The association between salt intake and adult systolic blood pressure is modified by birth weight\textsuperscript{1–3}

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ABSTRACT

Background: Epidemiologic evidence suggests that prenatal growth influences adult blood pressure. Nutritional factors, including salt intake, also influence blood pressure. However, it is unknown whether prenatal growth modifies the association between salt intake and blood pressure in later life.

Objective: Our aim was to examine whether the relation between salt intake and adult blood pressure is modified by birth weight.

Design: We studied 1512 participants of the Helsinki Birth Cohort Study who were born between 1934 and 1944. Information on birth weight was abstracted from birth records, and preterm births were excluded. During a clinical study, at the mean age of 62 y, blood pressure, weight, and height were measured. Diet was assessed with a validated food-frequency questionnaire. The relation between salt intake and blood pressure was tested by a piecewise multivariate regression analysis with the best fitting breakpoints to birth weight and salt intake.

Results: An inverse association was observed between birth weight and systolic blood pressure (SBP) ($P = 0.02$). No significant association between salt intake and SBP was observed in the whole study population. Of those whose birth weight was $\leq 3050$ g, a 1-g higher daily salt intake was associated with a 2.48-mm Hg (95% CI: 0.40, 4.52 mm Hg) higher SBP ($P = 0.017$) until the saturation point of 10 g. Of those whose birth weight exceeded 3050 g, SBP was not significantly associated with salt intake. For diastolic blood pressure, no significant relations were observed.

Conclusion: Adult individuals with low birth weight may be particularly sensitive to the blood pressure–raising effect of salt. Am J Clin Nutr 2011;93:422–6.

INTRODUCTION

Elevated blood pressure is a major risk factor accounting for more than one-half of all strokes and approximately one-half of all ischemic heart disease (1, 2). In addition, a small body size at birth has been associated with elevated blood pressure levels in later life in several studies, regardless of socioeconomic status (3). One underlying biological explanation could be that persons born with a low birth weight have a reduced number of nephrons in the kidneys (4), which might result in elevated blood pressure and hypertension over time.

High sodium and salt intake is another major contributor to elevated blood pressure. Intervention studies have shown reductions in cardiovascular events after reduced sodium intakes (5). Furthermore, it was previously shown that birth weight might be negatively associated with the salt sensitivity of blood pressure (6). This could play a major role in the maintenance of elevated blood pressure in persons born with a small body size.

To our knowledge, no previous study has focused on the possible interactions between birth weight, salt intake, and blood pressure levels in later life. The aim of the present study was to assess whether intrauterine growth modifies the association between salt intake and adult blood pressure in a large cohort of men and women born in Helsinki, Finland, between 1934 and 1944.

SUBJECTS AND METHODS

Design and study population

The subjects in this study are all participants in the Helsinki Birth Cohort Study, originally consisting of 4630 men and 4130 women. As previously described (7), they were born as singletons at Helsinki University Central Hospital between 1934 and 1944, attended child welfare clinics in the city, and lived in Finland in...
Dietary assessment

Diet was assessed with a validated, self-administered 128-item food-frequency questionnaire (FFQ) (9, 10). The FFQ was designed to assess the ordinary diet over the previous 12 mo. The subjects were asked to indicate the average intake frequency of each food item and mixed dish presented as 12 subgroups, eg, dairy products and vegetables. The 9 possible frequency categories ranged from never or seldom to ≥6 times/d. The portion sizes were fixed, eg, a glass or a slice of bread.

At the clinic, subjects completed the FFQ, which was then checked by a study nurse. The food intake data were entered and processed at the National Institute for Health and Welfare, Helsinki, Finland, by using the in-house calculation software Fineli, which uses the National Food Composition Database FINELI (11). Energy and salt intakes (sodium intake × 2.548) were calculated by multiplying the frequency of food consumption by fixed portion sizes to obtain the weight of each listed food item consumed as an average per day. Salt intake included the natural sodium content of raw foods, the salt added in cooking in average recipes, and the salt that is used in manufactured foods. Salt intake values were energy-adjusted by using the residual method (12).

Subjects were excluded if their FFQ had ≥10 blank food items (n = 2) or if their calculated energy intake was <650 or >6100 kcal/d, corresponding to 0.5% at each end of the self-reported daily energy intake scale (n = 20). In all, 122 subjects were excluded because their gestational age at birth was <259 d, ≥309 d, or not recorded. In addition, BMI was not recorded for 2 subjects and for one it was considered too high to be included in the analysis (68.39). Subjects whose energy intake was <1.27 × the basal metabolic rate, which is the minimum survival requirement and is used when habitual diet is measured (13), were defined as underreporters (n = 182 men and 161 women) and were removed from the analysis. The basal metabolic rate was estimated by using WHO equations, which take into account weight, age, and sex (14). The final analysis included 1512 subject, 512 of whom reported using antihypertensive medications.

