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Original article

Dietary acid load and blood pressure development in pregnancy: The Generation R Study

Myrte J. Tielemans [a, b, *], Nicole S. Erler [a, c], Oscar H. Franco [a], Vincent W.V. Jaddoe [a, b, d], Eric A.P. Steegers [e], Jessica C. Kiefte-de jong [a, d, f]

[a] Department of Epidemiology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands
[b] The Generation R Study Group, Erasmus MC, University Medical Center, Rotterdam, The Netherlands
[c] Department of Biostatistics, Erasmus MC, University Medical Center, Rotterdam, The Netherlands
[d] Department of Pediatrics, Erasmus MC, University Medical Center, Rotterdam, The Netherlands
[e] Department of Obstetrics and Gynecology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands
[f] Leiden University College, The Hague, The Netherlands

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SUMMARY

Background & aims: Dietary intake could induce a mild maternal metabolic acidosis that might lead to a higher level of blood pressure. Because studies in pregnancy are scarce, we evaluated the association between maternal dietary acid load and changes in blood pressure during pregnancy, pregnancy-induced hypertension and pre-eclampsia.

Methods: We included 3411 pregnant women of Dutch ancestry from a prospective population-based cohort (Rotterdam, The Netherlands). Dietary data was self-reported via a food-frequency questionnaire in early pregnancy. Four dietary acid load measurements were calculated: dietary potential renal acid load (dPRAL), net endogenous acid production (NEAP), animal protein/potassium ratio, and vegetable protein/potassium ratio. Diastolic blood pressure (DBP) and systolic blood pressure (SBP) were measured three times during pregnancy. Information on pregnancy-induced hypertension and pre-eclampsia was obtained from medical records. Linear mixed models and logistic regression were used and adjusted for sociodemographic and lifestyle factors.

Results: The results indicated that dPRAL, NEAP and animal protein/potassium ratio were not associated with DBP or SBP in pregnancy. One standard deviation higher vegetable protein/potassium ratio was associated with lower DBP (−0.30 mmHg [95% CI −0.54; −0.06]) but not with SBP (−0.29 mmHg [95% CI −0.60; 0.01]). Dietary acid load measurement was neither associated with the prevalence of pregnancy-induced hypertension nor with pre-eclampsia.

Conclusions: Dietary acid load was not associated with changes in DBP or SBP during pregnancy, although women with a higher vegetable protein/potassium ratio had a slightly lower DBP. Dietary acid load was not associated with pregnancy-induced hypertension or pre-eclampsia.

1. Introduction

Hypertensive disorders occur in 2–8% of all pregnancies and have been associated with adverse perinatal outcomes, such as preterm birth and fetal growth restriction, and with the development of cardiovascular disease of the mother later in life [1].

Studies have suggested that the development of hypertension may be influenced by the acid-base balance in the body, amongst other mechanisms [2]. This acid-base homeostasis needs to remain within a small range, and is therefore on the short term controlled by the lungs by altering the amount of CO_2 excretion [3]. On a longer term, the kidneys contribute to a stable acid-base homeostasis by eliminating excessive acids [2]. Additionally, dietary intake can influence this acid-base homeostasis, which has been shown also in healthy individuals [4]. Whereas a higher intake of sulfur-containing amino acids and phosphorus will increase a diet-dependent acid load, a higher intake of potassium, magnesium

* Corresponding author. Department of Epidemiology, Erasmus MC, University Medical Center, Office Na-922, PO Box 2040, 3000 CA Rotterdam, The Netherlands. Fax: +31 (0) 10 7044657.
E-mail address: m.tielemans@erasmusmc.nl (M.J. Tielemans).

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and calcium will increase a diet-dependent base load [2,5]. A Mediterranean diet, which is characterized by a high consumption of fruits and vegetables, is an example of a diet with a high diet-dependent base load. Adherence to this diet during pregnancy has been associated with blood pressure in the Generation R Study [6].

Observational studies in non-pregnant populations have suggested that a higher dietary acid load (e.g. a high diet-dependent acid load) may be associated with hypertension [7,8], although another study found no association [9]. Studies have also indicated that the severity of metabolic acidosis may increase independent of diet due to a decline in kidney function [10]. Currently, it is unknown whether dietary acid load is associated with blood-pressure increase in pregnancy. During pregnancy, changes in a woman's body include alterations in circulating volume, body composition, and changes in the blood flow of the uterus. Additionally, physiological changes occur in the acid-base homeostasis due to changes in the respiratory system. This may result in lower arterial CO_2 tension, higher oxygen tension and to changes in the renal system, resulting in a reduction in plasma bicarbonate amongst others [11]. In addition to physiological changes, dietary intake may alter in pregnancy. For example, the US Institute of Medicine advises pregnant women to increase their protein intake, a major contributor of dietary acid load, for optimal fetal growth and development [12].

To our knowledge, there are no studies that have evaluated the influence of dietary acid load on blood pressure or hypertensive complications in pregnancy. Yet, individual food groups or food components that contribute to dietary acid load have been studied in relation to pre-eclampsia [13–16]. For example, calcium supplementation, which is a contributor of diet-dependent base load, has been shown to reduce the risk to develop pre-eclampsia [13].

