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RESEARCH ARTICLE

Correlation between Selective and Non-selective α-Blocker Drugs with Age, Prostate Volume and Different Benign Prostate Hyperplasia (BPH) Indicators

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Abstract

Objective: This study aimed to evaluating the correlation between(age, prostate size) and different BPH indicators such as (PSA , IPSS , testosterone , estrogen ,Testosterone/Estrogen {T/E} ratio) among two groups (one treated with selective and another treated with non-selective α-blocker drugs) and untreated group. Methods: The study is a randomized control clinical trial carried out in Urology department during the period from September /2018 to May /2019.The study was based on 60 cases of symptomatic Benign Prostatic Hyperplasia, 30 patients treated with selective α-blocker drug (tamsulosin) and 30patients treated with non-selective α-blocker drug (alfuzosin) and 30 cases of newly diagnosed patients with BPH but did not take treatment for BPH disease, the range of their age was between (50-90). The variables age, prostate size, PSA, IPSS, testosterone, estrogen, T/E ratio were examined and appropriate statistical tests were employed for data analysis. Results: The results showed that there was a significant difference in correlation between age with IPSS and between age with testosterone ($p \leq 0.05$)among treated and untreated groups and also showed a significant difference in linear correlation between PSA ,Testosterone, Estrogen indicators levels and the prostate size ($p \leq 0.05$) among treated and untreated groups Conclusion: In men with biopsy-proven BPH , both International Prostate Symptom Score IPSS and testosterone increased and altering with ageing. Prostate size demonstrated significant positive correlations with Prostate Specific Antigen PSA, Testosterone, Estrogen among treated and untreated groups in this study.

Keywords: *BPH, Testosterone, Estrogen, PSA, IPSS, Tamsulosin, Alfuzosin.*

Introduction

Benign Prostatic Hyperplasia (BPH) is a pathological change that occurs in the prostate, leading to enlargement. It's a condition that greatly affects the quality of life of middle-aged and elderly men, causing Bladder Outlet Obstruction (BOO) and resulting in Lower Urinary Tract Symptoms(LUTS) [1].The precise molecular etiology of BPE/BPH is complicated and poorly understood, although several risk factors for the development of BPE/BPH and LUTS conditions have been identified.

These include age, genetics, hormones, growth factors, inflammation, and lifestyle factors [2]. Benign Prostatic Hyperplasia listed together with sign and symptoms range from nocturnal polyuria, overactive bladder, underactive bladder, bladder tumours,urinary stones, urinary tract

infection and all other causes of obstruction like urethral [3]. Practically speaking, BPH is a diagnosis of exclusion. When men over age 50 years complain of Lower Urinary Tract Symptoms, the following tests can be used to rule out all other possible causes before arriving at a BPH diagnosis [4].1-International Prostate Symptom Score (IPSS) are subjective questionnaires that can be used to help evaluate lower urinary tract symptoms and their effect on patients suffering from BPH [5]. 2-Prostate specific antigen (PSA)is an established biomarker for prostate cancer but can also be used in the diagnoses of BPH and provides important information on its progression[6].

3-Dihydrotestosterone(DHT), the most potent androgen in men, is metabolized from testosterone through the activity of 5α -reductase enzyme.

DHT plays a crucial role in the differentiation and growth of the prostate gland during fetal development as well as in the development of male external genitalia and secondary sexual characteristics [7]. Inhibition of the production or actions of DHT can result in the inhibition of the growth of the prostate gland. There is substantial clinical evidence that androgen and DHT play a key role in the development of BPH [8].

4-Estrogen plays an important role during prostate development and studies have shown that excessive estrogenization during prostatic development may contribute to the high incidence of BPH cur-rently observed in the aging male population [9].A more profound knowledge of the pathogenesis.

The natural history, and the risk of the Progression enabled more differentiated therapy of elderly men with BPH.the specific approach used to treat BPH depends upon a number of factors like age, prostate size, weight, prostate-specific antigen level, and severity of the symptoms [10]. Treatment options for BPH include: Watchful waiting is the monitoring of a patient without medical or surgical intervention, generally recommended for men with mild-to-moderate symptoms whose quality of life is not impaired and who have no disease complications [11]. Medical therapy for clinical benign prostatic hyperplasia (BPH) has advanced significantly in the last 2 decades.

