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ORIGINAL ARTICLE

HORMONAL INDUCTION OF BENIGN PROSTATIC HYPERPLASIA IN RATS: EFFECTS ON SERUM MACROMOLECULAR METABOLISM

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ABSTRACT

Benign prostatic hyperplasia (BPH) was induced in rats using a mixture of dihydrotestosterone (DHT) and estradiol valerate (ratio 10:1). The fasting blood glucose levels, serum lipid profile and pro-atherogenic indices of the rats were estimated using standard procedures, and compared to those of rats in a control group. The results show that rats in the test group had significantly ($p<0.05$) lower fasting blood glucose and serum total cholesterol levels, while the other lipid and lipoprotein parameters and serum lipid pro-atherogenic indices were similar ($p>0.05$) in both groups. Though BPH is thought to be related to metabolic derangements, it appears that BPH can be induced without a collateral disruption of serum macromolecular metabolism.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a neoplastic enlargement of the prostate gland that is common in elderly men (Paglone, 2010). The etiology of BPH is still poorly understood. However, it is clear that the growth and cytodifferentiation of the prostate gland (including aberrant growth) are under hormonal control (Ball and Risbridger, 2003). A complex relationship between androgens, estrogens, prolactin, sex hormone binding globulin, among other factors, is believed to be central to BPH pathogenesis (Ejike and Ezeanyika 2008; Ejike and Ezeanyika 2009).

Furthermore, there have been suggestions that BPH is associated with the metabolic syndrome (Kasturi *et al.,* 2006; Ozden, 2007). Furukawa *et al.* (2004) report that the metabolic syndrome is associated with systemic inflammation and oxidative stress – factors thought to promote a prostatic growth path, characterized by BPH (Wang *et al.,* 2004).

It is however not clear if the association between BPH and metabolic derangements is causal in any direction. Since BPH is known to be inducible in animals using dihydrotestosterone (DHT) and estradiol in a ratio of 10:1 (Jeyaraj *et al.,* 2000; Herber, 2002), this study examined the serum macromolecular metabolic profile of rats in which BPH was induced hormonally, in relation to a control set of rats.

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MATERIALS AND METHODS

Ten 4-week old albino rats, weighing approximately 109g each, were used for this study. The rats were acclimatized to the animal house environment for one week prior to the commencement of the study. They were randomly assigned to two groups of 5 rats each, housed in standard plastic rat cages (one for each group) and exposed to 12 hour light/dark cycles under humid tropical conditions. The rats had free access to feed and tap water.

Rats in the test group were given 0.2ml sub-cutaneous injections of hormones containing 9mg/kg body weight DHT and 0.9mg/kg body weight estradiol valerate dissolved in olive oil every other day for 28 days, while rats in the control group were given 0.2ml sub-cutaneous injections olive oil in place of the hormones. At the end of 28 days, the rats were fasted overnight and bled exhaustively by cardiac puncture, under light chloroform anesthesia. A few drops of whole blood was immediately removed and used for the fasting blood glucose assay, while the rest were allowed to clot before centrifugation for 5 minutes at 2000g. The serum was carefully pipetted into clean, properly labeled sample containers, and used for the other analyses.

Total cholesterol, triacylglycerol and HDL-cholesterol levels in serum were determined using the methods of Allain *et al.,* (1974), Tietz (1990) and Lopes-Virella *et al.* (1977) respectively. LDL-, VLDL-, and Non-HDL-cholesterols, and serum lipid pro-atherogenic indices were derived using equations described by Friedwald *et al.* (1972), Tietz (1990), Packard and Saito (2003) and Budzynski *et al.* (2003) respectively. Fasting blood glucose levels were estimated by the bioamperometry

principle, using the Accu-Check Glucometer and Advantage II test strips. All chemicals used were of analytical grade and were purchased from reputable companies. Means and standard deviations of the data were calculated, and differences between means separated by one way ANOVA. A significant threshold of $p < 0.05$ was employed for the analysis. All data analyses were done using SPSS for windows version 11.0 (SPSS Inc., Chicago, IL).

