Canned Beverages and Blood Pressure

Exposure to Bisphenol A From Drinking Canned Beverages Increases Blood Pressure Randomized Crossover Trial

Sanghyuk Bae, Yun-Chul Hong

Abstract—Bisphenol A (BPA) is a chemical used in plastic bottles and inner coating of beverage cans, and its exposure is almost ubiquitous. BPA has been associated with hypertension and decreased heart rate variability in the previous studies. The aim of the present study was to determine whether increased BPA exposure from consumption of canned beverage actually affects blood pressure and heart rate variability. We conducted a randomized crossover trial with noninstitutionalized adults, who were aged ≥60 years and recruited from a local community center. A total of 60 participants visited the study site 3 times, and they were provided the same beverage in 2 glass bottles, 2 cans, or 1 can and 1 glass bottle at a time. The sequence of the beverage was randomized. We then measured urinary BPA concentration, blood pressure, and heart rate variability 2 hours after the consumption of each beverage. The paired t test and mixed model were used to compare the differences. The urinary BPA concentration increased after consuming canned beverages by ≥1600% compared with that after consuming glass bottled beverages. Systolic blood pressure adjusted for daily variance increased by ≈4.5 mm Hg after consuming 2 canned beverages compared with that after consuming 2 glass bottled beverages, and the difference was statistically significant. The parameters of the heart rate variability did not show statistically significant differences. The present study demonstrated that consuming canned beverage and consequent increase of BPA exposure increase blood pressure acutely. (Hypertension. 2015;65:313-319. DOI: 10.1161/HYPERTENSIONAHA.114.04261.) ● Online Data Supplement

Key Words: aging ■ bisphenol A ■ blood pressure ■ crossover trials

Bisphenol A (BPA) is a chemical used in the production of polycarbonate plastic and epoxy resins, which are used in a wide range of products, including plastic bottles, food containers, optical discs, dental fillings, and on the inner coating of cans. Therefore, BPA exposure is ubiquitous and has been detected in >95% of the population in the United States. BPA shows affinity for the estrogen receptor and may alter its function by blocking or mimicking the action of estrogen. Previous epidemiological studies have reported the associations between BPA exposure and adverse health effects on the reproductive and endocrine systems. BPA exposure had also been associated with cardiovascular disorders. We had previously reported that increased urinary BPA concentration was associated with higher blood pressure (BP) and decreased heart rate variability (HRV) in a panel study with elderly participants. A previous study that analyzed the National Health and Nutrition Examination Survey data set also reported that increased urinary BPA concentration was associated with hypertension. Furthermore, other studies had reported that increased urinary BPA was associated with heart and peripheral artery diseases, of which hypertension and decreased HRV are important risk factors. Considering that most of the previous epidemiological studies examined the cross-sectional associations between urinary BPA concentration and health outcomes, a randomized intervention trial can provide a higher level of evidence and may elucidate the health effect of BPA more clearly.

Canned food is one of the known BPA exposure sources. Previous studies have reported that BPA in the epoxy lining of the can containers could leach into food. A randomized crossover trial showed that eating canned soup for 5 consecutive days increased urinary BPA concentration by >1000% compared with eating soup cooked with fresh ingredients. The increase exceeds the range of exposure previously reported to be associated with increased risk of cardiovascular disorders in the previous epidemiological studies. However, we could not find any report on the health effect of such increased exposure caused by consuming canned food.

In the present study, we conducted randomized crossover intervention trial to examine whether consuming canned beverage and consequent increase of BPA exposure actually affect BP and HRV.
Methods

We conducted a randomized, crossover intervention trial involving 60 noninstitutionalized elderly participants, who were aged ≥60 years between February 2014 and March 2014. We chose the elderly because they are more susceptible to environmental exposure, making it more likely to observe the effect of BPA. Those with the medical history of heart diseases, cancer, liver diseases, and endocrine diseases were excluded. We established a study site at a local community welfare center and recruited the participants from the visitors.

We obtained informed consents from all participants, and the study protocol was approved by the Institutional Review Board at College of Medicine, Seoul National University (1312-027-539). The procedures followed in the present trial were in accordance with Declaration of Helsinki and institutional guidelines.

