Pediatr Nephrol (2016) 31:349–351
DOI 10.1007/s00467-015-3270-8

EDITORIAL COMMENTARY

Cardiovascular risk among hypertensive adolescents and the potential benefit of a screen-and-treat strategy

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Received: 2 November 2015 / Accepted: 4 November 2015 / Published online: 2 December 2015

Abstract To evaluate whether screening for hypertension should start early in life, information on the risk of diseases associated with the level of blood pressure in childhood or adolescence is needed. The study by Leiba et al. that is reported in the current issue of Pediatric Nephrology demonstrates convincingly that hypertensive adolescents are at higher risk of cardiovascular death than normotensive adolescents. Nevertheless, it can be shown that this excess risk is not sufficient to justify a screen-and-treat strategy. Since the large majority of cardiovascular deaths occur among normotensive adolescents, measures for primordial prevention of cardiovascular diseases could have a much larger impact at the population level.

Keywords Cardiovascular disease · Hypertension · Screening · Primordial prevention

Introduction

Elevated blood pressure is the largest single cause of premature morbidity and mortality in adults [1]. It is a major risk factor for cardiovascular diseases (CVD), causing over 9 million deaths yearly [1]. Although CVD manifest typically in late adulthood, the atherosclerotic process caused by elevated blood pressure and other CVD risk factors starts early in life [2]. Further, blood pressure in childhood tracks into adulthood, and children or adolescents with elevated blood pressure have a high risk of hypertension later in life [3]. Early detection and early intervention to reduce hypertension and/or other CVD risk factors have therefore been advocated as a strategy to decrease the lifetime risk of CVD [4].

Screening for hypertension in adults has been recommended [5]. Whether such screening should start in childhood or adolescence, however, is an old debate which has recently re-emerged [6–8]. Several issues need to be addressed in order to determine whether individuals should be screened for elevated blood pressure (or any other CVD risk factor) in childhood and adolescence with the aim to prevent CVD. Of these, the most notable issue is having sufficient knowledge of the absolute CVD risk associated with any given level of blood pressure [5, 9]. Estimation of this risk necessitates large cohort studies with decades of follow-up in order to accumulate a sufficient number of cardiovascular events for analysis. This estimation is essential to any assessment of the potential impact of a screen-and-treat strategy beginning early in life [5, 8].

Cardiovascular diseases risk estimation

In an article published in this issue of *Pediatric Nephrology*, Leiba et al. have partly filled this important gap in our knowledge [10]. These authors assessed the association between hypertension and CVD mortality in a cohort of 2.3 million individuals who underwent a compulsory medical examination prior to military service, at the average age of 17.4 years. At baseline, 8720 adolescents had hypertension, which corresponds to a prevalence of 0.4 %. After a follow-up of more than 20 years, the hypertensive adolescents were found to have an

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Table 1 Number of subjects and deaths due to cardiovascular disease in the study by Leiba et al. [10][a]

Data	Normotensive adolescents	Hypertensive adolescents	All adolescents
Number of subjects	2,289,410	8720	2,298,130
Number of deaths due to CVD	2879	39	2918
Absolute risk of mortality due to CVD	0.13 %	0.45 %	0.13 %
Absolute risk difference between hypertensive and normotensive		0.32 %	
Number of deaths due to CVD potentially preventable if all hypertensive individuals were treated during the 20-year follow-up		28	
NNS to prevent 1 death due to CVD			81,976
NNT during the 20-year follow-up to prevent 1 death due to CVD			311

CVD Cardiovascular disease

[a] These data were used to compute absolute risks, absolute risk differences, number needed to screen (NNS), and number needed to treat (NNT)

increased mortality risk due to CVD compared to the normotensive adolescents (hazard ratio of 1.5), which was, however, no longer significant upon adjustment for body mass index. More specifically, an increased risk for stroke mortality was observed (hazard ratio of 3.0) but not for coronary heart disease mortality or sudden death.

Several limitations to this study have to be highlighted. First, blood pressure was not measured using a standardised protocol. Second, no adjustment for CVD risk factors, such as smoking, dyslipidemia, or diabetes was made, leaving room for residual confounding. Further, no data were available on non-fatal CVD. The major strengths of the study are the large and population-based sample and the long follow-up with the accumulation of data on a large number of cardiovascular deaths.

This study by Leiba et al. [10] is important because it allows quantification of the CVD mortality risk associated with hypertension in adolescence and also estimation, albeit a rough one, of the potential benefit of a screen-and-treat strategy beginning at that age (Table 1). Hence, out of the 2918 cardiovascular deaths recorded over the 20 years of follow-up, 2879 occurred among normotensive adolescents and 39 among hypertensive adolescents. Based on these numbers, it is easy to compute the absolute risk of CVD mortality, i.e., 0.13 % among normotensive individuals and 0.45 % among hypertensive individuals. Assuming that the relationship is causal and not confounded, the absolute excess risk of CVD mortality due to hypertension in adolescence would be 0.45 % − 0.13 %= 0.32 %. If we now suppose (1) that all hypertensive adolescents were treated and continued to be treated during the 20 years of follow-up and (2) that treatment would have completely reversed the excess risk (both assumptions being highly optimistic), one can estimate that 28 cardiovascular deaths could have been prevented. This means that a screen-and-treat strategy in adolescence would prevent—at best—1 % of all cardiovascular deaths in this population, with the largest number of deaths occurring in individuals who were normotensive during adolescence.

The number needed to screen (NNS) is the number of individuals that need to be screened to prevent one event, and the number needed to treat (NNT) is the number of individuals that need to be treated to prevent one event [11]. Based on data generated in the study by Leiba et al. [10], about 80,000 adolescents would have had to be screened and 300 would have had to be treated during the 20 years of follow-up to prevent one death due to CVD (Table 1). The NNT is often expressed over 5 years of treatment. If we assume that the risk reduction due to antihypertensive treatment was linear over these 20 years, the 5-year NNT would be more than 1200. For comparison, the 5-year NNT of antihypertensive treatment to prevent one death among adults at high risk for CVD has been estimated to be around 125 [12] and the 5-year NNT of statin treatment to prevent one death in adults with known heart disease has been estimated to be less than 100 [13].

Conclusion

The impressive study by Leiba et al. is important because it shows that hypertensive adolescents have a higher risk for cardiovascular mortality, particularly due to stroke [10]. However, the increased risk found in their study is not sufficient to justify a screen-and-treat strategy beginning at that age. Our estimates are very rough and based on highly optimistic (and non-realistic) assumptions, and NNT for the prevention of non-fatal CVD would be smaller. Further, the NNT should be estimated based on results of clinical trials rather than derived from cohort studies [11]. Nevertheless, the small difference in the absolute risk and the very large NNT suggest at best a modest potential benefit of hypertension screening beginning in adolescence, which is consistent with the findings of a modeling study which showed only a modest cost-effectiveness of blood pressure screen-and-treat strategies in adolescents for the prevention of CVD [14].

More striking in the study by Leiba et al. is the finding that 99 % of cardiovascular deaths occurred among individuals

who were not hypertensive adolescents [10]; these deaths would not have been prevented by any screen-and-treat strategy beginning at that age. To the contrary, these observations suggest that primordial prevention of CVD, for example, through environmental and/or educational population-wide interventions that aim to shift the whole blood pressure distribution toward the optimal level, should be preferred to have a substantial impact on the cardiovascular health of a population [15–17].

Compliance with ethical standards

Conflict of interest None

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