Considering this, we evaluated whether maternal dietary acid load during the first trimester of pregnancy is associated with higher systolic and diastolic blood pressures during pregnancy. We also evaluated whether maternal dietary acid load is associated with pregnancy-induced hypertension and pre-eclampsia.

2. Material and methods

2.1. Study design

This project is embedded in the Generation R Study, an ongoing multi-ethnic prospective cohort. Pregnant women living in the area of Rotterdam (the Netherlands) and who had an expected delivery date between April 2002 and January 2006 were approached to participate. Details of this birth cohort have been described in detail previously [17]. We obtained written informed consent from all participating women. The study was approved by the Medical Ethics Committee of the Erasmus Medical Center Rotterdam (the Netherlands) and was in accordance with the World Medical Association Declaration of Helsinki.

2.2. Population of analysis

During pregnancy, 4096 women of Dutch ancestry enrolled into the Generation R Study and were therefore eligible for this analysis. We restricted our population of analysis to women with valid dietary information and who gave birth to a live singleton new born (n = 3478). Women with pre-existing hypertension (n = 64) were excluded as well as women (n = 3) who did not have their blood pressure measured, leaving 3411 women for the study at hand (Fig. 1).

2.3. Dietary acid load

Dietary intake was assessed using a 290-item semi-quantitative food-frequency questionnaire (FFQ) which covered the average dietary intake over the previous three months. The FFQ was handed out at enrolment (median gestational age of 13.4 (interquartile range (IQR): 12.2–15.5) weeks). The FFQ included questions on foods that are frequently consumed in a Dutch diet, the portion sizes and frequency of consumption as well as the methods of preparation, and the food additions. The FFQ was initially developed to assess the dietary intake in an elderly Dutch population [18]. A validation study was performed in 80 elderly to compare the FFQ with fifteen 24 h food records (collected over a 1-y period) and 24 h urinary urea secretion (collected over 4 non-consecutive days) [18]. This validation study showed Pearson correlation coefficients for the within-person variation of 0.66 for total protein, 0.59 for vegetable protein, 0.52 for potassium, 0.72 for calcium, 0.74 for phosphorus, and 0.71 for magnesium. The Spearman correlation coefficient between protein intake estimated from the FFQ and from the urinary urea collection was 0.67 [18].

Dietary acid load was calculated using four different formulas. First, we estimated dietary acid load using the following formula: dPRAL (mEq/d) = 0.4888*protein(g/d) + 0.0366*phosphorus(mg/d) − 0.0205*potassium(mg/d) − 0.0263*magnesium(mg/d) − 0.0125*calcium(mg/d) [9,19]. The second formula was NEAP (mEq/d) = 54.5*protein(g/d)/potassium(mEq/d) − 10.2 [20]. Third, we calculated the animal protein/potassium ratio as follows: animal protein/potassium ratio = animal protein(g/d)/potassium(g/d) [21]. Finally, we calculated the vegetable protein/potassium ratio by using the following formula: vegetable protein/potassium ratio = vegetable protein(g/d)/potassium(g/d) [21].

The dPRAL formula proposed by Remer [19] considers average intestinal absorption rates of acid precursors (protein and phosphorus) and of base precursors (potassium, magnesium and calcium). This formula has been previously validated against urine pH in healthy adults [22]. The NEAP and the animal protein/potassium ratio use for their estimation of dietary acid load only protein (as acid precursor) and potassium (as base precursor). The NEAP formula has been validated previously in healthy adults using renal net acid excretion [20]. The animal protein/potassium ratio has been found to be a predictor for resorption of bone, an important reservoir of ions that can reduce excess acid loads [21].

2.4. Blood pressure

Maternal blood pressure was measured using a validated Omron 907® automated digital oscillometric sphygmomanometer (OMRON Healthcare Europe B.V. Hoofddorp, the Netherlands) at the research center that women visited at median gestational ages (IQR) of 12.9 (12.1–14.4), 20.4 (19.9–21.1), and 30.2 (29.9–30.8) weeks. Before the systolic blood pressure (SBP, mmHg) and diastolic blood pressure (DBP, mmHg) were measured twice during each visit, the women had to rest for 5–10 min. The mean values were calculated and used in the analysis. We collected 2831 (83%) blood pressure measurements during the first visit, 3299 (97%) measurements during the second visit, and 3321 (97%) measurements during the third visit. The blood pressure was measured during all three visits in 2706 women (79.3%), 628 women (18.4%) had two measurements, and 77 (2.3%) women had their blood pressure measured once.

2.5. Pregnancy-induced hypertension and pre-eclampsia

Information of hypertensive complications during pregnancy was obtained from medical records. All medical records of women who were suspected to have any kind of hypertensive complication or fetal growth retardation were reviewed in detail to confirm the presence of pregnancy-induced hypertension or pre-eclampsia [6]. Pregnancy-induced hypertension was defined as the development

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