Soy milk from the same manufacturer (Chung Food, Chungju, Chungchungbuk-do, Korea) in different packaging (glass bottle or can) was purchased from a supplier. The beverages were then stored together at the same temperature. We randomly selected 3 each from the glass bottled and canned beverages, and sent these samples to a laboratory (NeoDiM Medical Institute, Seoul, Korea) to measure BPA concentration in the beverage using high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS; Agilent 6410 triple Quad LCMS; Agilent, Santa Clara, CA).

Participants were asked to visit the study site 3 times with a 2-week interval between visits. All participants were asked to fast for ≥8 hours and visit the study site at 9 AM. We provided 2 servings (195 mL per serving) of the beverage to the participants in 3 different combinations at each time; 2 cans (CC), 2 glass bottles (GG), or 1 can and 1 glass bottle (CG). Figure 1 shows the flow of the crossover trial. The randomization list with 12 per block was generated using a random number generation method at the Seoul National University, and the combination of beverage for each visit was assigned to the participant registration number. The assignment was notified to research assistants at the study site, when the participants visited. The participants were blinded. Those who measured BP and analyzed samples were also blinded; however, those who provided the beverage were not.

Urine samples were collected from the participants 2 hours after the consumption. During that 2 hours, the participants were asked not to eat or drink any other food. Urine samples were sent to the laboratory, where the beverage samples were analyzed, in <90 minutes after collection. Samples were stored at −20°C before analysis. Urinary BPA concentrations were also measured using HPLC-MS, as described previously.10 Standard solutions with BPA concentrations were replaced by lower limit of detection divided by square root 2>0.999. When the measured sample concentration was not within 20% of the standard calibration curve, the measured concentration in the beverage using high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS) was also measured using the same method.

The procedures followed in the present trial were in accordance with Declaration of Helsinki and institutional guidelines. The procedures followed in the present trial were in accordance with Declaration of Helsinki and institutional guidelines.

The paired t test was used to compare ΔSBP and ΔDBP of each period; CC and CG were compared with GG separately. Our sample size provided 80% power (2-tailed α=0.05) for detection of a difference of 4 mm Hg, allowing a 5% drop out. Because of the crossover design, the time unvarying confounders were canceled out, while conducting paired analyses. However, a time-varying factor can be an important confounder. For instance, daily ambient temperature is inversely associated with BP, and it varies day to day. To examine the association between assigned beverage and health outcomes after adjusting potential time-varying confounders, we constructed mixed effect models. The demographic characteristics (age, sex, and weight), medical history (hypertension and diabetes mellitus), lifestyle (smoking status, alcohol consumption, and sleep time), date and mean daily temperature (°C) of the examination day, and the sequence of the visit were included in the model. The model had an unstructured correlation matrix within a person, and the sequence of visit of each individual was included as a random variable. The daily mean temperature of Seoul was obtained from the Korea Meteorological Administration observation database, and other covariates were obtained by conducting a survey at the time of enrollment. The date was included as a linear variable because it was associated with ASBP linearly in univariate analysis. We also analyzed the association between the assigned beverage and ΔSBP among the participants, who did not report the previous history of hypertension or diabetes mellitus.

The nonparametric associations of urinary BPA concentration and BP were examined by constructing a generalized additive mixed model, which included the same covariates to examine the association between cumulative exposure of BPA and BP. Because the urinary BPA concentration measured 2 hours after the consumption of beverage reflects not only the increase of exposure after the consumption of beverage but also the cumulative exposure before the intervention, we presented the association between urinary BPA concentration and BP as the outcome of this analysis instead of ΔBP, which was considered as the effect of increase of BPA exposure from the beverage only (Table S1 in the online-only Data Supplement). PROC MIXED of SAS version 9.3 (SAS institute, Cary, NC) and the package gamm4 of R version 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria) were used for statistical analyses.

Figure 1. Flow of the trial. CC indicates 2 canned beverages; CG, 1 canned and 1 glass bottled beverages; and GG indicates 2 glass bottled beverages.
**Results**

The enrollment and the first visits were from February 6 to 21, 2014. The second and third visits were from February 20 to March 10 and from March 6 to 18, respectively.

Characteristics of participants are shown in Table 1. The mean age of the participants was 73.1±4.2 years. Among the 60 participants, 56 were women. Among the participants, 27 and 9 answered that they have hypertension and diabetes mellitus, respectively. All but 1 hypertensive participant received medication. All the participants completed the trial as assigned and 180 measurements were conducted.

The means of BPA concentration directly measured from the beverage in glass bottles and cans were 0.31±0.01 and 8.22±0.82 μg/L, respectively.

