Research Article

# Unravelling the Link Between Benign Prostatic Hyperplasia and Butyrylcholinesterase

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**ABSTRACT**

Benign prostatic hyperplasia (BPH) is a common disease in men over 50 years of age may be viewed as inflammatory prostatitis whose pathogenesis may be triggered by multiple factors. Butyrylcholinesterase(BChE) levels in plasma has been shown to increase in various diseases like diabetes mellitus, cancer, where inflammatory processes are the key contributing factors. The study aims at unraveling the link between BPH and BChE. Serum albumin, globulins, prostate specific antigen, BChE and other liver enzymes (ALT, AST and ALP) were estimated in 25 healthy men and 25 with BPH. PSA was estimated by ECLIA and all the other parameters spectrophotometrically. PSA was significantly elevated (p=0.00) and BChE showed an apparent increase in BPH patients compared to controls. Further, there was a positive correlation(r=0.813, p=0.000) between BChE and PSA in BPH patients. Serum globulins increased significantly and all other hepatic enzymes remained in the normal range in these patients. Increase in globulins may be secondary to inflammatory response in BPH. It can be concluded that BChE can be considered as an inflammatory marker, though not specific for BPH. Search for biomarkers specific for BPH that could stratify patients at risk and complicated outcomes remains open.

**Keywords:** Benign prostatic hyperplasia, Butyryl choline esterase, PSA.

## INTRODUCTION

BPH refers to proliferation of the epithelial cells and smooth muscle cells within the prostate whose etiology is still not well understood.[1] Prostatic inflammation may be a mechanism for hyperplastic changes in prostate in BPH. In addition to androgen signaling, various growth factors, chemokines and cytokines released following bacterial or viral infection have been implicated in proinflammatory process within prostate which may lead to prostatic growth in BPH.[2] PSA produced in prostate epithelial cells as a response to androgen is markedly increased in BPH. The release of prostatic self antigens specially PSA subsequent to tissue damage may sensitize immune system to further release proinflammatory molecules.[3] On the contrary one of the hypotheses suggests that interaction between steroid hormone metabolism and inflammatory reactions regulate PSA expression.[4] Acetyl choline is an anti-inflammatory agent, whose levels increase in local and systemic inflammation with a concomittent increase in the enzymes acetyl choline esterase and butyrylcholinesterase.[5] Anticholinergics are used in the treatment of BPH.[6]

Increased BChE activity has been reported in hypertension, obesity, diabetes, where, low grade systemic inflammation plays a major role in the pathophysiology.[7,8]

Thus studies have shown that this enzyme can be a biochemical marker of inflammation. Hence, the present study aims to estimate BChE, PSA in BPH, correlate the two parameters and also attempts to establish the role of BChE in inflammatory processes of BPH.

## MATERIALS AND METHODS

The study population consisted of 25 normal males and 25 patients aged between 30 and 60 years. BPH was diagnosed by ultrasound and patients with BPH confirmed by absence of malignancy on the basis of histological reports of biopsy samples were considered for the study. Patients with hypertension, diabetes mellitus, dyslipidemias, and patients who were on drugs that could affect PSA levels were excluded from the study. 2 mL of blood was collected in vacutainers without any anticoagulant from controls and patients with BPH. The sample was allowed to clot for half an hour and centrifuged at 3000 rpm for 5 minutes to separate serum. Serum PSA was determined by ECLIA in Cobas 6000.[9] Serum BChE was estimated spectrophotometrically based on the yellow color formation by the reaction of DTNB with thiocholine formed from the hydrolysis of acetylthiocholine by the enzyme.[10] Liver function tests were also done by routine spectrophotometric methods as BChE is also synthesized by liver.[11] Data were analysed statistically by students t test and Pearsons correlation.

Statistical analysis was done by using SPSS software version 20. Differences of $p < 0.05$ were considered significant.

## RESULTS

Mean PSA concentration was significantly high in patients with BPH compared to normal males. There was an apparent increase in serum BChE in BPH patients compared to normal (Table 1). Further, there was a significant positive correlation between PSA and BChE in BPH patients (r=0.813, p=0.000) (Table 2). Furthermore,

serum globulins were significantly increased in BPH compared to normal subjects. However, other liver enzymes viz., ALT, AST and ALP did not show any variations in BPH (Table1). Further, correlation of these enzymes in BPH patients with BChE or PSA was insignificant (Table 2, 3).

