Urinary Benzophenone-3, Bisphenol A, and Triclosan Levels on Serum Measures Related to Prostate Health: NHANES 2005-2010 & 2011-2012

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INTRODUCTION

Chemical agents have been used for decades to enhance safety, contribute to healthy, modern lifestyles, and increase the human lifespan. However, these exogenous compounds have been scrutinized for their unintended health effects. Data from National Health and Nutrition Examination Survey (NHANES), collected by the Centers for Disease Control and Prevention, have shown widespread exposure to Bisphenol A (BPA) (i.e., ingredient used in some plastics), Benzophenone-3 (BP-3) (i.e., major ingredient in sunscreen), and triclosan (TCS) (e.g., an antimicrobial) within the U.S. general population (Tyrrell et al. 2013; Zamoiski et al. 2015). Because of the existing concerns surrounding the evidenced and associated health effects of these known endocrine disruptors and the limited information surrounding exposure health implications on the human prostate gland, this study evaluated the topic of concern in US males above the age of 40, by use of the publicly available NHANES data.

OBJECTIVES

Evaluate the associated effects of BP-3, BPA, and TCS on the reproductive indicators of prostate health in American men ages 40 and above.

METHODS: NHANES data 2005-2010 & 2011-2012 (total testosterone only) was collected for the purposes of this study. The analytical method conducted for all variables of interest is provided in the table on the right. To conduct these analyses, SAS 9.4 Survey procedures were employed to properly analyze the complex weights of these probability survey sample data. Exposures to BPA, BP-3, and TCS were measured in terms of urinary output and associated with serum markers of prostate health. Exposures were recoded as categorical quartiles (Q1 – lowest exposure to Q4 – highest exposure). These variables include total prostate specific antigen (PSA), creatinine, and total testosterone.

METHODS

Dependent	Independent	Covariates	Test
Total PSA, Creatinine, Testosterone, BPA, BP-3, TCS	Age Race/Ethnicity Education Marital Status	No	Independent T-Test
Total PSA, Creatinine, Testosterone	BPA, BP-3, TCS	Yes (two models: (1) one exposure variable and (2) three exposure variables	Multiple Linear Regression

Note: Multiple linear regressions were adjusted by age, race/ethnicity, education, marital status, body mass index, poverty income ratio, season of collection, time of venipuncture, and natural-log transformed urinary creatinine, total serum cholesterol, and serum cotinine. In a second model, further adjustments were made for the two excluded exposures.

RESULTS

Nationwide Distribution (2005-2010: n = 1371 and 2011-2012: n = 788)

Total PSA: 0.970 (0.027) Creatinine: 1.000 (0.006) Total Testosterone: 71.340 (5.455) Urinary BPA: 0.970 (0.027) Urinary BP-3: 0.275 (0.007) Urinary TCS: 1.000 (0.006)

Table 1. Total PSA Distribution NHANES 2005-2010

Total PSA	N	Geometric Mean	SE	95% CL	
Age					
40-49	378	0.716	1.043	0.658	0.779
50-59	360	0.964	1.051	0.873	1.065
60-69	316	1.215	1.066	1.069	1.381
70-79	206	1.599	1.075	1.383	1.848
>=80	111	1.667	1.116	1.336	2.080
Race/Ethnicity					
Mexican American/Other Hispanic	312	0.957	1.053	0.863	1.061
Non-Hispanic White	755	0.967	1.034	0.904	1.034
Non-Hispanic Black	253	1.023	1.072	0.890	1.176
Other	51	0.940	1.148	0.712	1.241
Education					
Less than High School	397	1.0687	1.0668	0.9383	1.2171
High School/GED	341	0.9987	1.0459	0.9124	1.0931
More than High School	633	0.9280	1.0382	0.8606	1.0008
Marital Status					
Married/Living with Partner	981	0.9545	1.0345	0.8916	1.0220
Widowed	81	1.3341	1.1429	1.0198	1.7452
Divorced/Separated	212	1.0343	1.0782	0.8889	1.2036
Never Married	97	0.8551	1.1024	0.7029	1.0403

Table 2. Total Testosterone (TT) NHANES 2011-2012

		Model 1			*Model 2*		
	Urinary BPA (ng/mL)	**% Change**	**95% CL**		**% Change**	**95% CL**	
Q1	Reference						
Q2	0.978 – 1.835	24.259	-26.288	109.489	3.252	-35.345	64.889
Q3	1.835 – 3.380	30.578	-18.511	109.258	13.179	-27.682	77.128
Q4	≥3.380	81.212	8.250	203.345	27.724	-15.583	93.267
		$p < 0.1151$			$p < 0.6367$		
	Urinary BP-3 (ng/mL)	**% Change**	**95% CL**		**% Change**	**95% CL**	
Q1	Reference						
Q2	2.872 - 9.624	36.520	-0.274	86.899	29.888	-4.125	75.980
Q3	9.624 – 44.876	1.511	-33.628	55.255	-0.994	-36.218	53.680
Q4	≥44.876	158.183	64.132	306.129	140.320	53.449	276.331
		$p < 0.0004$			$p < 0.0005$		

Table 3. Creatinine (NHANES 2005-2010)

		Model 1			*Model 2*		
	Urinary BPA (ng/mL)	**% Change**	**95% CL**		**% Change**	**95% CL**	
Q1	**Reference**						
Q2	0.978 – 1.835	3.207	0.034	6.481	3.254	0.097	6.510
Q3	1.835 – 3.380	3.075	-0.296	6.559	3.117	-0.242	6.588
Q4	≥3.380	3.039	-0.876	7.108	3.017	-0.927	7.117
		$p < 0.1780$			$p < 0.1664$		

The results provided here are those that were significantly associated with the serum outcome of interest. The nationwide distribution is provided at the top of this section, providing geometric means (standard error (SE)) for the variables of interest. Table 1 shows total PSA levels distributed in this study sample. Overall, total PSA increased with age. When compared between racial and ethnic backgrounds was highest in African American men and lowest in those who classified as "Other". Additionally, total PSA saw decreasing levels with higher levels of education. Finally, with regard to marital status, widowed men saw significantly higher levels, indicating poorer health. This was a pattern seen for the other serum variables of interest, as well (i.e., marker levels projecting towards that of poorer health: most total PSA and creatinine, in addition to the lower levels of TT (not shown here)). Table 2 and 3 provides the regressions for BPA and BP-3 with TT and BPA with creatinine, respectively. BPA and BP-3 positively associated with TT. Only BP-3 was globally associated with TT, specifically with exposures noted at ≥44.876 ng/mL of urinary BP-3. Table 3. shows a non-global association between BPA and creatinine. The result provides a significantly positive percent change as compared to the first quartile.

CONCLUSIONS

To date, this is the first known study to investigate the associations of environmental phenols within the context of older men's health, particularly regarding the prostate gland. Exposure to BP-3 was the only agent to produce global significant effects on one of the variables of interest, TT. In this cross-sectional study, a significant direct association between BP-3 and serum TT was presented in men ≥40 years of age that were participants of the 2011-2012 NHANES cycle. These findings provide that that BP-3 may have androgenic effects on older men. However, given the cross-sectional nature of this study, further studies will be needed to validate these findings.

"The old construct was that 'prostate cancer was fire and testosterone was gasoline,' said Dr Köhler. 'But a better analogy is that prostate cancer is a tree and testosterone is water,' he said. 'You need a certain amount of testosterone for prostate cancer to develop, but if you keep piling on more and more testosterone [water], the tree doesn't develop into a sequoia.' This is known as the 'saturation model,' ' he explained."

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