RESULTS

The final analysis included 680 men and 832 women. With respect to SBP, the best obtained breakpoint to birth weight was 3050 g and to salt intake was 10.0 g (based on an energy intake of 2500 kcal). The model with the breakpoints was significantly better than the one without breakpoints (adjusted P = 0.003). With respect to DBP, no consistent statistically significant trends were found.

The basic characteristics of the subjects are described in Table 1. Subjects whose birth weight was >3050 g were taller and heavier in adulthood than were subjects whose birth weight was ≤3050 g. However, there was no significant difference in BMI between the groups. SBP was significantly lower in those whose birth weight was >3050 g than in subjects with a lower birth weight. Birth weight was ≤3050 g in 15% of the men and in 26% of the women. Although the women were, on average, smaller at birth than were the men, the optimal birth weight breakpoint in the model was 3050 g for both sexes. Salt and energy intake in adult life did not differ between the low- and high-birthweight groups. As expected, women were lighter and smaller in adulthood than were men in both birth weight groups (P < 0.001). However, BMI did not differ significantly between men and women. In addition, DBP but not SBP was significantly lower in women than in men in both birth weight groups (P < 0.001). Although men had higher salt (P < 0.001) and energy (P < 0.001) intakes than did women, energy-adjusted salt intake did not differ significantly between men and women.

An inverse association was observed between SBP and birth weight (P = 0.058, P = 0.02). No such association was observed between birth weight and DBP (P = 0.010, P = 0.71). In the entire study population, a positive association was observed
between unadjusted salt intake and unadjusted DBP ($P = 0.070, P = 0.006$) but not with unadjusted SBP ($P = 0.004, P = 0.89$).

Of those whose birth weight exceeded 3050 g, salt intake was not significantly associated with SBP or DBP. Of those whose birth weight was $\leq 3050$ g, a 1-g higher daily energy-adjusted salt intake was associated with a 2.48-mm Hg higher systolic blood pressure ($P = 0.025$) until the saturation point of 10 g (Figure 1). After the saturation point of 10 g, the average SBP was estimated to be 4.72-mm Hg higher in those whose birth weight was $\leq 3050$ g than in those with a higher birth weight (95% CI: 1.96, 7.48; $P < 0.001$). The modifying effect of birth weight on the association between salt intake and SBP did not differ significantly between men and women (data not shown). After the exclusion of subjects taking antihypertensive medications from the analyses (data included 445 men and 555 women), the modifying effect of birth weight on the association between salt intake and SBP became smaller, and it was not significant (1.20 mm Hg; $P = 0.42$). Salt intake was not significantly associated with DBP when studied within the 2 groups separately.

**DISCUSSION**

We examined elderly men and women from a large epidemiologic cohort of people born in Helsinki, Finland, between 1934 and 1944. Our results suggest a close relation between salt intake and adult blood pressure in subjects born with a low birth weight but who were not preterm. The association between salt intake and SBP was observed in subjects with a birth weight of $\leq 3050$ g but not in subjects with a higher birth weight.

Several epidemiologic studies have shown an inverse relation between low birth weight and adult hypertension, as reviewed in the report by Gamborg et al (3). Also, we previously reported that participants in our cohort with a diagnosis of hypertension in adulthood had a lower birth weight, were shorter in length, and had a lower BMI at birth than did those with no diagnosis of hypertension (17). In addition, 2 small intervention studies suggest an association of birth weight with salt sensitivity of systolic blood pressure. Salt intake $\cdot$ 3050 g \[x = observed value, solid bold line = fitted model \] or \[= observed value, dashed bold line = fitted model; P for interaction of birth weight \times salt intake \times systolic blood pressure = 0.0174\]. The thin dotted lines, obtained by locally weighted scatter plot smoothing (LOWESS method), are given for comparison.

![FIGURE 1. Systolic blood pressure adjusted for sex, current age, BMI, use of antihypertensive medication, gestational age, and energy as a function of energy-adjusted salt intake for those whose birth weight was $\leq 3050$ g \[n = 318; x = observed value, solid bold line = fitted model \] or \[> 3050$ g \(n = 1194; = observed value, dashed bold line = fitted model; P for interaction of birth weight \times salt intake \times systolic blood pressure = 0.0174\]. The thin dotted lines, obtained by locally weighted scatter plot smoothing (LOWESS method), are given for comparison. The vertical solid thin line represents the regression breakpoint (10 g) for those whose birth weight was $\leq 3050$ g. For those whose birth weight was $\leq 3050$ g, a 1-g higher daily salt intake was associated with a 2.48-mm Hg higher systolic blood pressure ($P = 0.017$) until the saturation point of 10 g.
blood pressure in adults (6) and children (18). To our knowledge, our study was the first to examine how birth weight modifies the relation between salt intake and adult blood pressure in a large study population.

