Solar UV Radiation: A Potential Modifiable Risk Factor for Hypertension

Vikas Kapil, MBBS, PhD; Ajay K. Gupta, MBBS, MD, PhD

Increased blood pressure (BP) is one of the leading risk factors for cardiovascular morbidity and mortality worldwide, eclipsing smoking and alcohol, with the lowest risk associated with a usual systolic BP (SBP) between 110 and 115 mm Hg, well within the normotensive range.1 BP is regulated by a myriad of endogenous (eg, neural, cardiac, and endocrine) and exogenous (eg, diet and exercise) factors that can adversely serve to lead to hypertension and excess cardiovascular risk. Currently, treatment strategies to reduce BP and subsequent cardiovascular risk are underpinned by various pharmacological approaches. However, despite the availability of numerous antihypertensive agents (and easy availability of their cheap generic versions), BP control at population level seems to be elusive, even in the resource-rich western world.2 On the other hand, public health strategies promoting diet and exercise to prevent and manage hypertension have not shown desired results either; almost all guidelines emphasize lifestyle modifications, particularly dietary and exercise-based interventions, in conjunction with antihypertensive agents.3

This focus on dietary and exercise-type advice is in part because of the relative ease with which these 2 interventions are amenable to design and conduct of clinical trials, although there are clearly challenges to such trials, such as blinding and adherence to intervention. However, there are protean environmental factors associated with increased BP that may also be amenable to modification through population strategies to lower excessive cardiovascular risk related to BP, including ambient noise and atmospheric pollution, among others.4

Further atmospheric conditions (namely, ambient air temperature) have long been known to be associated with seasonal variation in usual BP5 that constitutes one of the long-term patterns of BP variability, both measured in the office and out of office.6 The mechanisms relating to these seasonal associations of BP and ambient temperature have been proposed to include cold-induced sympathetic-induced vasoconstriction and renin-angiotensin-aldosterone system activation,7 among others. However, interpretation of epidemiological data is confounded by daily sunlight (ie, there are longer daytime solar hours in summer). This therefore invokes the possibility that it is solar exposure rather than (or more likely, in synergy with) ambient temperature that is mechanistically important for BP regulation. Indeed, for much of the past 20 years, extensive research has been performed to determine whether vitamin D, which is produced in the skin in response to solar radiation exposure, is important in BP regulation. Large observational studies have shown that low vitamin D levels are a risk factor for hypertension,8 although conversely meta-analysis of numerous vitamin D intervention trials has shown no overall benefit on BP.9

To date, no large data set combined solar radiation exposure and ambient temperature to tease out the relative importance of one or other of these mechanisms for BP regulation. In this issue of the Journal of the American Heart Association (JAHA), Weller and colleagues10 have used an extremely large data set of 340 000 patients from >2000 hemodialysis centers in the United States, covering extremely different geographies and environmental conditions, with >45 million predialysis BP records. They used 2-stage analysis: mixed effect model for repeated measures at each center level and combining these individual center-level records using random-effects meta-analysis models, to evaluate the relative importance of UV light exposure and daily average temperature at the locality of each center.10

The major finding of the study is that UV radiation intensity is inversely related to predialysis SBP independent of ambient temperature, although there appeared to be an interaction...
between the 2 environmental factors, especially for patients with self-identified white ethnicity. The authors postulate that the mechanism of BP lowering may be caused by UV-induced mobilization of constituents of the noncanonical (or alternative) NO synthesis pathways. NO is a key vasoprotective molecule produced in the cardiovascular system, predominantly from canonical endothelial NO synthase in response to shear-stress or circulating agonist, such as acetylcholine or bradykinin; and tonic NO production is associated with vasorelaxation and antiatherogenic and antiplatelet phenotypes. Conversely, all cardiac risk factors (including hypertension) and cardiovascular diseases, as well as chronic kidney disease, are associated with reduced NO bioavailability that is thought to be pathogenic in disease initiation and progression.

