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COMMENT

Combination of genetic and environmental factors for childhood hypertension: a simple indicator of family history remains useful

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Hypertension is a multifactorial disease involving both genetic and environmental factors. Common gene polymorphisms associated with hypertension are also linked to the onset of hypertension [1]. An international consortium identified 118 new polymorphisms associated with hypertension [2], and a subsequent meta-analysis with data from 757,601 individuals from the UK Biobank and The International Consortium for Blood Pressure GWAS 1000G analyses (ICBP-1000G) identified 535 new sites. Overall, 901 gene polymorphisms have already been identified [3]. Nevertheless, when calculating the genetic risk score (GRS) based on these 901 loci, the odds ratio for hypertension is only 3.5 times higher in the highest-risk 10th decile than in the lowest-risk first decile. Hence, even with the GRS, possible genetic factors based on a combination of genetic and environmental factors have not been fully elucidated. Therefore, genetic factors must be currently estimated from family history.

Birth weight, an indicator of the prenatal environment, is related to hypertension, but whether it is a cause or a result remains undetermined. Maternal hypertension-related genes can cause fetal growth suppression through the intrauterine environment [4]. Zheng et al., by means of a Mendelian randomization-based causal analysis, showed that birth weight had no effect on hypertension risk [5]. Moreover, the HUNT study, after adjusting for children's GRS by Mendelian randomization, showed no effect of birth weight on cardiometabolic factors [6]. On the other hand, the integrated UK Biobank and HUNT studies showed no association between parental scores and cardiometabolic factors in offspring, suggesting the intervention of intrauterine mechanisms [7].

Parental longevity and hypertension history are also associated with blood pressure levels in adult offspring [8–10]. Longitudinal studies evaluating hypertension since childhood have already been conducted [11], allowing a meta-analysis to confirm that elevated blood pressure during childhood is a risk factor for hypertension in adulthood [12]. Therefore, if high-risk populations could be identified earlier, intervention strategies could be implemented.

As shown in Fig. 1, parental hypertension is also the result of the combination of genetic and environmental factors and can also be used as a predictor of hypertension in offspring. On the other hand, a child's genetic background is inherited from both parents. Moreover, the environmental factors that affect a child are shared with both parents. Furthermore, child characteristics (i.e., age, BMI, and lipid profile), which we can directly examine, result from the combination of a child's genetic and environmental factors. Thus, when examining the degree of association between parental and child hypertension, we can make estimations from analyses that are adjusted only for child age and from analyses that are adjusted for the basic characteristics of children. This is because child characteristics are thought to be a partially intermediate factor between the effects of parental and child hypertension.

Seoyun Jang et al. conducted a cross-sectional analysis using data from 3996 children and adolescents aged 10–18 years, together with data from their parents. These data were extracted from the Korean National Health and Nutrition

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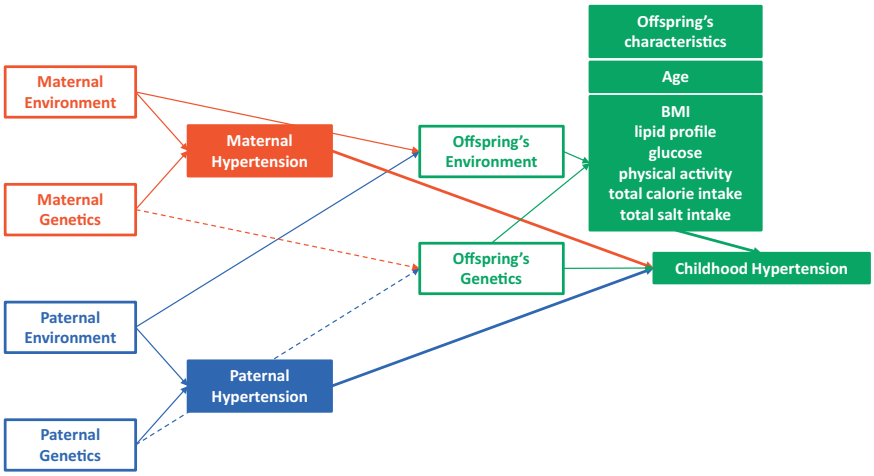

Fig. 1 Causal diagram of genetic and environmental factors and basic characteristics for childhood hypertension

Survey to investigate the parent–child association of hypertension in Korea. The risk of hypertension in the children was approximately twice as high if one parent had hypertension and more than four times higher if both parents had hypertension compared to the control group whose parents were did not have hypertension [13]. In this article, a family history of parental hypertension is clearly associated with the risk of hypertension in children. Moreover, parental hypertension is considered a marker for childhood hypertension.

However, regarding this study, it should be emphasized that this association remains uncertain in the following two cases: first, when parental hypertension was the only hypertension identified by the time the survey was conducted, and second, when child hypertension was the only hypertension identified by the time the survey was conducted. Moreover, not all children developed hypertension. To analyze the association between the individual cumulative risk of hypertension and parent–child hypertension at a specific time, studies examining family relationships, followed by individual analyses, are required [14]. Nevertheless, as reported by Wang et al., parental hypertension is a risk factor for hypertension in offspring. However, this risk is increased with a history of hypertension at a younger age [10]. In other words, it is possible that the present study effectively detected the risk of childhood hypertension among a high-risk population whose parents developed hypertension at a relatively young age.

Therefore, this study confirms that hypertension in parents is a good marker for hypertension in children. Given the future risks, early detection and intervention during childhood before the onset of hypertension are considered effective strategies.

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Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

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