Low birth weight can be a result of slow fetal growth or short gestation, both of which independently confer a risk of high blood pressure (3, 17, 19, 20). In this study, we focused on subjects not born preterm, and we adjusted for gestational age at birth. Therefore, our results regarding low birth weight likely reflect slow intrauterine growth rather than short duration of gestation.

Our findings support the hypothesis of early programming of adult diseases. It has been suggested that low birth weight may reflect the effect of fetal undernutrition, which may result in a reduced number of nephrons and lead to increased glomerular filtration rate, which thereby increases the risk of glomerulosclerosis and elevated blood pressure (4). In animal studies, it has been shown that maternal dietary protein restriction during pregnancy leads to hypertension in adult offspring (21–23). In addition, severe maternal dietary protein restriction reduced the number of glomeruli, influenced arterial pressure, and programmed salt-sensitive adult hypertension in rat offspring (24).

We observed that, in those whose birth weight was low (≤3050 g), a 1-g higher daily salt intake resulted in a 2.48-mm Hg increase in SBP. Previously, it was shown that even a 2-mm Hg reduction in SBP in adults could decrease stroke mortality by ≈10% and ischemic heart disease or other vascular causes of mortality by ≈7% (25). Thus, even a small persistent reduction in blood pressure could have major implications for public health. In our study population, salt intake was higher than the daily intake (7 g for men and 6 g for women) recommended by government organizations (26). On average, salt intake was 140% and 130% of the recommended intake for men and women, respectively. Therefore, if participants whose birth weight was ≤3050 g decrease their salt intake to the recommended level, their SBP could decrease by ≥5 mm Hg. If these findings are replicated in other studies, reductions in salt intake should be especially beneficial for those born with a low birth weight.

It has been shown in epidemiologic and clinical studies that a high salt intake increases blood pressure, as reviewed in the report by He and MacGregor (5) and Strazzullo et al (27). In our study, we also saw a relation between salt intake and unadjusted DBP but not between salt intake and unadjusted SBP within the entire study population. However, when the subjects were divided into 2 groups according to their birth weight and when salt intake and DBP were adjusted, the association between salt intake and DBP was no longer observed. It is well known that adjustment for these variables may affect results, which may explain these different findings.

The main strength of the current study was the use of a large study population consisting of both men and women. In addition, birth data were obtained from reliable records and were not based merely on recalled values. A further strength of the study was the use of an FFQ, which measures the whole diet and was found to rank intake merely on recalled values. A further strength of the study was the use of an FFQ, which measures the whole diet and was found to rank intake merely on recalled values. A further strength of the study was the use of an FFQ, which measures the whole diet and was found to rank intake merely on recalled values. A further strength of the study was the use of an FFQ, which measures the whole diet and was found to rank intake merely on recalled values. A further strength of the study was the use of an FFQ, which measures the whole diet and was found to rank intake merely on recalled values. A further strength of the study was the use of an FFQ, which measures the whole diet and was found to rank intake merely on recalled values. A further strength of the study was the use of an FFQ, which measures the whole diet and was found to rank intake merely on recalled values.

We previously discussed the limitations of the Helsinki Birth Cohort Study (8, 28). Our study was restricted to persons who had attended child welfare clinics in Helsinki. Most of the children attended these clinics free of charge at that time. The social class distribution of the children in our study, as defined by their father’s occupation, was similar to that in Helsinki as a whole. The participation rate was 69% of those invited. However, our results were based on internal comparisons within the sample. Selection bias would be expected to affect the results only if the relation between prenatal growth, salt intake, and adult blood pressure were different between participants and nonparticipants. This was unlikely but could not be ruled out.

Our study had some potential limitations related to the use of the FFQ, ie, its potential for information bias. It is challenging to measure sodium or salt intake from food-consumption data. However, the continually updated Finnish food-composition database has included sodium content values since the 1980s (29). In addition, our database was validated against 24-h urinary sodium excretion, and it was previously shown that there is a substantial correlation between dietary and urinary sodium measurements (29, 30). When salt intake is estimated with an FFQ, it is not possible accurately to measure the salt used in cooking and at the table. However, a validation study showed that sodium intake, as measured with our FFQ, was similar to intakes determined by using diet records (10). Furthermore, the average salt intake in our study was at the same level as that observed in the National FINDIET 2002 study (30). Therefore, we believe that limitations of the FFQ in estimating salt intake did not affect the results.

In conclusion, our study showed a positive association between salt intake and SBP in adult Finnish individuals born with a low birth weight. Thus, persons with a low birth weight may especially benefit from a reduction in dietary salt intake. Even though the modifying effect of birth weight on the association between salt intake and SBP was modest, it might well have public health implications. However, our observations need to be confirmed in other populations and in different ethnic groups.

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