**Table 1:** Base line data depicting liver function and PSA in normal and BPH patients

| | Normal (n=25) | BPH (n=25) | P value |
|---|---|---|---|
| **Age** | 56.1 ± 10.26 | 60.6 ± 9.6 | 0.101 |
| **Total protein(g/dL)** | 7.2 ± 0.41 | 7.3 ± 0.25 | 0.187 |
| **Albumin (g/dL)** | 4.49 ± 0.18 | 4.26 ± 0.36 | 0.068 |
| **Globulin(g/dL)** | 2.71 ± 0.31 | 3.09 ± 0.44* | 0.018 |
| **AST(IU/L)** | 25.7 ± 9.65 | 24 ± 7.41 | 0.581 |
| **ALT(IU/L)** | 35.8 ± 17.52 | 25.38 ± 9.41 | 0.103 |
| **ALP(IU/L)** | 68 ± 11.61 | 84.42 ± 34.34 | 0.152 |
| **BChE(µmol/mL)** | 57.12 ± 3.72 | 59.72 ± 5.61 | 0.18 |
| **PSA(ng/mL)** | 1.51 ± 0.66 | 9.67 ± 1.66*** | 0.00 |

n= sample size

**Table 2:** Correlation of BChE with other hepatic markers and age in BPH patients

| | r value | p value |
|---|---|---|
| **Age** | 0.122 | 0.56 |
| **Total protein** | 0.344 | 0.098 |
| **Albumin** | 0.350 | 0.094 |
| **Globulin** | -0.192 | 0.369 |
| **AST** | -0.255 | 0.188 |
| **ALT** | -0.273 | 0.197 |
| **ALP** | -0.217 | 0.833 |
| **PSA** | 0.813 | 0.000 |

**Table3:** Correlation of PSA with other hepatic markers and age in BPH patients

| | r value | P value |
|---|---|---|
| **Age** | -0.10 | 0.962 |
| **Total protein** | 0.289 | 0.156 |
| **Albumin** | 0.294 | 0.163 |
| **Globulin** | -0.197 | 0.356 |
| **AST** | -0.250 | 0.174 |
| **ALT** | -0.273 | 0.197 |
| **ALP** | -0.233 | 0.273 |
| **BChE** | 0.813 | 0.000 |

## DISCUSSION

BPH is a common disease that accounts for morbidity and mortality in men over 50 years of age.[12] The pathophysiology of which is still unclear. Inflammation of prostate may be one of the causes for hyperplastic changes in BPH. BPH may be viewed as inflammatory prostatitis whose pathogenesis may be triggered by multifactorial pathways.[13] There are several proposed mechanisms for the basis of inflammation which includes production of proinflammatory cytokines and chemokines following bacterial or viral infection, infiltration of lymphocytes and macrophages and oxidative stress. Infiltrating cells may provide sources of free radicals that may promote proliferation of prostate epithelial cells leading to prostatic hyperplasia.[2] BChE is an enzyme synthesized by liver, has been significantly increased in the initial stages of diseases like diabetes mellitus, hyperthyroidism, Alzheimer's disease, oral cancer where inflammatory processes are key contributing factors,[14] whereas in the advanced stages of the disease the enzyme activity is low.[5] Butyryl cholinesterase catalyzes hydrolysis of acetyl choline in CNS and ANS. Its exact function in blood remains to be explored. In the present study plasma BChE has increased in patients with BPH, while the other liver enzymes remained in normal range. The significant increase in serum globulins observed may be secondary to inflammatory response in BPH that could be due to increased synthesis. Significant increase in PSA in these patients can be attributed to increase in volume of secreting prostate tissue. Subsequent to tissue damage, several prostatic self antigens including PSA will be released which sensitize immune system, activate CD4 cells to release proinflammatory cytokines and interleukins. More interestingly, there was a strong correlation of BChE with PSA levels in BPH patients. However, BChE as well as PSA levels did not show any correlation with age in BPH patients. This finding is in agreement with the results of previous studies.[15,16] Literature survey showed that Lampon[8] reported a significant positive correlation between BChE and hsCRP in patients with acute inflammation. Acetyl choline when bound to nicotinic receptors on tissue macrophages leads to decrease in production of proinflammatory cytokines. Acetyl choline by activation of cholinergic anti-inflammatory pathway acts as an anti-inflammatory agent.[5] Furthermore, anticholinergic agents are used in the treatment of BPH.[6] BChE is an enzyme found in serum, pancreas, liver and CNS which hydrolyses acetyl choline, hence, BChE concentration will indirectly reflect reduced concentration of acetyl choline in the tissues. This hypothesis clearly explains the role of BChE in the etiology of inflammation in BPH. Earlier studies have shown that steroid hormones increase hepatic synthesis and secretion of BChE.[17] Certain studies have revealed that declining testicular function with increase in intra prostatic androgen level leads to BPH.[18] Hence, a similar phenomenon is likely in prostate gland where secretion of PSA is dependent on androgen activation and same may be true with the increased secretion of BChE.

Although a number of potential markers like CRP, interleukins, MDA have been evaluated in BPH, none of them are specific to prostate. Since, BChE also remains in the list of non specific markers, search for biomarkers

that could be used to stratify patients with risk or with related outcomes of BPH still remains open.

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