The urinary BPA concentration showed a similar pattern. The BPA concentration after consuming CC and CG was significantly higher than that after consuming GG (P<0.0001). Adjusting for urinary creatinine did not change the pattern (Table 2). The BP_{after} was the lowest after consuming GG and the highest after consuming CC, but the differences did not show statistical significance. However, ΔSBP was significantly higher after consuming CC by 5.0 mm Hg compared with that after consuming GG (P=0.0160). The parameters of HRV did not show significant differences.

Table 3 shows the relative differences of BP and HRV estimated with a mixed model according to the assignment in the CG and CC compared with the GG consumption. Similar to the paired analysis, ΔSBP was significantly higher after consuming CC by 4.5 mm Hg compared with that after consuming GG. When we restricted the analyses to those who did not report the previous history of hypertension or diabetes mellitus, the result showed a similar pattern.

Figure 2 shows the nonparametric association between the urinary BPA concentration and BP_{after}, using a generalized additive mixed model to examine the effect of cumulative BPA exposure. As the urinary BPA increased, SBP_{after} and DBP_{after} increased linearly. The regression coefficient of SBP_{after} and DBP_{after} for 10 μg/g creatinine increment of urinary BPA estimated with linear models was 1.6 mmHg (SE=0.71; P=0.0204) and 0.5 mm Hg (SE=0.35; P=0.1592), respectively. ΔSBP also increased linearly, but ΔDBP did not (Figure S1).

**Discussion**

In the present study, we demonstrated that consuming canned beverage significantly increased the urinary BPA concentration compared with consuming the same beverage in the glass bottle, which contained a lower concentration of BPA than beverage in the can. The change of BP 2 hours after the consumption of canned beverage compared with BP measured before the consumption was higher than that after the consumption of beverage in glass bottles. However, the parameters of HRV did not show statistically significant difference.

Although all possible routes of exposure are not known, most BPA exposure is thought to occur through the oral route. Several previous studies have reported that BPA in the inner coating of cans may leach into the food based on measurements of BPA concentrations in various canned products. BPA concentrations in the canned beverage in the present study were comparable with the results of previous studies. For instance, Lim et al reported that mean BPA concentrations in canned beverages were 8.30 μg/kg, with the range being nondetectable to 14.26 μg/kg. The mean concentration of BPA in the canned beverage measured in the present study was 8.22 μg/L, and the range was 7.62 to 9.38 μg/L.

Two previous trials examined cumulative BPA exposure >1 week or 5 consecutive days. Unlike previous trials, the present study examined only 1 time of exposure. However, this was sufficient to increase urinary BPA concentration by >1600%. The urinary BPA concentration varied in a day, and our results showed that a relatively small amount of contaminated food can significantly increase BPA exposure, possibly explaining the daily variation.

In the present study, we demonstrated that exposure to BPA increases BP, and the result was consistent with that of previous epidemiological studies, which reported the positive association of BPA concentration and BP. Hypertension is a risk factor of cardiovascular diseases, and the 20 mm Hg increase of systolic BP doubles the risk of cardiovascular disease. In light of this, the 5 mm Hg increase observed in the present trial may cause a clinically significant increase of risk of cardiovascular disorders, such as heart diseases and peripheral arterial diseases, which were associated with increased BPA concentration in the previous epidemiological studies. However, the increase of BP followed by BPA exposure does

<table>
<thead>
<tr>
<th>Variables</th>
<th>Parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>60</td>
</tr>
<tr>
<td>Age, y, mean±SD</td>
<td>73.1±4.2</td>
</tr>
<tr>
<td>Sex, female, n, %</td>
<td>56 (93.3)</td>
</tr>
<tr>
<td>Weight, kg, mean±SD</td>
<td>57.9±7.6</td>
</tr>
<tr>
<td>Hypertension, n, %</td>
<td></td>
</tr>
<tr>
<td>Yes, with treatment</td>
<td>26 (43.3)</td>
</tr>
<tr>
<td>No</td>
<td>33 (55.0)</td>
</tr>
<tr>
<td>Diabetes mellitus, n, %</td>
<td></td>
</tr>
<tr>
<td>Yes, with treatment</td>
<td>9 (15.0)</td>
</tr>
<tr>
<td>Yes, without treatment</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>No</td>
<td>51 (85.0)</td>
</tr>
<tr>
<td>Drinker, n, %</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13 (21.7)</td>
</tr>
<tr>
<td>No</td>
<td>47 (78.3)</td>
</tr>
<tr>
<td>Smoker, n, %</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3 (5.0)</td>
</tr>
<tr>
<td>No</td>
<td>57 (95.0)</td>
</tr>
<tr>
<td>Average sleep time, n, %</td>
<td></td>
</tr>
<tr>
<td>≤5 h/d</td>
<td>17 (28.3)</td>
</tr>
<tr>
<td>6–7 h/d</td>
<td>20 (33.3)</td>
</tr>
<tr>
<td>8–9 h/d</td>
<td>15 (25.0)</td>
</tr>
<tr>
<td>≥10 h/d</td>
<td>6 (10.0)</td>
</tr>
<tr>
<td>Completed trial, n, %</td>
<td>60 (100.0)</td>
</tr>
</tbody>
</table>
Hypertension February 2015

