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Consideration of drug therapy in benign prostatic hypertrophy

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ABSTRACT

Benign prostatic hypertrophy (BPH) has become a major global health problem both in its frequency by which it determines the complications and the problems of diagnosis and treatment it requires. BPH is a heterogeneous disease. The symptoms attributed to BPH may have other coexisting causes and growth factors both androgen-dependent and independent, which promotes prostate enlargement. It is well known that prostate size correlates poorly with the symptoms so that reducing prostate using 5-alpha-reductase or alphablocants inhibitors may not always be sufficient. A better understanding of the pathophysiology of BPH and its interactions with other drugs will help the development of new substances with a better efficiency. This present work aims to be a modest contribution related to medical treatment in benign prostatic hyperplasia and the role that the generalist practitioner should play in managing of this urinary disease quite common in elderly men.

Keywords

Benign prostatic hypertrophy, medical drugs, alphablocants

Introduction

Clinical research in this study is mainly aimed at studying the effectiveness of non invasive treatment of prostate adenoma were used as methods of therapy drug therapy (alpha-blockers, 5a-reductase inhibitors, combination therapy) and active surveillance of patients suffering from this condition. For efficiency and purposefulness main monitor and set the weight of each type of non-invasive treatment and medication, performing correlations between patient age and the treatment used. Also analyzed the effects or side effects of medical treatments applied.

It attempts to identify prognostic factors according to the applied therapy, outlining an algorithm for noninvasive treatment of prostate adenoma and conduct of medical and professional factors based on collaboration between urologist and specialist physicians. These considerations are based on male patient suffering from the disease of old age, the ultimate goal being to improve clinical symptoms easing the natural evolution of the disease and the patient's social integration.

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Material and method

Clinical research conducted in this study has as main purpose the effectiveness of medical treatment with alpha-blockers, 5-alpha-reductase and their combined therapy. I aimed to establish the proportion of each type of non-invasive or medical treatment and studied the correlation between age and the treatments used. I studied the side effects of drugs, identification of prognostic factors and the failure of medical treatment.

I performed a retrospective study on a lot size of 384 patients aged between 50 and 87 years, prostate adenoma, treated non-invasive or medical treatment or by active surveillance (watchfull waiting). Diagnosis of prostate adenoma or benign prostatic hyperplasia was established within the Cabinet of Urology - Professor PhD. Viorel Tode Constanta Romania (202 patients) and the Cabinet of Athens Eye Hospital Polyclinic Urology - Athens, Greece (182 patients). Patients were monitored in the cabinets above and in the office of primary care - family, diagnostician collaboration between specialist urologist and general practitioner, family. The study was conducted between January 2009 - June 2013, during this time period being monitored both patients already in treatment and newly diagnosed patients.

Results and discussions

It have been established criteria of inclusion/exclusion in the study, the essential criteria in smooth pursuit in patients treated medically. In this sense, the study excluded patients with a history of proliferation/tumor urothelium of patients with neurogenic bladder patients with diabetes and patients with surgery or lower urinary tract diagnosed with malignant tumors [1].

Fixing these exclusion criteria is due to the influence of the conditions listed drug and

combination therapeutic effects of the underlying disease treatment effects of prostate adenoma [2,3].

Most patients studied have been shown to lower urinary tract symptomatology (LUTS) - 325 cases, the remaining patients are presenting with complications of prostate adenoma: acute urinary retention - 12 cases, hematuria - 8 cases, infectious complications - 39 cases, including cystitis, acute/chronic - 17 cases, acute prostatitis - 12 cases, acute orchi epididymitis / acute epididymitis - 10 cases.

Lower urinary tract symptoms are not specific only to BPH, they running through a number of other pathological processes similar symptoms. History and physical examination can distinguish them, and further investigations are necessary when the diagnosis is unclear for BPH. Recommendations of the European Association of Urology in 2004, established the explorations that are recommended and even those recommended for the diagnosis of BPH [5.6].

Recommended tests are: history, physical examination including digital rectal examination, prostate symptom score international determination of serum prostate specific antigen levels and the levels of serum creatinine, urine analysis exam "meter". Optional exams are studies pressure, flow, uretrocistoscopia, upper urinary tract imaging, imaging of the prostate and bladder, micturition calendar. Examinations are recommended: intravenous urography, filling cystometry, uretrografia retrograde computed tomography, magnetic resonance transrectal.