Table 1. Serum lipid profile and fasting blood glucose concentrations in rats in the test and control groups

	Test	Control	P value
T.Chol (mmol/l)	2.2 ± 0.1	2.7 ± 0.4	*0.038
HDL (mmol/l)	1.1 ± 0.3	1.2 ± 0.3	0.580
LDL (mmol/l)	0.8 ± 0.3	0.9 ± 0.5	0.686
Non-HDL (mmol/l)	1.1 ± 0.3	1.5 ± 0.5	0.244
VLDL (mmol/l)	0.7 ± 0.2	1.3 ± 0.8	0.060
TAG (mmol/l)	0.3 ± 0.1	0.6 ± 0.4	0.059
FBG (mmol/l)	9.1 ± 1.7	15.5 ± 4.0	*0.001

TAG, TChol, HDL, LDL, VLDL and FBG represent Triacyglycerol, Total Cholesterol, High Density Lipoprotein Cholesterol and Low Density Lipoprotein Cholesterol, Very Low Density Lipoprotein Cholesterol and Fasting Blood Glucose respectively.
* indicates values that are significantly different

Table 2. Serum lipid pro-atherogenic indices of rats in the test and control groups

	Test	Control	P value
T.Chol/HDL	2.2 ± 0.6	2.4 ± 0.8	0.785
NonHDL/HDL	1.2 ± 0.6	1.4 ± 0.8	0.785
LDL/HDL	0.8 ± 0.5	0.8 ± 0.6	0.975

TCHOL, HDL and LDL represent Total Cholesterol, High Density Lipoprotein Cholesterol and Low Density Lipoprotein Cholesterol, respectively.

RESULTS AND DISCUSSION

Table 1 shows that the serum total cholesterol of the test group was significantly ($p<0.05$) lower than that of the control group. However, the other serum lipids and lipoproteins were each similar ($p>0.05$) between the two groups. Cholesterol is the precursor for steroid hormone biosynthesis. Its availability and conversion to pregnenolone are a rate limiting factor and step, respectively, in the biosynthesis of steroid hormones (Bruiggemier, 2005). Mitropoulous *et al.* (2004) and Parsons *et al.* (2008) report that hypercholesterolemia may affect the sex steroid axis and result in BPH, while Ezeanyika *et al.* (2006) showed that serum total cholesterol levels correlated positively with BPH symptoms. However, the data presented here, show a significantly lower level of serum cholesterol in rats in which BPH was induced hormonally [and its presence confirmed histologically (data not shown)], relative to their control counterparts. It appears that though hypercholesterolemia (and dyslipidemia, generally) may lead to a cascade of events culminating in diseases like BPH, BPH can exist without dyslipidemia.

The fasting blood glucose levels, like the total cholesterol levels, were also significantly ($p<0.01$) lower than that of their control counterparts (Table 1). Though elevated fasting blood glucose concentrations (as is characterized in diabetes mellitus) is thought to play a role in the etiology of BPH (Stamatiou *et al.,* 2009) and clinical markers of BPH have been shown to correlate with diabetes mellitus (Sarma *et al.,* 2008), the data presented here show that the induction of BPH in rats by hormonal means does not result in a concomitant elevation of their blood glucose level.

There were no significant differences ($p>0.05$) in the serum lipid pro-atherogenic indices of rats in control and test groups. The serum lipid pro-atherogenic indices are good markers of adverse cardiovascular events (Budzynski *et al.,* 2003), and cardiovascular disorders, especially hypertension have been linked to BPH (Hammarsten and Hogstedt, 1999). It therefore appears that BPH sufferers may have a higher risk of cardiovascular events. This report however, suggests that the test rats were not at more risk of cardiovascular events than the control rats.

In conclusion, the data presented here show that in rats, the induction of BPH may not present with a corresponding increase in blood glucose concentrations, serum lipids and lipoproteins, and lipid pro-atherogenic indices. The relationship between BPH and metabolic abnormalities as seen through macromolecular metabolism therefore may not be a 'straight-jacket affair' and deserves more attention.

REFERENCES

Allain CC, Poon LS, Chan CSC, Richmond W, Fu PC. 1974. Enzymatic colorimetric method for cholesterol estimation. *Clin Chim*., 20: 470-475

Ball, E.M.A. and Risbridger, G.P. 2003. New perspectives on growth factor-sex steroid interaction in the prostate. *Cytokine Growth Factor Review,* 14: 5-16.

