Biochemical Changes In Patients With Benign Prostate Hyperplasia

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Abstract:

Benign prostate hyperplasia BPH is the most common benign tumor in aging men. The present study aims to assess the serum prostate specific antigen (Total PSA and Free PSA), Prostatic Acid phosphatase (PAP), Malondialdehyde (MDA) and Lactate Dehydrogenase (LDH) status in patients with BPH. This study included 50 patients with BPH who reviewed the Hilla General Teaching Hospital in addition to 50 non-infected (control). All samples are divided into 3 groups according to age (50-59, 60-69, 70-75) years old. Aged as mean ± SD (54.23±3.15, 63±3.4, 72.8±2.6) respectively. The results indicate a high level of TPSSA (14.92±1.27, 15.90±1.63, 16.75±1.60 ng/ml) in patients compared with control (1.73±0.42, 1.86±0.24, 4.54±1.14 ng/ml) respectively. The FPSA values (5.91±0.54, 5.98±0.84, 6.24±0.56 ng/ml) are significantly increased compared with control (0.50±0.18, 0.57±0.15, 1.84±0.60) respectively. The PAP values of patients are (1.76±0.56, 1.83±0.59, 2.41±0.73 IU/L) and in control are (0.43±0.13, 0.46±0.12, 0.47±0.11 IU/L) respectively. The values of MDA levels are increased in patients (2.30±0.76, 2.42±0.76, 2.95±0.94 µM/L) compared with control (0.63±0.18, 0.65±0.21, 0.66±0.12 µM/L) respectively. Also, LDH activity in patients (88.89±12.88, 95.93±19.35, 111.93±34.05 IU/L) is higher compared with (81.50±10.31, 82.55±23.66, 84.59±20.52 IU/L) in control. The result indicates the high significant value (p<0.05) in these parameters for all patients compared with control groups.

Key words: Benign prostate hyperplasia, Malondialdehyde, Lactate dehydrogenase enzyme.

الخلاصة:

يعتبر مرض تضخم البروستات الحميد (BPH) من الأمراض الأكثر شيوعاً الذي يصاب كبار السن. تهدف هذه الدراسة إلى تقييم حالة مرضى البروستات الخاص الكلي (Total Prostate Specific Antigen – TPSA)، (Prostatic Acid Phosphatase), (Free Prostate Specific Antigen – Free PSA) والملانون ثنائي الدياهيد (Malondialdehyde) لدى الأشخاص المصابين بمرض تضخم البروستات الحميد. تضمنت هذه الدراسة 50 مريض من راجعوا مستشفى التعليم العام بالإضافة إلى 50 من غير المصابين بالمرض (الكامل). تم تقسيم جميع العينات إلى 3 مجموعات حسب الفئة العمرية (50-69، 70-75). وقد أظهرت النتائج وجود زيادة مماثلة في مستوى الـTSSP (14.92±1.27، 15.90±1.63، 16.75±1.60) في المرضى (√104 (49.25±7.43، 26.22±8.32، 30.81±10.49) في المرضى و1.73±0.42، 1.80±0.32) في المرضى عندمقارنة مجموعة السطح FSSA (4.54±1.14) على التوالي. وكذلك هناك زيادة مماثلة في مستوى الـPSA (5.91±0.54، 5.98±0.84، 6.24±0.56) على التوالي. أما مستوى الـPSA في المرضى (1.76±0.56، 1.83±0.59، 2.41±0.73) في حالة كانت (0.50±0.18، 0.57±0.15، 1.84±0.60) على التوالي. بينما لم تظهر الفرق الـMSSA (0.53±0.18، 0.65±0.21، 0.66±0.12) على التوالي. أما مستوى الـMSSA في المرضى (2.30±0.76، 2.42±0.76، 2.95±0.94) في حالة كانت (0.63±0.18، 0.65±0.21، 0.66±0.12) على التوالي. بينما لم تظهر الفرق الـMSSA (0.53±0.18، 0.65±0.21، 0.66±0.12) على التوالي. أما مستوى الـLDH في المرضى (88.89±12.88، 95.93±19.35، 111.93±34.05) في حالة كانت (81.50±10.31، 82.55±23.66، 84.59±20.52) على التوالي. أظهرت النتائج وجود زيادة مماثلة في جميع المرضى مقارنة بمجموعة السطح عند اعتماد مستوى احتمالية (p<0.05).
I. Introduction:

Benign prostatic hyperplasia, or (BPH), is a highly prevalent disease of older men caused by nonmalignant, unregulated growth of the prostate gland (Miller, 1996). Kristal et al., in (2008) estimation the BPH prevalence approximately 40-50% of males age 50 years to greater than 80% of men over 70 years. Histologically, it is characterized by a proliferation of the epithelial and stromal elements within the prostate tissue. It is arises in the periurethral and transition zones of the prostate gland (Lepor, 2005). Current scientific evidence suggests that the prostate cancer is more common in patients with BPH than those without it (Orsted et al., 2011). For diagnosis and Prognosis of prostate disease, biomarker can be used, included DNA-based markers, RNA-based biomarkers, and protein markers (such as serum markers PAP, PSA, FPSA, and TPSA) (Ludwing and Weinstein, 2005). The prostate specific antigen is still used together with prostatic acid phosphatase the major marker for prostate disease (Dulinska et al., 2002).