not necessarily lead to chronic elevation of BP. The present study only accounted for the acute effect of BPA exposure. The positive association between urinary BPA concentration and SBPafter suggests possible chronic effects on increment of BP, but the associations of repeated or chronic BPA exposure with cardiovascular diseases are still to be evaluated in further longitudinal study.

Unlike the previous report, the parameters of HRV were not significantly decreased with higher exposure to BPA. This may be because of 2 reasons. First, the sample size of the present study was not calculated to detect the differences of parameters of HRV. The previous study analyzed observations from >500 participants, and the sample size of the present study was relatively small. Second, the change of HRV observed in the previous study may not be the result of acute exposure. Further study with larger sample size and study design, which can account for a longer time frame, is needed to elucidate the effect of exposure to BPA on HRV.

We used crossover trial design because we tried to evaluate the relationships between the short-term exposure and the acute health effects. Previous studies showed that the serum concentration of BPA reaches its peak at 1.3 hours after consumption of the beverage.

### Table 2. Means of Urinary BPA, BP, and Parameters of Heart Rate Variability According to the Assigned Beverage

<table>
<thead>
<tr>
<th>Variables</th>
<th>GG, n=60</th>
<th>CC, n=60</th>
<th>CC, n=60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary BPA, μg/L</td>
<td>1.13±1.76</td>
<td>7.93±6.01</td>
<td>16.91±12.55</td>
</tr>
<tr>
<td>Urinary BPA, μg/g creatinine</td>
<td>1.25±2.26</td>
<td>9.43±5.01</td>
<td>20.65±6.61</td>
</tr>
<tr>
<td>SBP&lt;sub&gt;after&lt;/sub&gt;, mm Hg</td>
<td>134.9±18.2</td>
<td>135.8±18.4</td>
<td>131.9±14.4</td>
</tr>
<tr>
<td>DBP&lt;sub&gt;after&lt;/sub&gt;, mm Hg</td>
<td>80.0±9.4</td>
<td>80.5±11.2</td>
<td>80.0±8.5</td>
</tr>
<tr>
<td>SBP&lt;sub&gt;after&lt;/sub&gt;, mm Hg</td>
<td>127.0±14.0</td>
<td>128.2±16.0</td>
<td>129.0±14.8</td>
</tr>
<tr>
<td>DBP&lt;sub&gt;after&lt;/sub&gt;, mm Hg</td>
<td>76.5±7.8</td>
<td>77.0±9.3</td>
<td>77.1±9.0</td>
</tr>
<tr>
<td>ΔSBP, mm Hg</td>
<td>−7.9±14.3</td>
<td>−7.6±11.0</td>
<td>−2.9±10.6</td>
</tr>
<tr>
<td>ΔDBP, mm Hg</td>
<td>−3.5±7.4</td>
<td>−3.5±5.7</td>
<td>−2.8±5.9</td>
</tr>
<tr>
<td>SDNN, ms</td>
<td>31.3±30.9</td>
<td>26.4±12.7</td>
<td>26.4±16.1</td>
</tr>
<tr>
<td>RMSSD, ms</td>
<td>25.0±19.7</td>
<td>22.8±17.3</td>
<td>24.3±22.7</td>
</tr>
</tbody>
</table>

Compared using the paired t test. ΔDBP indicates DBP<sub>after</sub>−DBP<sub>before</sub>; ΔSBP, SBP<sub>after</sub>−SBP<sub>before</sub>; BP, blood pressure; BPA, bisphenol A; CC, 2 canned beverages; CG, 1 canned and 1 glass bottled beverages; GG, 2 glass bottled beverages; HRV, heart rate variability; RMSSD, root mean square of successive differences; SBP<sub>after</sub> and DBP<sub>after</sub> systolic BP and diastolic BP measured 2 hours after consumption of the beverage; SBP<sub>before</sub> and DBP<sub>before</sub> systolic BP and diastolic BP measured before consumption of the beverage; and SDNN, SD of normal-to-normal intervals.