For each patient entered the study was prepared by a table IPSS guidance needed to assess clinical pain, studying and lower urinary tract disorders. The patient self-evaluation points giving 1 to 5 for each of the seven signs or symptoms. They investigated the initial dysuria, decreased size and force urine flow, intermittent urinating and feeling incomplete emptying of the bladder, which are three irritative obstructive symptoms: nocturnal urinary frequency, urinary frequency and daytime micturition [7] (TablesI and II).

Table I -Quality of life index

Quality of life according to urinary symptoms	If you were to spend the rest of life in the current situation
Pleased	0
Satisfied	1
More than satisfactory	2
Equally satisfied and dissatisfied	3
More dissatisfied	4
Infelicitous	5
Appalling	6

Determination of prostate specific antigen is the most valuable specific marker of prostatic tissue. You do not have any medical treatment recommended before performing a digital rectal and PSA assay[8]. A raised PSA is found in prostate cancer, but sometimes in BPH, prostatitis, acute urinary retention, recent biopsy of the prostate, but without clinical significance

of PSA. The threshold level is set to 4 ng/ml, but recent studies have decreased to 2.5 ng/ml.

The frequency of false positive results caused by benign prostate disease can be reduced by 20-40% by determining unbound PSA - free PSA [9]. Determination of free PSA has become the practice to increase the specificity of total PSA in diagnosis of prostate cancer when its values are between 4 and 10 ng/ml [10]. If the free PSA is less than 19% of the total PSA, it is estimated that perhaps prostate cancer patient has to be certified by biopsy and histopathology.

Sometimes useful PSA density (PSA Secic / prostate volume > 0,15), PSA velocity (increases greater than or equal to 0,75 mg/ml/year correlated with age - the serum level increases with age) [11,12]. PSA and the amount of the prostate can be used as parameters of the evaluation of the natural history of benign prostatic hyperplasia, a risk of urinary retention or surgery [13,14,15].

Based on the results I divided patients

Table II - Evaluation of IPSS (International Prostate Symptom Score)

Symptoms score	Not at all	Less than once per day	Less than half from time	Approximately half from time	More than half from time	Almost always
In the last month how often have you had the feeling that you have not completely emptied your bladder after you finished urinating?	0	1	2	3	4	5
In the last month how often you had to urinate again less than 2 hours after the last urination?	0	1	2	3	4	5
In the last month how often it happened that, while urine stream to stop and then to resume?	0	1	2	3	4	5
In the last month how often did you find it difficult to postpone the urination?	0	1	2	3	4	5
In the last month how often have you had a weak urinary stream?	0	1	2	3	4	5
In the last month how often had to push or force start urination?	0	1	2	3	4	5
In the last month how often you wake up to urinate at night?	0	1	2	3	4	5

completing IPSS questionnaire into three categories (Table III):

Table III - IPSS types identified at patients from the studied group

Item no.	IPSS	No. of cases	%
1	Small 0-7	28	7,29%
2	Medium 8-19	248	64,58%
3	Severe 20-35	108	28,12%

Treatment with alpha-blockers (Tamsulosin) at studied group patients

It were treated with alpha-blockers the patients with IPSS low and medium prostate volume less than 40 cc and PSA less than 1.4 ng/ml. There were thus included in the study 276 patients, representing a rate of 71.88%. Follow-up period of these cases ranged from 6 weeks to 76 months, analyzing the short-term efficacy and long-term.

After 6 weeks in 54 of the 276 patients (19.56% of the patients treated with alpha-blockers) have been no changes in the IPSS. Patients whose therapy failed and IPSS at 6 weeks did not change were removed from the study.

Comparative analysis of non-response to therapy with alpha-blockers showed no significant association failures. Nonparametric chi-square test which compared the number of failures reported with alpha-blockers therapy showed a lower correlation coefficient $r=0.2$ and a high value level of significance $p < 0.05$, confidence interval being 95%.

For those who respond (222 cases), I measured the degree of improvement in the therapeutic efficacy of the IPSS. Overall, Tamsulosin therapy resulted in a rapid improvement in symptoms, IPSS falling short at a rate of 80.44% of patients treated with alpha-blockers, which represents 57.81% of the total group of patients included in the study.

