side effects that limits their use.

5-Alpha Reductase Inhibitor

In 1963, Farnsworht and Brown discovered that testosterone is metabolized in the prostate gland to DHT by 5-alpha reductase.

Soon thereafter, Bruchovsky and Wilson (1968) as well as Anderson and Liao (1968) suggested that DHT is the main intracellular androgen regulating prostate growth. These findings paralleled those of Imperato-McGinley and associates (1974) who described the 5-alpha reductase deficiency syndrome in men characterized by pseudohermaphroditism, and, more importantly, a small to absent prostate which never grew in size. These men were also sexually potent and able to ejaculate. These findings stimulated a search for a 5-alpha reductase inhibitor to block the formation of DHT.

Finasteride

The first successful 5-alpha reductase inhibitor to be synthesized was a neutral 4-azasteroid compound named finasteride by Rasmusson and associates (1984). It acts as a pure 5-alpha reductase subtrate inhibitor by acting as a testosterone analogue binding to the 5 (- reductase enzyme complex. Early studies with 4MA, a finasteride like compound demonstrated ventral prostate growth inhibition in rats and a reduction in prostate volume by 64% in beagles (Brooks, 1981). In humans, Stoner (1990, 1992) demonstrate a reduction of 18% on 5mg/day dosing in three months with shrinkage up to 28% in a 6 month study. More importantly, the early trials of finasteride demonstrate few adverse side effects while significantly reducing the plasma levels of DHT. At 5 mg /day, the incidence of decreased libido, impotence and ejaculatory disorders were 5% or less. In the recent placebo controlled phase III trial by the Finasteride Study Group (1993), and Gormley and associates (1992), the 5mg / day dosage produce an average fall of 3.3 points in the AUA symptom score while producing an average 22% increase in maximum urinary flow rate (1.7ml/s) with a 22% decrease in prostate volume. Tamela and Kontturi (1993) as well as Kirby and associates (1993) also demonstrated an interesting fall in maximum voiding pressure that was concomitant with falls in AUA symptom scores and increases in maximum urinary flow rate.

Based on the recent AUA BPH guidelines, the patient population to offer finasteride as a treatment option are those with moderate to severe AUA symptom scores. The recommended dosage is 5mg/ day and patients should be advised that although symptoms may improve soon after commencing therapy, maximal effect may take 6 to 12 months. Of the adverse side effects, most are mild and consist mainly of decreased libido, impotence and ejaculatory disorders. Overall, finasteride is a well tolerated drug with no known significant drug interactions.

The Future

On the horizon for future development and clinical evaluation is another 5 (- reductase inhibitor, episteride, which unlike finasteride is a product inhibitor (DHT analogue) (Issacs, 1993). Episteride appear to have a higher binding affinity for the specific 5-alpha reductase type 2 isozyme isomer present in the prostate (Levy, 1994) and in animal studies, it has similar effects on DHT and prostate tissue as finasteride (Lamb, 1992). How this will evolve clinically remains to be studied.

ALPHA ADRENORECEPTOR BLOCKADE

Introduction

In what has proven to be a fascinating pharmacophysiologic approach to the treatment of BPH is the application of alpha adrenoreceptor blockers. While it was known that alpha adrenoreceptors innervated the bladder neck and pharmacotherapies were initiated to treat outflow obstruction in neurogenic voiding dysfunction in the early 1970s (Kleenan, 1970; Krane, 1973), it was not until Caine and associates (1975, 1976) identified these receptors within the prostate stroma and capsule that alpha adrenoreceptor blockage for treatment of BPH developed formally. Since then, numerous investigators has reinforced and focused the concept of increased tone contributing a factor to prostatic obstruction.

The prostate gland in BPH contains more smooth muscle than a normal prostate. Intracellular studies of smooth muscle cells in BPH show an increased number of organelles such as mitochodria implying increased activity and thus tone (Bartsch, 1979). Autonomic innervation studies have demonstrated that adrenergic fibers which release noradrenaline stimulate specific adrenoreceptors in the prostate (Lepor, 1984). Lepor and Shapiro (1984), Hedlund and

associates (1985) and numerous others have demonstrated that two specific adrenoreceptor populations reside in the prostate, alpha-1-adrenoreceptors and alpha -2-adrenoreceptors. There is an increased in alpha- 2- adrenoreceptors in BPH stroma. However, these receptors have been identified mostly in the glandular basement membrane and blood vessels of the prostate (Hedlund, 1985). Alpha-1 -adrenoreceptors appear homogeneously distributed in the prostate gland. In vitro studies of prostatic smooth mucle with alpha-1 and alpha-2 adrenoreceptor agonists and antagonist have demonstrated alpha-1-receptors to be primarily responsible for smooth muscle contraction (Lepor,1984). Further subtyping of alpha 1 adrenoreceptors into alpha 1a, alpha 1b and alpha 1c have been accomplished (Ruffolo,1991). Subsequent studies have pointed to the alpha-1c adrenoreceptor as the subtype responsible for smooth muscle contraction in the prostate gland (Lepor,1993). But how do these strong pharmacophysiologic finding pointing towards potential phamaceutical control of prostatic tone translate into functional clinical significant applications for BPH?