### Table 3. Estimated Relative Difference of BP and Heart Rate Variability in the CG and CC Compared With That of the GG Consumption

<table>
<thead>
<tr>
<th>Variables</th>
<th>CG</th>
<th>CC</th>
</tr>
</thead>
<tbody>
<tr>
<td>All, n=60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP&lt;sub&gt;after&lt;/sub&gt;, mm Hg</td>
<td>2.1697</td>
<td>1.7953</td>
</tr>
<tr>
<td>DBP&lt;sub&gt;after&lt;/sub&gt;, mm Hg</td>
<td>0.8361</td>
<td>0.4782</td>
</tr>
<tr>
<td>ΔSBP, mm Hg</td>
<td>0.1236</td>
<td>4.5101</td>
</tr>
<tr>
<td>ΔDBP, mm Hg</td>
<td>−0.1627</td>
<td>−0.7825</td>
</tr>
<tr>
<td>SDNN, ms</td>
<td>−5.0372</td>
<td>−4.9536</td>
</tr>
<tr>
<td>RMSSD, ms</td>
<td>−2.1233</td>
<td>0.9315</td>
</tr>
</tbody>
</table>

No previous history of hypertension, n=33

ΔSBP, mm Hg | 0.4485 | 5.8678 |
ΔDBP, mm Hg | 1.3405 | 5.2726 |

No previous history of diabetes mellitus, n=51

ΔSBP, mm Hg | −0.5558 | 5.4570 |
ΔDBP, mm Hg | −0.3742 | 5.2134 |

Adjusted for age, sex, weight, smoking, alcohol consumption, medical history of hypertension and diabetes mellitus, sleep time, mean daily temperature, and date of examination. ΔDBP indicates DBP<sub>after</sub>−DBP<sub>before</sub>; ΔSBP, SBP<sub>after</sub>−SBP<sub>before</sub>; BP, blood pressure; CC, 2 canned beverages; CG, 1 canned and 1 glass bottled beverages; GG, 2 glass bottled beverages; HRV, heart rate variability; RMSSD, root mean square of successive differences; SBP<sub>after</sub> and DBP<sub>after</sub> systolic BP and diastolic BP measured 2 hours after consumption of the beverage; and SDNN, SD of normal-to-normal intervals.
ingestion of a BPA gelatin capsule, and the urinary concentration of BPA reached its peak at 2.2 hours after consumption of a diet rich in canned food. The half-life of BPA absorbed through the oral route is believed to be >6 hours. Thus, there is little possibility of carryover effects with >1 week of washout periods between the interventions and ≥8 hours of fasting before the intervention.

Most of the potential confounders, such as demographic characteristics, medical history, and potential effects of soy milk on BP, are canceled out because of the crossover design, by which the comparison was conducted within each participant. However, time-varying variables could still affect the results. One of the possible time-varying confounders was daily temperature. Because the BP is known to decrease as the ambient temperature increases, and the present trial had proceeded from February to March, the changing temperature could have influenced the outcomes. However, the result from the analysis adjusting the daily mean ambient temperature using a mixed model did not differ from that of the paired analysis (Table 3).

We also adjusted the daily variance of BP by subtracting the baseline BP (BPbefore) of every visit day, calculating ΔBP.

The SBP before of CC was the lowest without statistically significant difference. Because the BP was measured with an automatic sphygmomanometer and those who measured BP were blinded to the assignment of the beverage, potential bias in the measurement of BP were probably minimal. We instructed the participants to maintain their routines, such as taking antihypertensive medication, and it is unlikely that there was any difference in medication status between visit days.

Other possible sources of BPA may also play roles as time-varying potential confounders. To control for the confounders, we instructed the participants to maintain their daily routines and not to consume any food for ≥8 hours before the trial. In addition, interventions and samplings were conducted at the same time of the day for each visit. These measures might control the exposure to other sources of BPA, but possibility of exposure from other sources still remained. However, the remaining random variance in BPA concentration may have moved the statistical significance toward the null. The sequence of the intervention may influence the association in the crossover trial. We included the sequence of visit in the mixed model. However, the sequence of the model did not show significant association, and including or excluding the sequence of visit from the model did not change the result significantly (data not shown).

