



## Preponderance of Bisphenol a in Primary Hypertensive Subjects

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### ABSTRACT

Primary or essential hypertension accounts for about 95-97% of cases of hypertension. It has no clear underlying etiology but appears to be as a result of interplay of complex genetic and environmental factors. Bisphenol A (BPA) is an industrial chemical used primarily in polycarbonate plastic and epoxy resins. Its exposure in humans is mainly through diet. BPA acts, through a variety of physiological receptors, such as genomic estrogen receptors 1 and 2, membrane-bound estrogen receptors, and alteration in blood pressure. This study was designed to examine Bisphenol A and estrogen levels in known hypertensive subjects by determining serum BPA, estrogen, and basic metabolic index (BMI). A total of 172 known hypertensive subjects (test group) from medical out-patient clinic, Central hospital, Benin City and 60 normotensive subjects (control groups) were recruited for this study. Serum estrogen and Bisphenol A were estimated using ELISA method. Level of significant was taken at  $p < 0.05$ . Results showed that there was no statistical significant difference in the mean levels of BMI ( $P = 0.351$ ) and estrogen ( $p = 0.884$ ) in the test groups when compared with the control groups. BPA was significantly higher in hypertensive subjects ( $p = 0.000$ ) when compared with normotensive subjects. Significantly raised BPA was found in known hypertensive subjects compared with normotensive subjects, which indicates that, individuals with primary hypertension may have been exposed to high environmental Bisphenol A. BPA accumulation in blood may be a contributory factor or a result of primary hypertension.

**Keywords:** Bisphenol A; Estrogen; Primary hypertension

### INTRODUCTION

Hypertension is defined as persistently elevated blood pressure; that is a pressure that exceeds an arbitrary set level of normalcy. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII) recommends that the diagnosis of hypertension be made when the average of two or more diastolic blood pressure measurements on at least two subsequent visits is 90 mmHg or more, and when the average of multiple systolic blood pressure readings on two or more subsequent visits is consistently 140 mmHg or more. Isolated systolic hypertension is defined as systolic blood pressure 140 mmHg and diastolic blood pressure 90 mmHg [1]. Hypertension is broadly classified as Primary or essential hypertension (95-97%) which has no clear underlying cause but appears to be the result of an interplay of complex genetic and environmental factors, and secondary hypertension (3-5%) caused by a specific underlying disorders usually involving kidneys or endocrine system. Several pathophysiological mechanisms contribute to the development of

primary hypertension. The factors include: genetics, high salt intake, low physical activity, obesity, insulin resistance, renin-angiotension system, sympathetic nervous system, malnutrition, alcohol and acute stress [2].

Bisphenol-A (BPA) (4,4-dihydroxy-2,2-diphenylpropane), is an industrial chemical synthesized by condensation of two phenol groups and one acetone molecule. BPA was first synthesized in 1891, its estrogenic properties were hypothesized in the 1930s [3] Since the year 1940, BPA has been predominantly used as a monomer in the manufacturing of polymers such as polycarbonate (PC), epoxy resins, polysulfone, or polyacrylate, as an antioxidant and inhibitor of end of polymerization in polyvinyl chloride plastics (PVC) and as a precursor for the synthesis of the flame retardant tetrabromobisphenol-A [4,5].

Polycarbonate is used in materials like; reusable plastic bottles, feeding-bottles, plates, goblets, cups, microwave ovenware, storage containers, etc., whereas the epoxy resins are used for internal coating of food and beverage cans.(4) Other uses of polycarbonates, epoxy resins, polysulfone, and polyacrylates are sunglasses, building materials, CD-ROM, medical devices, dental materials, thermal paper etc. [6]. Therefore, it is estimated that food contributes to more than 90% of the overall BPA exposure, while exposure through dust ingestion, dental surgery, and dermal absorption remains below 5% in normal situations [7]. BPA is also said to be an endocrine disruptor. It can imitate the body's hormones, disrupting the production, secretion, transport, action, function, and elimination of these natural hormones [8]. It does this by acting through a variety of physiological receptors, such as genomic estrogen receptors 1 and 2, membrane-bound estrogen receptors, androgen receptor, peroxisome proliferator-activated receptor  $\gamma$ , thyroid hormone receptor, and alteration in blood pressure [9].