Phenoxybenzamine

The earliest studies with alpha adrenoreceptor blockers were performed with phenoxybenzamine, a non-selective alpha-1- and alpha-2- adrenoreceptor blocker. In two early placebo controlled studies by Caine et al (1981)and Abrams et all (1982), there were improvement in symptoms and urodynamic parameters such as maximum urinary flow rates. However, adverse effects such as dizziness, lethargy, palpitations nasal congestion and postural hypotension were encountered and thought due to the alpha 2 effects of the drug. In addition, phenoxybenzamine, a chemical relative of nitrogen mustard has been associated with gastric carcinomas in rodent studies (Caine, 1986).These adverse effects have limited its use. Phentolamine, another non-selective alpha blocker, is limited in its use and not widely studied due to its poor oral absorption, short duration and hypotensive complications (Kirby, 1993). These factors are important in the selection and design of alpha blockers to treat BPH.

Prazosin

Since alpha-1-adrenoreceptors are responsible for prostatic smooth tone and the side effects of phenoxybenzamine are due mostly to it alpha 2 adrenorecptors, it seemed logical to employ selective alpha-1 adrenoreceptor blockers. Design initially and used clinically as an antihypertensive agent, prazosin became the first of many alpha -1 adrenoreceptor blockers to be studied for the treatment of BPH. Shapiro and associates (1981) demonstrated that prazosin inhibited the contraction of strips of prostate capsule and adenoma. In several small double blind studies with placebo, both symptoms and urodynamic parameters were improved (Hedlund, 1983; Martorana; 1984; Kirby, 1987). Chapple et al (1990, 1992), for example, demonstrated a 34% increase in maximum flow rate along with a mean decrease of 20.7% in maximum detrusor voiding pressure along with symptom improvements. Currently, praxoxin is FDA approved for hypertensive applications and is available for use. The drug has a rapid response and is short acting with peak plasma levels attained within 3 hours and a half life of 2 to 3 hours. For BPH treatment, this translates to a recommended twice to three times a day dosing schedule which is started at 0.5 mg at each dose and increased gradually to 2 mg over several weeks. Like most short acting alpha blocker, there is an increased chance of postural hypotension in the first few days of use. The short acting nature of this drug is its main disadvantage. However, it is still one of the most widely prescribed alpha-1-adrenoreceptor blocker for BPH in the world and its current lower cost compared to other longer acting agents have made this drug a available choice for BPH treatment (Jonler, 1994).

Other Alpha adrenoreceptor blockade

Many other alpha adrenoreceptor blockers have been studied such as nicergoline, thymoxamine, ketranserin, alfusosin and indoramin (Kirby, 1993). Most of the series were small and the drugs are not widely available, Therefore, their usage for BPH in the United States is limited in clinical practice. However, most have shown similar improvements in treating BPH. Alfusosin is not FDA approved but has been studied in many large European studies. Lukacs et al and Jardin et al in 1994 reported on 5849 and 983 patients respectively and reported significant improvement in Boyarsky-modified symptoms scores compared to placebo. Of those that are well prescribed and attaining greater popularity in the United States as a alpha adrenoreceptor blocking medical therapy for BPH, terazosin (currently FDA approved for the treatment of the symptoms of BPH) and doxazosin (FDA filed in 1993) are both widely available and currently approved by the FDA for hypertension treatments.

Terazosin

Terazosin and doxazoxin are both long acting selective alpha 1 adrenoreceptor blockers. Terazocin is well absorbed orally and attains it peak plasma level at 1 hour. It has a serum half-life of 12 hours. As such, terazocin is amenable to a once a day dosing and due to its rapid action, it has a potential first dose effect like that of prazocin (Jonler, 1994). First reported for the study of BPH by Dunzedorfer in 1988 in a small series indicating improvement over placebo, terazocin has been extensively studied by many including several series by Lepor and associates. In 1990 in a small series of 39 patients, Lepor demonstrated not only symptom improvements and increases in peak urinary rates, but that these improvement appeared to be dosage dependent especially with regard to peak urinary rates. In a multicenter study, Lepor (1992) reported on 285 patient receiving either placebo of 2,5,10 mg daily. He found all patients demonstrated an improvement in Boyarsky symptom scores and an increase in peak flow rates of 1.7 and 3.0 ml/sec in the 5 mg and 10 mg per day group respectively compared to placebo. What was interesting was that these improvements demonstrated a clear dose-dependent response that does not seem to plateau at 10 mg suggesting that a higher dosage if tolerable might provide a better clinical response. In addition, the response appears to be durable (Lepor,1993).