Many new α1 antagonists (selective α1 receptor blocker (tamsulosin) and non-selective α1- blocker receptor (alfuzosin) drugs and 5α -Reductase inhibitors (5α-Ri) are now commercially available. The practicing urologist must decide on the most appropriate medication for his patients, taking into consideration various factors like efficacy, dosing regime, adverse effects, cost, patient's socioeconomic background, expectations, drug availability and his own clinical experience [12]. Surgical treatment of BPH is necessary, and referral to an urologist is warranted if medical treatments fail, or if benign prostatic obstruction causes renal insufficiency, urinary retention, recurrent urinary tract infections, and bladder calculi [13]. The aim of this study is to evaluate the outcomes and effectiveness of selective therapy with alpha one blocker and non-selective alpha blocker drugs in patients with Benign Prostate Hyperplasia.

Materials and Methods

Study Design

The present study is a randomized control clinical trial carried out in Urology department during the period from September /2018 to May /2019. In this study we have three patients groups:

New Diagnosis (untreated)

Patients group with Benign Prostate Hyperplasia {did not take medication for BPH disease}.They were 30male new diagnosis with BPH depending on specific parameters examination(prostate size, International Prostate Symptom Score (IPSS), Prostate Specific Antigen (PSA) ,testosterone, estrogen, T/E ratio) range of their ages was (50-90) years old.

Treated Groups

Treated with Selective α1 Receptor Blocker Drug

They were 30male diagnoses with BPH and give to them selective α1 receptor blocker Tamsulosin oral tab once daily for one month. After this month measuring to them the following parameters (prostate size, IPSS, PSA, testosterone, estrogen, T/E ratio) range of their ages was (50-90) years old.

Treated with Non-selective α-receptor Blocker Drug

They were 30 male diagnosis with BPH and give to them non-selective α1 receptor blocker Alfuzosin oral tab once daily for one month .after this month measuring to them the following parameters(prostate size, IPSS, PSA, testosterone, estrogen ,T/E ratio) range of their ages was(50-90)years old. After we get the result of all groups we make the comparison between them depending on statistical analysis.

Methods

Measurement of Prostate Size

Accurate prostate volume measurement relies heavily on Ultrasound (US) which is a widely used and well-tolerated imaging

modality for evaluation of the prostate. Plays a central role in the detection, localization and staging of patients who have BPH and this made by special urologist [14].

Measuring of International Prostate Symptom Score (IPSS)

The International Prostate Symptom Score (IPSS) is a scoring system used to screen for and diagnose Benign Prostatic Hyperplasia (BPH) as well as to monitor symptoms and guide decisions about how to manage the disease. The IPSS is based on the answers to eight questions, seven regarding disease symptoms and one question related to the patient's quality of life [5].

Blood Sample Collection

Five ml of blood was drown in situ using a disposable 5ml syringe. A tourniquet was applied directly on the skin around the arm. The skin over the vein sterilized with 70%ethyl alcohol, and then collected blood poured on the walls of the plain tube. Then the blood is centrifuged for 10 min. at 3000 rpm to to get a clear solution of blood plasma (blood serum) in the upper phase which is labeled by the patients name serum ,then collected for measuring the following parameters:(Prostate Specific Antigen (PSA), testosterone, estrogen, T/E ratio) calculate the level of them for all three groups.

The procedure made by using Roche Cobas E411 auto analyzer instrument. All assay steps and assay temperature are controlled by this instrument, the total duration assay is 1hr and the level of Estrogen parameter calculate, also and The procedure is made by using The VIDAS® Estradiol II (E2 II) assay is intended for use on the instruments of the VIDAS family (VITEK Immunodiagnostic Assay System) as an automated quantitative Enzyme-Linked Fluorescent immunoassay (ELFA) for the determination of total estradiol concentration in human serum. All assay steps and assay temperature are controlled by this instrument.

Ethical Approval

Ethical approval for this study was obtained from research ethical committee in college of medicine, University of Babylon-Iraq.