Estrogen is important for maintaining and repairing endothelium mediated by estrogen receptor alpha ( $ER\alpha$ ) through increase in numbers and cyclooxygenase resulting in vasorelaxation [10]. Oestrogenic endocrine disruptor chemicals, such as BPA is a selective estrogen receptor modulator and can act as agonist and antagonist of estrogen for estrogen receptor alpha ( $ER\alpha$ ) but acts only as an agonist for estrogen receptor beta ( $ER\beta$ ). Activation of estrogen receptor beta ( $ER\beta$ ) can reduce systematic arterial pressure through autonomic influence [11,12]. During development, endocrine disruptors can influence normal hormonal homeostasis and lead to immediate and/or lifelong consequences. This study was therefore designed to evaluate bisphenol A, and estrogen levels in known hypertensive subjects.

## MATERIALS AND METHODS

A total of 232 human subjects aged between 40 and 60 years were recruited for this study. 172 of the subjects were already diagnosed hypertensive patients attending Medical out Patient (MOP) clinic at Central hospital, Benin City, Nigeria, while 60 apparently healthy subjects aged between 40-60 years with blood pressure <140/90 mmHg were recruited as controls. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Measurements of blood pressure were performed using mercury sphygmomanometer with appropriate arm cuffs. Prior to measurement, participants rested for 5 min in a sitting position according to the standard protocol [13-15].

Blood samples (5 ml) were drawn from each subject with which serum Estrogen and bisphenol A were analyzed using competitive Enzyme Linked Immunosorbent Assay (ELISA). Statistical Package for Social Science (SPSS) version 20.0 was used for the statistical analysis. The values obtained are expressed as mean and standard deviation (SD). The independent standard t-test was used to determine the significant difference between variables. Level of significance was taken at  $p < 0.05$ .

## RESULTS

A total of 232 human subjects aged between 40 and 60 years were recruited for this study. 172 of the subjects were already diagnosed hypertensive patients attending Medical out Patient (MOP) clinic at Central hospital, Benin City, Nigeria, while 60 apparently healthy subjects aged between 40-60 years with blood pressure <140/90 mmHg were recruited as controls. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Measurements of blood pressure were performed using mercury sphygmomanometer with appropriate arm cuffs. Prior to measurement, participants rested for 5 min in a sitting position according to the standard protocol.

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## DISCUSSION

Bisphenol A (BPA) is a widely used chemical in the production of plastic food containers in many consumer products and of epoxy resins in dental fillings [16,17]. Exposure to BPA is very common and is majorly orally. The present study revealed that serum BPA was significantly increased in the hypertensive subjects when compared with normotensive subjects. This increase could imply that these individuals (the hypertensive subjects) may have been exposed to some of the consumer products made with BPA. Increase in BPA as seen in the hypertensive subjects could also be the cause of the hypertension or could be worsening the condition owing to the endocrine-disrupting effect of BPA on the estrogen receptors [18]. Little is known about the mechanism of how BPA affects the cardiovascular system but BPA is suspected to have various mechanisms of action in humans, and the estrogenic action is considered to be one of the mechanisms [19,20]. Estrogen affects the cardiovascular system, but whether exogenous estrogen protects or harms the cardiovascular system is controversial. The cells of the cardiovascular system have estrogen receptors ( $\alpha$  and  $\beta$ ). These receptors are involved in antiatherogenic actions, vasodilation and preservation of vascular integrity, cardiomyocyte survival, and regulation of excitability of smooth muscle cells [21,22]. As a xenoestrogen, BPA may alter these functions of estrogen receptors by mimicking or blocking the action of estrogen [23]. If BPA mimics the vasodilatory function of estrogen, it will cause more reduced vascular resistance, expansion of ECF blood volume, increased venous return, increased heart rate, increased cardiac output and all giving rise to high blood pressure (hypertension).

## CONCLUSION

From the results of this study, it is seen that both test and control participants studied are exposed to Bisphenol A – a substance used in the production of polycarbonates, plastics, cans, etc., and can migrate from these products into the body. Also, it is seen that there is higher preponderance of this chemical in the primary hypertensive subjects studied. It may be inferred that BPA accumulation may be a contributing factor in the development or pathogenesis of primary hypertension, or may worsen the effect of the existing condition. Conversely, its accumulation in the blood may be a consequence of the primary hypertension.

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