The long-term study efficacy of alpha-blockers included 222 patients with favorable response to short-term assessment. Long-term efficacy was assessed by the lack of alpha-blockers on treatment failure. Failure was defined as the increase in IPSS 12-15 months. Thus, in this study I have lost a total of 71 cases in which the IPSS increases almost as the initial values.

Of the total 276 patients treated with tamsulosin (alpha-blockers) was found efficiency at 183 patients (66.3%), which demonstrates an average efficacy of therapy with alpha-blockers.

Treatment with the 5-alpha-reductase inhibitors (Dutasteride)

Out of the 108 patients with IPSS severe, a number of 33 patients were treated with 5-alpha-reductase inhibitors. The reason for this number of cases was the value of PSA and prostate volume, being included in the dutasteride therapy patients whose PSA value did not exceed 1.4 ng/ml and ultrasound prostate volume exceeded 40 ml.

I analyzed the efficacy of the 5-alpha-reductase inhibitors both short term (6 months) and long term.

I found that for 8 of the 33 patients treated with the 5-alpha-reductase inhibitors, there has been no change ultrasound prostate volume and IPSS values maintained severe, these 8 patients (24.24% of those treated with 5 alpha reductase) were excluded from the study.

At 25 patients (75.76%) remained in the study have undergone evaluation at 12-15 months observing that IPSS improved by reducing rates values between 12 and 18%, demonstrating the effectiveness of treatment with 5-alpha-reductase inhibitors long term, a total of 6.51% of patients in the total group was improved by this treatment.

Treatment with combined therapy (Duodart - tamsulosin 0.4 mg and dutasteride 0.5 mg)

Since January 2003 AUA introduced in patients with severe IPSS, prostate volume 40 cc and higher PSA values of 1.4 ng/ml, combination therapy (5-alpha-reductase associated with alpha-blocker inhibitors). The criteria imposed by ARUA, our group patients were in number of 75 (19.53% of the total lot 384). These patients received combined therapy Duodart form a single tablet containing both alpha-blockers (tamsulosin 0.4 mg) and 5-alpha-reductase inhibitor (dutasteride 0.5 mg). Follow-up period of these patients ranged from 6 months to 24 months, thus assessed the effectiveness of short-term and long-term therapy applied.

After 6 months of combination therapy, for a total of 7 patients out of 75 (at the rate of 9.33%) was observed treatment failure (IPSS has not improved, the life quality of patients being unchanged,

demonstrated also by ultrasound).

Favorable response to combination therapy has been shown to decrease prostate volume and IPSS improvements proven ultrasound. In this regard, short-term efficacy was found at a rate of 90.64% of patients with combined therapy (68 patients).

The 68 patients with IPSS improvement in short, remained in the study and were re-conducted long-term 12 to 24 months. Of these 68 cases, a total of 5 cases (7.35%) were found failures therapeutic IPSS worsening or complications (hematuria and infection) leading to surgical indication by TUR-P cases failed.

Of the 75 patients treated with the combination is found by evaluating the therapeutic efficacy both short and long term treatment of the success to a percentage of 84% of cases (63 patients).

Conclusions

1. Medical treatment, non-invasive plays an increasingly important role in the therapeutic arsenal indicated in benign prostatic hypertrophy.

2. Active surveillance as the sole means of non-invasive treatment is almost non-existent due to delayed presentation urologist most patients requiring drug therapy.

3. Studied group comprises of 384 patients aged 50 to 87 years, patients were divided into three categories according to the values of IPSS, prostate volume and PSA value.

4. Besides patients with mild symptoms, those with moderate pain may benefit from therapy with alpha-blockers.

5. Alpha-blockers are most commonly applied to medical therapy in patients with benign prostatic hyperplasia. This class of drugs generates a rapid and significant improvement in symptoms, as well as a significant increase in urine flow.

6. 5-alpha-reductase inhibitors causes a substantial reduction in prostate volume, but a more modest improvement in symptoms compared with

alpha-blockers.

7. 5-alpha-reductase inhibitors can be used successfully as monotherapy only in patients with severe IPSS, PSA below 1.4 ng/ml, and prostate volume over 40 cc.

8. Combined therapy is superior to the alpha-blockers, and 5-alpha-reductase inhibitors, both in the short term efficacy, as well as the long term.

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