Statistics Analysis

All data were collected and analyzed by using SPSS (statistical package for social sciences) version 23,Variable were presented as mean ± SD. Student T-test was used to assess significant difference among the means of the data .P value was set <0.05 as significant where the P value less than 0.05 was considered to be statistically significant.

Results

Correlation between Age and Different BPH Indicators among Treated and UN Treated Groups

The results showed that there was a significant difference in correlation between age with IPSS and between age with testosterone ($p \leq 0.05$) among treated and untreated groups. While showed no significant difference in correlation between age with (Prostate size, PSA, Estrogen, and T/E ratio) ($p > 0.05$) among treated and untreated groups as shown in Table (1).

Table 1: Correlation between age and different BPH indicators among treated and untreated groups

	Mean± Sd	*Rho* value	P value
age	69.2222 ± 8.66710	0.046	0.668
Prostate size	52.6 ± 22.755		
age	69.2222 ± 8.66710	0.244	0.021*
IPSS	19.9333 ± 5.81126		
age	69.2222 ± 8.66710	-0.062	0.564
PSA	3.9111 ± 4.34785		
age	69.2222 ± 8.66710	0.209	0.048*
Testosterone	4.7037 ± 1.91569		
age	69.2222 ± 8.66710	0.079	0.458
estrogen	34.2807 ± 15.60839		
age	69.2222 ± 8.66710	0.058	0.526
T/E ratio	0.1559 ± 0.07376		

Linear Correlation Figures between Both PSA, IPSS, Testosterone, Estrogen, T/E Ratio Indicators Levels and the Prostate Size among Treated and Untreated Groups

The results showed that there was a significant difference in linear correlation between PSA, Testosterone, Estrogen indicators levels and the prostate size ($p \leq 0.05$) among treated and untreated groups. While Showed no significant difference in linear correlation between IPSS indicator level and the prostate size between treated and untreated groups As show in Figures (1), (2), (3) and (4).

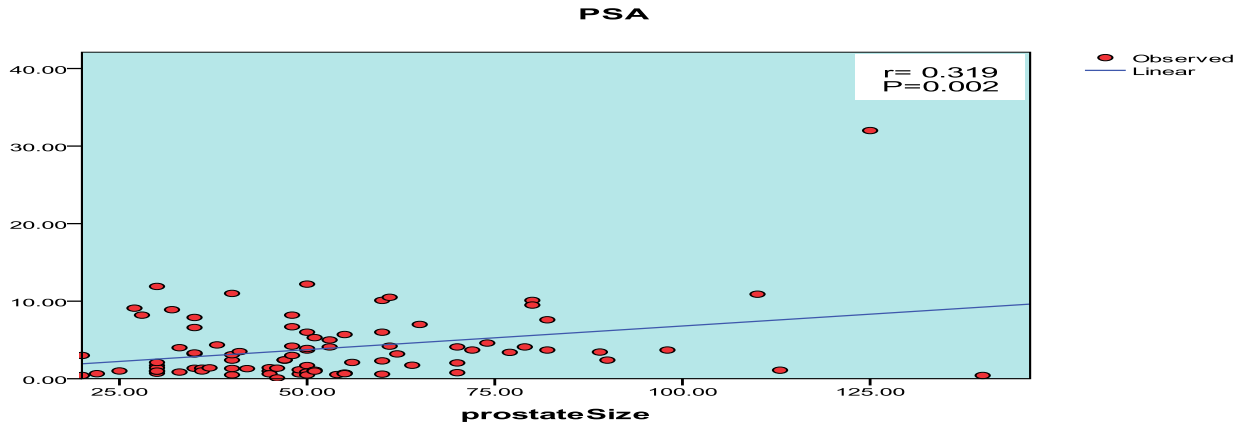

Figure 1: The linear correlation (significant difference) between PSA level and the prostate size between treated and untreated groups