Brueggemeier RW (2005) Sex hormones (male): analogs and antagonists. In: Meyer RA (Ed) Encyclopedia of Molecular Cell Biology and Molecular Medicine. 2nd Edition Volume 13. Weinheim, Wiley-VCH Verlag GmbH & Co KGaA pp 3-7

Budzynski J, Klopocka M, Swiakowski M, Pulkowski G and Ziólkowski1 M. 2003. Lipoprotein(a) in alcohol-dependent male patients during a six-month abstinence period. *Alcohol & Alcoholism,* 38:157–162

Ejike CECC and Ezeanyika LUS 2008. Metabolic syndrome in sub-Saharan Africa: "smaller twin" of a regions prostatic diseases? *Int Urol. Nephrol.,* 40:909-920

Ejike CECC and Ezeanyika LUS 2009. Lifestyle changes in Nsukka metropolis in relation to prostate cancer and benign prostate hyperplasia. *Nig J Biochem Mol Biol.,* 24: 55-59

Ezeanyika LUS, Ejike CECC, Obidoa O and Elom SO 2006. Prostate disorders in an apparently normal Nigerian population 2: Relationship with some biochemical parameters. *Biokemistri.,* 18:133-139

Friedewald WT, Levy RI and Fredickson DS. 1972 Estimation of the concentration of LDL cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*., 18: 499-502

Furukawa S, Fujuta T, Shimabukuro M, Iwaki M, Yamada Y, Nakajima Y, Nakayama O, Makishima M, Matsuda M and Shimomura I. 2004. Increased oxidative stress in obesity and its impact on metabolic syndrome *J Clin Invest.,* 114:1752-1761

Hammarsten J and Hogstedt B. 1999. Clinical, anthropometric, metabolic and insulin profile in men with fast annual growth rates of BPH. *Blood Press,* 8:29-36

Herber D. 2002. Prostate enlargement: the canary in the coal mine? *Am J Clin Nutr.,* 75: 605-606

Jeyaraj DA, Uduyakumar TS, Rajalakshmi M, Pal PC and Sharma RS. 2000. Effects of long term administration of androgens and estrogen on Rhesus monkey prostate: possible induction of benign prostatic hyperplasia. *J Androl*., 21:833-841

Kasturi S, Russell S and McVary KT. 2006. Metabolic syndrome and lower urinary tract symptoms secondary to benign prostatic hyperplasia. *Curr Urol Rep.,* 7:288-292

Lopes-Virella MF, Stone P, Ellis S. 1977. Cholesterol determination in high density lipoprotein separated by three different methods. *Clin Chem*., 23: 882

Mitropoulous D, Plomidou K, Kyroudi-Voutgari A, Zervas A and Perea D 2004. Effect of hypercholesterol diet (HD) on sex steroid plasma levels in rats. *Eur Urol.,* 3:74

Ozden C, Ozdal OL, Urganioglu G, Kovuncu H, Gokkaya S and Mermis A. 2007. The correlation between metabolic syndrome and prostatic growth in patients with benign prostatic hyperplasia. *Eur Urol.,* 51:199-206

Packard CJ and Saito Y. 2003. Non-HDL cholesterol as a measure of atherosclerotic risk. *J Atheroscler Thromb* 11:6-14.

Paglone DR. 2010. Benign prostatic hyperplasia. *Clin Geriatr Med*., 26: 223-239

Parsons JK, Bergstrom J and Barrett-Connor E. 2008. Lipids, lipoproteins and the risk of benign prostatic hyperplasia in community-dwelling men. *BJU Int.,* 101: 313-318

Sarma AV, Burke JP, Jacobsen DJ McGree ME, St Sauver J, Girman, Lieber MM, Herman W, Macoska J, Montie JE, and Jacobsen SJ. 2008. Associations between diabetes and clinical markers of benign prostatic hyperplasia among community-dwelling black and white men. *Diabetes Care,* 31:476-482

Stamatiou K, Lardas M, Kostakos E, Koutsonasions V and Michail E. 2009. The impact of diabetes type 2 in the pathogenesis of benign prostatic hyperplasia: A review. *Adv Urol* doi:10.1155/2009/818965

Tietz NW. 1990. Clinical guide to laboratory tests. 2nd edition. WB Saunders Company, Philadelphia, USA, pp 554-546

Wang W, Bergh A and Damber JE. 2004. Chronic inflammation in BPH is associated with focal upregulation of cyclo-oxygenase-2, Bd-2 and cell proliferation in glandular epithelium. *Prostate.,* 61:60-72

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