As with prazocin, few adverse effects were reported and the drug is well tolerated. Dizziness, headache, asthenia and postural hypotension were the usual major complaints reported (Lowe, 1994). As described in the prescribing information insert, the recommended initial regimen for patients is 1mg/day for three days, then 2mg/day for 12 days and then a stepwise increase in dosage to 5 mg/day for six days, 10mg/day for six days and even 20 mg/ day as needed to balance clinical response and tolerability

of the drug. The drug is usually taken at bedtime. Currently, terazocin is the only alpha-1-adrenoreceptor blocker approved by the FDA for treatment of BPH.

Doxazocin

Doxazocin is the newest widely prescribed antihypertensive alpha-1-adrenorecptor blocker to be studied and prescribed for the treatment of BPH. It is a structural analogue of prazocin but has a longer plasma half-life of 22 hours. Peak plasma levels are attained at 2-3 hours (Prescribing Information Insert). As a antihypertensive agent, it is extensively utilized and has had minimal significant side effects (Jonler, 1994).

One of the earliest published series is by Chapple et al in 1991. In this multicenter placebo controlled study of 135 patients at 4mg per day dosage, they reported a significant improvement in symptoms with a mean maximum urinary flow rate improvement of 2.6 ml/second in the Doxazocin group. Christensen et all in 1993 who studied 100 patients in a European randomized, double blind, placebo controlled study reported an overall patient assessed improvement in symptoms of 79% in the doxazocin group versus 44% in the placebo group on 4mg per day dosing. Maximum urinary flow rate was improved in the doxazocin group by 1.5 mls/sec versus a deterioration of 0.3 in the placebo group. There was only minimal adverse side effects equally present in both groups.

Several ongoing reported clinical investigations are currently underway and seem to well demonstrate dozaxocin's efficacy and safety for the treatment of BPH. In the Multicenter Doxazocin Study Group reported by Mobley (1994), 566 men who were 45 years or older were studied in one of three double blind placebo controlled study, maximum and average urinary flow improved by 2.3-3.3 and 0.6-1.6 ml/sec in doxazocin and placebo groups respectively. In addition, symptoms were also improved significantly in the doxazocin group for doses 4-8 mg/day dosage. Significant efficacy was achieved within 3 weeks of initiation of therapy. Adverse effects reported were mainly dizziness, fatigue and headache. The effects of dozaxocin on normotensive patient's blood pressure was minimal in this study. Kirby et al (1994) has also reported minimal blood pressure changes in normotensive men compared to larger changes in hypertensive men. Fawzy and associates (1993) have also reported similar improvements in symptom score, urinary flow rates and adverse effects in their study with 4,8 and 12 mg per day dosing in their multicenter study of 216 patients.

Currently under FDA evaluation for approval for BPH applications, the suggested regimen for initiating and maintaining dozaxocin dosage is to start at 2 mg per day and titrate the dose in a stepwise manner to 4, 8 and potentially 12 mg per day dosing over several weeks. Patient should be particularly monitored for side effects such as postural hypotension as with all alpha 1 adrenoreceptor blockers. In addition, to the adverse side effect mentioned for other alpha blockers, doxazocin has been associated with lowering levels of serum insulin, glucose and cholesterol in some hypertensive patients (Lehtonen, 1990; Pool, 1991). This effect may be of benefit to some patients, but is an effect to consider and monitor in the diabetic patient on medications.

In a pilot study of 43 patients by Kaplan in 1992, the safety and efficacy of doxazosin (4mg/day) and terazosin (5mg/day) were compared in morning and evening once a day dosing schedules. With both drugs, there was significant improvements in Boyarsky symptom scores on medical therapy. However, there was no significant difference in scores between the drugs and between morning and evening dosing schedules. It is noteworthy that 7/8 adverse events occurred in patients randomized to the morning dose.

Tamulosin

In the search to develop a more selective and long acting alpha blocker for BPH applications, tamulosin, a specific alpha-1 adrenoreceptor blocker, was synthesized. The first published study was by Kawabe and Niijima in 1987. They treated 77 patients for two weeks. The reported an overall 80% improvement in patient symptoms with an increased in peak urinary flow rate of 3 ml/sec. In 1990, Kawabe reported a double blind placebo controlled study of 270 patients receiving either placebo or 0.1, 0.2, 0.4 mg. As in the previous study, there were significant improvements in symptoms and urinary flow with tamulosin compared to placebo. Of the adverse side effects reported, 5 patients had complaints of gastrointestinal discomfort and nausea. One patient in the 1987 study had a elevation of liver enzymes after two weeks of treatment. Tamulosin is currently not available in the United States but is undergoing FDA approval. It is a promising and interesting alpha-1 adrenoreceptor blocker because it is the only one available that demonstrates a high affinity for the alpha-1c adrenoreceptor, the receptor responsible for smooth muscle contraction in the prostate stroma (Kenny, 1994).