The estrogenic and antiandrogenic effects of BPA, and its binding to estrogen receptors, α and β, are suggested to be the mechanism of cardiovascular diseases associated with BPA exposure. Estrogen receptors, α and β, are thought to be responsible for repairing blood vessels and controlling BP; therefore, the action of BPA on these receptors is the probable mechanism. BPA also acts as an antagonist and disrupts the function of the thyroid hormone, and this may lead to an increase of BP. However, little is known about the molecular or physiological mechanism of increased BP after BPA exposure. Further research is warranted to elucidate the mechanism by which BPA increases BP.

We used soy milk to examine the effect of exposure to BPA leached from the container. We chose commercially available beverage to examine the effect of exposure occurring in daily lives. Soy milk was the ideal beverage because there was no known ingredient that elevates BP. However, in a previous intervention study, consuming soy milk lowered the BP in patients with mild to moderate essential hypertension. In addition, it has been reported that soy products were associated with lower BP. In the present study, we observed that the BP after was generally lower than BP before, and this might be the effect of soy milk. However, the effect of soy milk was canceled out in the analyses because we compared the difference of BP according to the container of the same soy milk within the same participants by using the crossover design.

The present study has limitations. We used spot urine to evaluate the exposure to BPA. We were unable to measure the total amount of BPA excreted in the urine or the time course of the BPA concentration, which would more accurately represent the exposure. However, considering the pharmacokinetics of BPA described above, the urinary BPA concentration measured from spot urine samples 2 hours after consumption may reflect the level of exposure from the beverage. Evaluating the time course of BPA concentration and BP may elucidate the physiological action of BPA on BP, but this was beyond the scope of the present trial. All participants were the elderly (age ≥60 years) and most of them were women, and these may limit the generalizability of the results. Only 4 of the participants were men, and we could not examine the difference of the effect between men and women. If there is a sex difference, the result could have been influenced by the difference. However, when we conducted an additional analysis, excluding male participants, the result was similar (data not shown).
We did not consider the possibility of other chemicals as confounders in the analyses. We could not find any literature about the effects on BP by chemicals leached from can or chemical reaction between soy milk and inner coating of can. However, residual confounding may have remained from unknown factors, including other chemicals in the canned beverage.

**Perspectives**

The present study demonstrated that the exposure to BPA was increased by consumption of canned beverage, and the exposure increased the BP in a relatively short-time frame. Considering that the use of epoxy resin for inner coating of canned food and BPA exposure from consumption of canned food are almost ubiquitous, the consequent increase of BP exposure increased the BP in a relatively short-time frame. The results suggested that participants should be considered to prevent exposure to BPA.

This study was supported by a grant of the Korean Health Technology Research Institute. The Korean Health Technology Research Institute is funded by the Ministry of Health and Welfare, Republic of Korea (HI13C0735).

**Acknowledgments**

Y.M. Choi and H. Yoo contributed in recruiting the participants and conducting the trial as research assistants. We are grateful for all the participants.

**Sources of Funding**

This study was supported by a grant of the Korean Health Technology R&D Project, Ministry of Health & Welfare, Republic of Korea (HI13C0735).

**Disclosures**

None.

**References**


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**Novelty and Significance**

**What Is New?**

- In the present randomized crossover trial, consuming canned beverage resulted in higher exposure to bisphenol A, an endocrine disruptor, and the exposure consequently increased the blood pressure in a short-time frame.

**What Is Relevant?**

- There had been reports from epidemiological studies that showed association between high-concentration of bisphenol A and cardiovascular diseases, including hypertension and heart diseases. The present study provides a higher level of evidence for the effect of BPA on blood pressure.