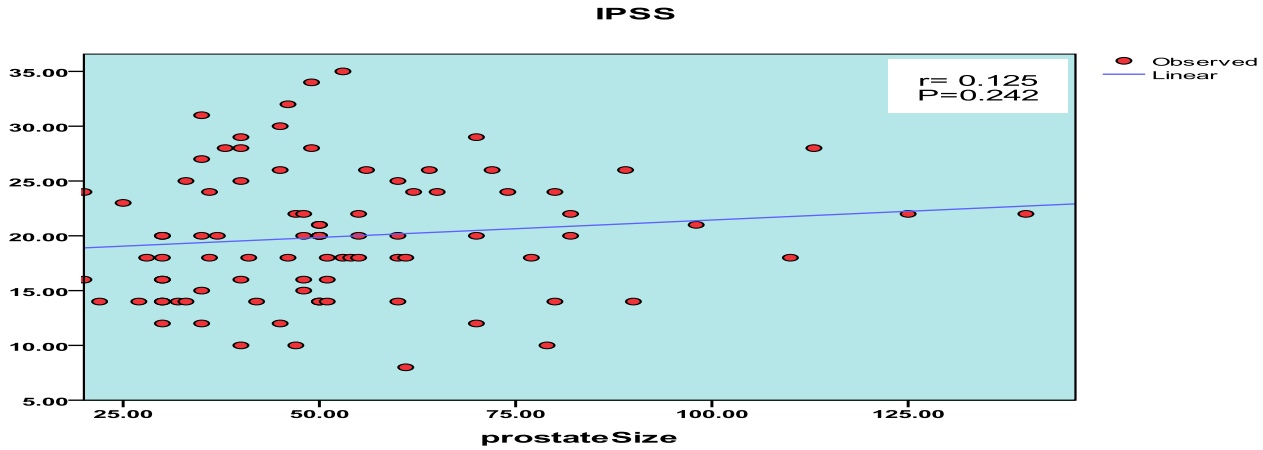

Figure 2: The linear correlation (no significant difference) between IPSS level and the prostate size between treated and untreated groups

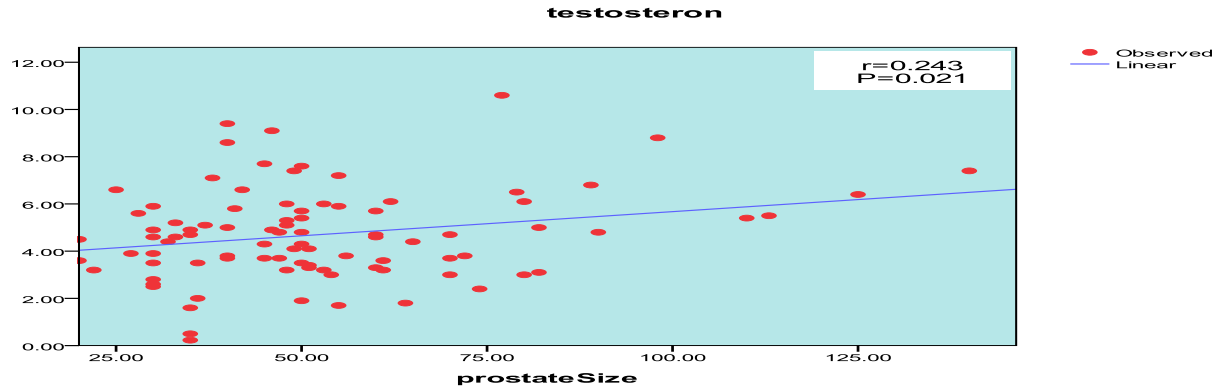

Figure 3: The linear correlation (significant difference) between Testosterone level and the prostate size between treated and untreated groups