In previous studies the etiology of BPH is not understood. Androgen, essential for normal prostate growth and development, plays a prominent role (Novara et al., 2006). However, there is evidence that metabolic disturbance may promote prostate hyperplasia pathogenesis (Savas et al., 2009). Reactive oxygen species (ROS) and free radical are produced during metabolic and physiological process which leads to oxidative stress when disrupts of the production/elimination balance, and plays a significant role in the ethiopathology of BPH (Aydin et al., 2006).

The lipid peroxidation process is auto oxidation of unsaturated fatty acids and Malondialdehyde is one of the major end products of lipid peroxidation process (LPO) in which reactive oxygen species degrade polyunsaturated lipid. Thus, measurement of MDA levels in serum provides a convenient index of lipid peroxidation to clarify the oxidative stress in BPH (Merendino et al., 2003). Lactate Dehydrogenase is one of the enzymes that secreted by prostate, it is a cytoplasmic enzyme that catalyses the oxidation of L-lactate to pyruvate. It is used to detect cell damage or cell death (Gisselsson and Lerche, 2008).

In this study we aimed to evaluate relationship between oxidative stress and BPH and this may be contributing to the explanation of the ethiopathogenesis of the disease.

II. Material and methods:-

A perspective study was carried out at AL-Hilla General Teaching Hospital. Fifty diagnosis men with benign prostate hypertrophy were enrolled in the study compared with fifty apparently healthy persons. All patients and control are divided into 3 groups according to age. Blood samples were taken before digital rectal examination (DRE). The samples were collected after phlebotomy in evacuated tubes and were centrifuged at 1600 xg for 15 min at 4 °C after the blood had clotted for 1 hour at room temperature and the sera were frozen at -20 °C and were not thawed (and frozen) before using.

Prostate Specific Antigen (BioMerieux, France):- Total PSA and free PSA level were measured using VIDAS instrument and commercial kits based on ELFA technique (Enzyme Linked Fluorescent Assay).

Prostatic Acid Phosphatase (Biolabo, France): - PAP activity was determined by enzymatic colorimetric method and used commercial kits.

Malondialdehyde: - was estimated according to (Yagi et al., 1987) method. This method is based on the formation of red pigment condensation of lipid peroxidation breakdown products like MDA with thiobarbituric acid TBA.

Lactate Dehydrogenase (Biolabo, France): - was measured by enzymatic colorimetric method (SFBC modified method) using commercial kits.
Statistical analysis: Data were reported as mean ± SD. The data were analyzed according to completely randomized design (CRD) to determine a significant difference between the results. Data with P values < 0.05 were considered to be statistically significant.

III. Results

A total of 50 diagnosis men with BPH were enrolled in this study and compared the result with 50 apparently healthy persons (control). All patient and control samples are divided into 3 groups according to age (50-59, 60-69, 70-77). Aged as mean ± SD (54.23±3.15, 63±3.4, 72.8±2.6) respectively. We determine serum PSA (TPSA, FPSA), PAP activities, MDA level and LHD activity in all patients and control by using immunological and colorimetric methods. An increase level (p < 0.05) of total PSA (14.92±1.27, 15.90±1.63, 16.75±1.60 ng/ml) was observed in BPH patients when compared with control (1.73±0.42, 1.86±0.24, 4.54±1.14 ng/ml) respectively (figure 1). Free PSA (FPSA) shows a significant increase in patients compared with control (5.91±0.54, 5.98±0.84, 6.24±0.56 ng/ml) (0.50±0.18, 0.57±0.15, 1.84±0.60 ng/ml) respectively as shown in (figure 2). Prostatic acid phosphatase PAP activity in BPH patients (1.76±0.56, 1.83±0.59, 2.41±0.73 IU/L) was increased when compared with control (0.43±0.13, 0.46±0.12, 0.47±0.11 IU/L) respectively (figure 3). We found a statistically rise in serum MDA level in the patients (2.30±0.76, 2.42±0.76, 2.95±0.94 µM/L) when compared the result with control (0.63±0.18, 0.65±0.21, 0.66±0.12 µM/L) respectively as shown in figure 4. An increase in the activity levels of serum Lactate Dehydrogenase in patients (88.89±12.88, 95.93±19.35, 111.93±34.05 IU/L) when compared with control groups (81.50±10.31, 82.55±23.66, 84.59±20.52 IU/L) respectively Shown in (figure 5). The results show an increase level of c and a positive correlation between them as shown in the table 1.