**Summary**

Considering the almost ubiquitous use of bisphenol A in daily lives, the increase of blood pressure consequence to the exposure poses substantial health risk.
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Hypertension. 2015;65:313-319; originally published online December 8, 2014;
doi: 10.1161/HYPERTENSIONAHA.114.04261

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/65/2/313

Data Supplement (unedited) at:
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**Title:** EXPOSURE TO BISPHENOL A FROM DRINKING CANNED BEVERAGE INCREASES BLOOD PRESSURE: A RANDOMIZED CROSSOVER TRIAL

**Authors:** Sanghyuk Bae1(2), Yun-Chul Hong1(2)(3)

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Table S1. The relative time frame of exposure, BP and BPA measurement

<table>
<thead>
<tr>
<th>Time</th>
<th>Exposure source</th>
<th>BP</th>
<th>BPA</th>
</tr>
</thead>
<tbody>
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<td>Before intervention</td>
<td>Cumulative</td>
<td>BP_before</td>
<td>Not measured</td>
</tr>
<tr>
<td>Intervention</td>
<td>Beverage</td>
<td>( \Delta BP(=BP_after - BP_before) )</td>
<td>Not measured</td>
</tr>
<tr>
<td>After intervention</td>
<td>Cumulative + Beverage</td>
<td>BP_after</td>
<td>Measured</td>
</tr>
</tbody>
</table>
Figure S1. Non-parametric associations of urinary BPA concentration with ΔSBP and ΔDBP in all observations.
罐装饮料和血压（摘要）

与摄入罐装饮料相关的双酚A暴露可升高血压：一项随机交叉试验
Exposure to Bisphenol A From Drinking Canned Beverages Increases Blood Pressure: Randomized Crossover Trial
Sanghyuk Bae, Yun-Chul Hong

双酚A（BPA）是一种常用于塑料瓶和饮料罐（易拉罐）内涂层的化学物质，与此同时，BPA暴露几乎无处不在。之前的研究所发现，BPA与高血压及心率变异性降低有关，而本研究的目的是观察摄入罐装饮料而增加BPA暴露是否明显影响了血压及心率变异性。为此，本研究在普通社区居民中进行了一项随机交叉试验，受试者年龄均≥60岁且全部来自于当地一个社区中心。试验中将相同的饮料分别装入2个玻璃瓶、2个饮料罐（易拉罐）或者1个玻璃瓶、1个饮料罐（易拉罐）中给受试者饮用，并且每次只随机发放其中一组饮料，共有60人完成了全部3次试验。在受试者摄入饮料2小时后监测其尿BPA浓度，血压和心率变异性，并以配对样本法和混合模型来比较各组结果间的差异。结果发现，与摄入饮料相比，摄入罐装饮料2小时后尿BPA浓度升高大于1600%，收缩压（调整每日变异性后）则升高约4.5 mmHg，此差异有统计学意义。心率变异性的差异则没有统计学意义。本研究证明了摄入罐装饮料增加BPA暴露后会使血压迅速升高。

(Hypertension. 2015;65:313-319.)

个体化行为干预（摘要）

个性化行为干预在提高血压控制率中的作用：一项随机对照试验的主要结果
Effectiveness of a Tailored Behavioral Intervention to Improve Hypertension Control: Primary Outcomes of a Randomized Controlled Trial
Jennifer P. Friedberg, Maria A. Rodriguez, Michelle E. Watsula, Iris Lin, Judith Wylie-Rosett, John P. Allegra, Stuart R. Lipsitz, Sundar Narayan

目前，高血压患者的血压控制率仍不理想。本研究选取533例血压控制不佳的高血压患者（经抗高血压药物治疗≥6个月），采用三臂随机对照试验的方法，给予2种行为干预来提高血压控制率。干预组采用个体化、阶段匹配式干预（stage-matched intervention, SMI）及非个体化健康教育干预（health education intervention, HIEI）的方式，给予目标饮食、运动及药物治疗6个月，对照组采用常规护理（UC）。各组的血压基线水平无差别。SMI组、HIEI组、UC组的基线血压控制率分别为42.6%、40.6%及44.6%（P=0.74），收缩压（SE）分别为136（0.89）、137（1.33）及137（0.96）mmHg。三组6个月时的血压控制率分别为64.6%（SMI）、54.3%（HIEI）及45.8%（UC）[与UC进行两两比较，P值分别为0.001（SMI）和0.108（HIEI）]。6个月后，SMI组、HIEI组、UC组收缩压（SE）分别为131.2（1.05）、131.8（0.99）及134.7（1.02）mmHg[与UC进行两两比较，P值分别为0.009（SMI）和0.047（HIEI）]。较UC而言，SMI组与UC组相比可以更好的降低收缩压并使血压控制率提高。对于血压控制不佳的高血压患者而言，SMI是一种全新、有效的方法去帮助其血压达标。

(Hypertension. 2015;65:440-446.)