The Future of Alpha Adrenorecptor Blockade

Future developments in alpha adrenoreceptor blockers are focusing on receptor subtype specificity. Since prostate smooth muscle activity is mediated by the alpha 1c receptor and related toxicity is mediated by the other two receptors, alpha 1a and alpha 1b, an highly specific alpha 1c adrenoreceptor blocker should demonstrate a important advantage over the presently available adrenoreceptor blockers for BPH.

Lastly, combination therapy is a concept that is theoretically attractive because it seeks to treat BPH through two different mechanisms. Using finasteride will shrinks the prostate gland in the glandular/epithelial portion of the prostate stroma. Using an alpha adrenoreceptor blocker relaxes and decreases muscle tone in the smooth muscle portion of the prostate gland. Theoretically, the additive effects should produce a more efficacious response than either alone. This combination therapy is currently under study in a Veterans Administration cooperative study of about 1,200 men that are randomized in a double blind study to placebo, terazosin, finasteride ,and terazocin and finasteride (McConnel, 1994).

The Impact of Pharmaceutical Therapy of BPH

In the United States, the recent political and socioeconomic conditions have driven the treatment of BPH towards studying and applying a formulated guideline for the accepted treatment of BPH. This guideline developed by the AHCPR applies the AUA symptom score to the treatment of uncomplicated BPH. Under these guidelines, interventional treatment are offered to those with moderate to severe symptoms scores. These treatments are currently classified to surgical and medical options. The surgical options are fur-

ther subdivided by their level of invasiveness. The viable option of medical therapy has only recently impact on the treatment of BPH especially in those patients with moderate symptoms. Previously, the choice to the physician and patients were watchful waiting or invasive surgical therapy, i.e.. TURP or open prostatectomy. Today, medical therapy and less invasive procedures are providing a spectrum of choice to both patient and physician. It is a currently complex choice involving many known and unknown variables that still currently being investigated. But in the realm of availability, choice and accepted efficacy, the pharmaceutical treatment provides an attractive alternative to many where there were none previously. BPH is a symptom driven disease process towards treatment. In the uncomplicated symptomatic patient, it is the patient who is the ultimate consumer of treatment and the one who will significantly influence choice of treatment.

As reviewed by the AHCHR, medical therapy confers a cost advantage for the patient and does not involve the morbidities associated with surgical options. This is very attractive to the patient. In analyzing treatment preference, medical treatment was a clear choice in those with moderate symptoms by BPH patients in the panels judges practice and by a panel of proxy judges. What is interesting in their small study is the positive view and favored choice of treatment that pharmaceutical therapy received in the mild symptom group. Although against the recommendation of the guidelines, this group of patients have the potential to utilize this medical therapy. The view of patients towards having medical therapy was equally favorable overall (McConnell, 1994). Recently, we reported on the usefulness of the AUA-BPH guidelines in 100 patients after one year of therapy. Patients were evaluated as per the AUA-BPH guideline and treatment offered based on their AUA symptom score (Te, 1994). Those with mild symptoms were offered watchful waiting; those with moderate symptoms were offered alpha adrenoreceptor blockade or finasteride; those with severe symptoms were offered alpha adrenoreceptor blockade, finasteride, laser TURP or TURP. In the mild symptom group composed of 34 men, 84% of patients remained on watchful waiting while the remaining progressed to pharmaceutical therapy. In the moderate symptom group of 46 men, 19 were placed on finasteride, of which 68% remained on this therapy at one year. 27 men were placed on alpha adrenorecptor blockade and 74% remained on this therapy at one year. What is interesting is that none progressed to surgery and treatment was changed to the alternate form of pharmaceutical medical therapy. The severe group of 23 men demonstrated a mixed group. 2 patients were placed on finasteride and both progressed to a laser TURP. Four patients chose alpha adrenoreceptor blockade and 1 progressed to a TURP. The remaining were treated with laser TURP and TURP. Of the 15 men who were treated with a laser TURP, 3 progressed to a TURP. Overall, 74% of the patients were placed and maintained on their original therapy. Pharmaceutical therapy in this study especially in the moderate symptom group appear to achieve good level of patient satisfaction based on the patient's commitment to stay on the therapy at one year. Even in the severe group, 50% remained on their pharmaceutical therapy at one year demonstrating its impact on surgery in this group.

Finally, many questions and studies still need to be performed about a disease that we have been treating for many years but have not fully understood. It is clear that with the advent of so many therapies, both surgical and medical, the indication for interventional management of BPH is still developing and evolving. STI

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