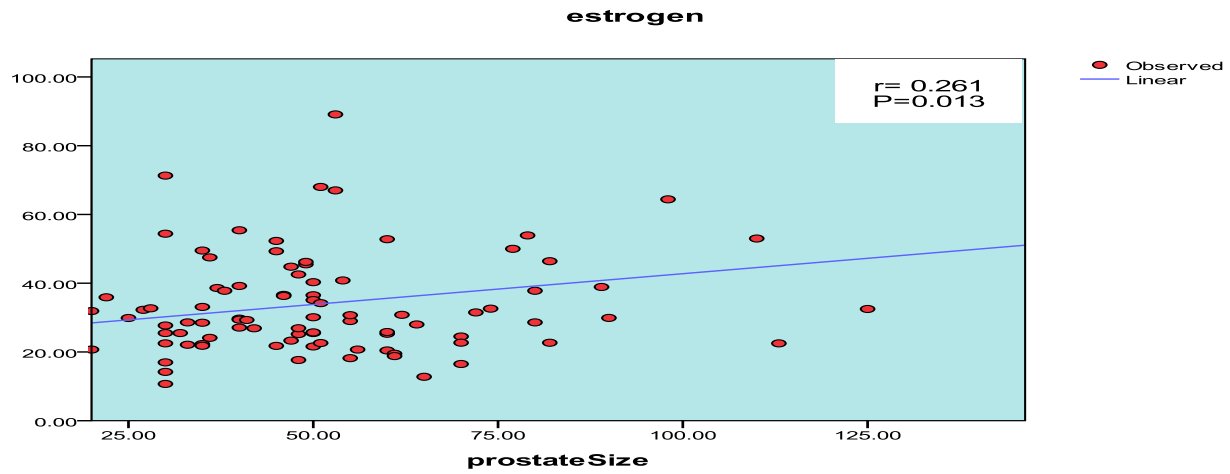

Figure4: The linear correlation (significant difference) between Estrogen level and the prostate size between treated and untreated groups

Discussion

The results of this study demonstrated that the administration of non- selective α-receptor blocker drug (Alfuzosin) and selective α1-receptor blocker drug (Tamsulosin) for one month as single daily dose have a positive effects on the enhancement of patients responsiveness in the treatment of BPH, with good tolerability, acceptability, and minimum hemodynamic adverse effects. alfuzosin and tamsulosin are comparable in their efficacy in the symptomatic management of BPH which found in this study by difference in BPH indicators between the three studied groups. BPH is age-related, and the prevalence increases with increasing age [15].

Among many factors that contribute to prostate enlargement in BPH, the two most well-known etiologic factors were aging and androgen [16]. In this study the Correlation between Age and different BPH indicators among treated and un treated groups, The results showed that there was a significant difference between age and IPSS ($p \leq 0.05$) among treated and untreated groups as shown in Table 1 and this result agree with (Suzuki ,2003) who reported that the results of IPSS were increased with age as BPH is a major cause of morbidity in the aging men and lead to disturbed voiding in men, which symptoms are collectively referred to as LUTS that was collected by IPSS question.

The results also showed a significant difference between age and testosterone ($p \leq 0.05$) between the two groups and this agree with (Qin-Song, 2012) who mentioned that the two etiologic factors that are largely accepted to play a role in the pathogenesis of the disease are aging and alterations in androgen levels. This study showed no significant difference ($p > 0.05$) between age and (Prostate size, PSA, Estrogen, and T/E ratio) among treated and untreated groups [16]. Linear Correlation between both(PSA, IPSS, Testosterone, Estrogen indicators levels) and the prostate size among treated and untreated groups: The results showed that there was a significant difference in linear correlation between PSA level and prostate size ($p \leq 0.05$) among treated and untreated groups. This result agree with (Putra ET al. 2016) and (Jozo Coric et al. 2015).

Who confirmed that there is positive correlation between PSA and the increase in prostate size, this is supported by the fact that prostate epithelial cells are responsible for circulating PSA, since PSA is an organ-specific biomarker of the prostate [17, 18].In this present study, the result ,also showed significant difference between testosterone level and prostate size ($p \leq 0.05$)and this agree with (Vincenzo,2010), (Joseph *et. al.*) who mentioned that in the prostate, testosterone is converted into the more potent androgen Dihydrotestosterone (DHT) by 5α-reductase type, And so DHT has a central role in BPH development and maintenance [19, 20].

Also this study showed a significant difference between Estrogen level and prostate size ($p \leq 0.05$) and this agree with (Schatzl ET al.2000) who found that a direct correlation between elevated estradiol levels

and prostatic volume [21]. The results Showed no significant difference ($p>0.05$) between IPSS indicator level and the prostate size and this compatible with (Gnyawali, 2014) who mentioned that no correlation between prostate size and IPSS, so the management of BPH patients should be considered on the bother symptom and not on the size of prostate [22].

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