



May probable cause of hypertension in hypertensive disorders of pregnancy be over expressing tyramine depending deterioration of microbiota composition



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To the Editor

The hypertensive diseases complicate 5–11% for all pregnancies in the pregnancy [1]. They are leading reasons for the maternal and fetal mortality and morbidity. The high blood pressure etiology showing up in the pregnancy period was not fully clarified at the present time. The hypertension is a case while the systolic blood pressure is above 140 mmHg; the diastolic blood pressure is above 90 mmHg. The hypertensive diseases are grouped as chronic hypertension, gestational hypertension, pre-eclampsia, superimposed pre-eclampsia, eclampsia and HELLP syndrome in the pregnancy [1–5].

The gestational hypertension is defined as hypertension, which first shows up after the 20th pregnancy week. It is seen at the rate of 5–8% [2]. It is classified as mild (140–149/90–99 mmHg), median (150–159/100–109 mmHg) and severe ($\geq 160/110$ mmHg) hypertension according to the blood pressure.

The pre-eclampsia is defined as an existence of one of the hypertension and coexisting systemic involvement findings (proteinuria, thrombocytopenia, renal failure, liver dysfunction, pulmonary edema, cerebral symptoms or visual symptoms) after the 20th pregnancy week. It is seen at the rate of 1–3%. While the non-concomitant form of serious complications is known as mild pre-eclampsia, the concomitant form of serious complications is classified as serious pre-eclampsia. The serious complications are the cases in which the systolic blood pressure is above 160 mmHg, diastolic blood pressure is above 110 mmHg and thrombocytopenia is smaller than 100,000/ μ L. The pre-eclampsia is classified as early-onset/placental (< 34 pregnancy weeks) and late-onset/maternal (> 34 pregnancy weeks) pre-eclampsia [3]. While it is defined as persistent hypertension in the patients having chronic hypertension, the case in which there is recent or worsening proteinuria or negative findings or development of the serious complications is described as superimposed pre-eclampsia [4]. The eclampsia is a clinical diagnosis based on showing up the tonic-clonic convulsions in cases with the pre-eclampsia diagnosis.

The HELLP syndrome diagnosis criteria are the cases in which there are hemolysis (microangiopathic smear, indirect bilirubin high, total

bilirubin increase > 1.2 mg/dL, haptoglobin low < 25 mg/dL, LDH increase nonspecific), increased aminotransferases (AST increase > 2 times) and which thrombocytopenia is smaller than < 100,000/ μ L. The partial incomplete HELLP is a case in which one or two of these criteria occur and may progress in the complete form. The hypertension and proteinuria are not found in 10–20% of the cases. It is seen 10–20% of the serious pre-eclampsia cases [5].

As mentioned above, a high blood pressure condition is discussed, as its reason is not known in the pregnant for these syndromes which are named as gestational hypertension or pre-eclampsia or eclampsia and HELLP syndrome. While a human body consists of 75 trillions of eukaryotic cells, it also hosts more than 100 trillions of prokaryotic cells (also for the bacteria) in 1000 different types least [with the genes more than 3 million (150 times more than the human genes)]. Most of these bacteria cells constitute our microbiota, our new organ, by maintaining their lives in our intestines [6,7]. The microbiota, which is similar to our individual id card (one-third is common for many humans, two-thirds is personally identifiable), may reach totally up to 2 kg [7]. We may face the many diseases including the obesity, psychological problems, cancer and hypertension when the population rates of these mini creatures change in our intestines [6]. For example, the tyrosine amino acid is converted into the tyramine by the aromatic-L-amino acid decarboxylase found in the intestinal bacteria (*Lactobacillus bulgaricus*; *Lactobacillus plantarum*; *Enterococcus faecalis*) [8,9]. If the bacteria number producing the aromatic-L-amino acid decarboxylase extremely colonizes in our intestines, the tyramine accumulation occurs. The tyramine accumulated causes to be extremely released of the norepinephrine (NE) from the sympathetic nerve endings and the epinephrine (E) from the adrenal medulla in the excessive amounts. The NE and E in the excessive amounts lead to the peripheral vasoconstriction, cardiac output increase and hypertension [10]. The probable cause of hypertension related to the pregnancy may be this situation.

As is known, the NE and E are the catecholamine family members. The catecholamines stimulate the growth of many bacteria including the *E. coli* [11]. The tyramine is not also produced by the bacteria but also found in many foods including the wine and cheese [12]. The

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tyramine existence in circulation causes the catecholamine synthesis, as its origin is the food intake or intestine bacteria produced by the circulation. It also leads to the dysbiosis of body flora by stimulating the growth of some bacteria in the intestine flora of catecholamines. It was stated that the butyrate amounts increased and these increased butyrate amounts cause the systolic and diastolic blood pressures of pregnant to go up when the microbiota composition changed in the pregnancy period [13].

As is firstly hypothesized herein, the increment of the butyrate amounts may probably result from the catecholamines extremely released by the tyramine. Because, it is known that the catecholamines stimulate the growth of bacteria producing the butyrate. Thus, if the butyrate amounts increase, the blood pressures in pregnant increase as well. We think that the hypertension in pregnancy may be probably eliminated, when it is kept away from the foods including tyramine by diet of the pregnancy.

As stated above, when the normal flora rates of microorganisms forming the body flora change, an increment or decrement for the metabolic products reveals. These metabolic products then lead to the various diseases including the hypertension. The tyramine is probably responsible for the hypertension, which is induced by the pregnancy period and of which reason is unexplained up to today, as it shows up depending on the disproportionately increase of bacteria number. Therefore, knowing the composition of intestine flora before the pregnancy and taking the measures (if necessary, making the transplantation of intestine flora) eliminated the occurrence of hypertensive diseases coming to existence of the maternal reasons and cause the maternal and fetal mortality and morbidity to decrease.

Conflict of interest statement

We disclose any financial and personal relationships with other people or organizations that could inappropriately influence this work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2018.11.011>.

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