Table 1: Correlation Coefficient (r) between TPSA, FPSA, PAP, MDA and LDH in patients with BPH.

<table>
<thead>
<tr>
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<th>TPSA</th>
<th>FPSA</th>
<th>PAP</th>
<th>MDA</th>
<th>LDH</th>
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<td>0.999</td>
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<tr>
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<tr>
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<td>0.992</td>
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</table>
Figure 1: Activity of serum Total Prostate Specific Antigen from Benign Prostate Hyperplasia patients and control groups.

Figure 2: Activity of Free Prostate Specific Antigen from patients with Benign Prostate Hyperplasia and control groups.

Figure 3: Prostatic Acid Phosphatase activity in Benign Prostate Hyperplasia patients and control groups.

Figure 4: Malondialdehyde level in patients with Benign Prostate Hyperplasia and control groups.

Figure 5: Lactate Dehydrogenase activity in Benign Prostate Hyperplasia patients and control groups.
VI. DISCUSSION

Benign prostatic hyperplasia (BPH) is one of the common benign tumors in older men (Edwards, 2008). It occurs when the prostate gland increase in size as a result of the proliferation of epithelial cells within the basal cell layer (Vitalone et al., 2001). For diagnosis and prognosis of prostate disease, different types of biomarkers can be used such as a serum marker (PSA, PAP, TPSA and FPSA) (Ludwing and Weinstein, 2005).

Prostate Specific Antigen is a serine protease that is synthesized by epithelial cells of the prostate under normal condition and is secreted into seminal fluid. Its function is thought to be liquefaction of seminal fluid through enzymatic action (Vihinen, 1994). The measurement of serum levels of PSA is the most widely used indicators to detect prostate disease (Malati et al., 2006). Several studies have correlated serum PSA with age and with total prostate gland volume. Oesterling et al. in (1993), studied 471 men aged 40-79 years who were randomly selected from the community. In this study a relationship was found between PSA and both prostate volume and age. In normal condition, PSA can only enter blood circulation by leaking into the extracellular fluid and diffusing into veins and capillaries. However, in BPH disease, tumor growth disrupts the basal cell layer and cell polarity is altered. The direction of PSA secretion is disturbed and PSA is released freely into circulatory system which leads to increase PSA level in patient (Shih et al., 1994). Frempong et al., in the (2008), suggested that BPH disease can be associated with elevated levels of PSA. These findings on PSA concentration agree with our result.

Prostatic acid phosphatase is one of the major proteins secreted by prostate tissue after puberty. PAP can be used as a prognostic indicator of prostate disease also it is used in forensic investigations in case of sexual abuse (Bull et al., 2002). Huggins and Hodges in (1941), observed that there was no correlation between the height of serum acid phosphatase in the prostate disease such as (BPH), in general, our data disagree with their findings because in case of prostate disease such as PBH, normal acinar connection to the ducts of the prostate do not develop. So that, in those proliferating cells some of the synthesizing and secretary integrity of the epithelium of the prostate continues thus there is accumulation of prostatic acid phosphatase which diffuse to the blood stream. Also some cells degenerate as a result of overgrowing which leads to accumulation of intracellular products and released directly to vascular channels, ultimately elevated blood level of PAP (Murphy et al., 1978).

MDA it is an end product of lipid peroxidation (LPO) which is a process where reactive oxygen species degrade polyunsaturated lipids. The present study shows increased MDA level (an indicator of lipid peroxidation). Increased lipid peroxidation can be destructive to various body tissues if not scavenged by an antioxidant defense mechanism which leads to oxidative stress (Palmieri and Sblendorio, 2007), and high level of free radical produced from cells in BPH patients (Radu et al., 2011). Also the level of MDA is accompanied with PSA (Merendino et al., 2003).

Lactate Dehydrogenase is a tetrameric enzyme that catalyzes the oxidation of lactate to pyruvate. Several studies documented that stress cause increase serum LDH activity which is an indication of tissue damage (Devaki et al., 2010). Mraz et al., in the (1979), demonstrates that the LDH activity increase with BPH. This finding on LDH activity agree with our results, however, hyperplasia cells produced more lactate which leads to increase LDH activity (Gisselsson and Lercbe, 2008).

IV. Conclusion

The present study has shown that there was a relationship between potency of oxidative stress and BPH. The data show an increase of TPSA, FPSA, PAP, MDA and LDH levels in BPH patients and a positive correlation between them as shown in
In conclusion, we describe a previously unknown relationship between PSA, PAP, MDA and LDH as an index of oxidative stress in BPH.

V. Reference