Over the past 25 years, there has been the discovery of an alternative pathway for NO generation involving the sequential reduction of inorganic nitrate and thence nitrite to bioactive NO. Increase in circulating nitrite levels, whether through infusion of sodium nitrite or through provision of fixed doses of either oral inorganic nitrate salts or dietary nitrate (usually in the form of beet juice), is associated with robust and reproducible reductions in BP in healthy volunteers and hypertensive patients that is associated with elevations of downstream canonical NO secondary messengers, confirming the production of bioactive NO. More important, for the hypothesis postulated within the linked article, both the authors and others have directly demonstrated that UV light exposure to human skin mobilizes nitrite (and other NO storage forms) into the circulation and the SBP was significantly and substantially. Indeed, the synergy between the 2 was apparent, with larger SBP reduction associated with UV radiation for each higher quartile of the temperature range. Unfortunately, whether UV radiation can be used therapeutically to lower BP chronically (given the sunlight-independent effect is noteworthy and novel. In considering the importance of these data, there are at least 2 different levels to consider. More important, these appear to be the first data to try to tease out the effect of sunlight versus ambient temperature on BP, albeit in an end-stage kidney disease population, and the interesting finding of a sunlight-independent effect is noteworthy and novel. However, these findings should not detract from the fact that the relationship between the ambient temperature and the SBP was significant and substantial. Indeed, the synergy between the 2 was apparent, with larger SBP reduction associated with UV radiation for each higher quartile of the temperature range. Unfortunately, whether UV radiation can be used therapeutically to lower BP chronically (given the sunlight-independent effect is noteworthy and novel). Secondly, the question follows how best to use such information to improve public or individual patient health. On this second point, it is simple to envisage a future guideline recommending a set amount of natural sun exposure per day, but how to determine to optimal amount and to balance the real carcinogenic risks of sun exposure will not be simple. Perhaps if the mechanism postulated is correct, one could simply eat an extra beet daily!

However, as in other cases, there appear to be more complexities, including the synergy between theUV radiation and temperature and their differential impact as per skin color or, perhaps, salt sensitivities. The fact that those living in the areas with a warmer climate and higher incident sunshine had a higher baseline SBP suggests the presence of these complex factors interplay with other factors that at times
outweigh the hypotensive effect of the sun and warmth. It is possible that the next phase of research on these novel and modifiable risk factors may potentially uncover further modifiable mechanisms, and may as yet help reduce the immense burden of hypertension and possibly cardiovascular disease.

Disclosures

Dr Gupta has received travel grants to attend a conference from Servier Inc in the past. Dr Kapil has no disclosures to report.

References

1. Collaborators GRF. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388:1659–1724.

2. Dorans KS, Mills KT, Liu Y, He J. Trends in prevalence and control of hypertension according to the 2017 American College of Cardiology/American Heart Association (ACC/AHA) Guideline. J Am Heart Assoc. 2018;7:e008888. DOI: 10.1161/JAHA.118.008888.

3. Whelton PK, Carey RM, Aronow WS, Carey KJ, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MaLaughlin EF, Muntner P, O’Meara ES, O’Neill JA Jr, Oparil S, Pearson TD, Sang Y, Spencer CA, Strohle A, Thombs BD, Vogel CH, Whelton PK. Hypertension control and control gaps 2015–2016. JAMA. 2017;318:2321–2335.

4. Munzel T, Sorensen M, Gori T, Schmidt FP, Rao X, Brook J, Chen L, Mancia G, Natali A, Oliva-Valencia V, Pizzoli C, Polderman KH, Poulter NR, Salvioli S, Speckmeier U, Taddei S, Webb DJ, Zanchetti A, Mancia G. Nitric oxide: role in vascular disease. PLoS One. 2015;10:e0117572.

5. Rose G. Seasonal variation in blood pressure in man. Nature. 1961;189:235.

6. Sorensen M, Gori T, Schmidt FP, Rao X, Brook J, Chen L, Mancia G, Natali A, Oliva-Valencia V, Pizzoli C, Polderman KH, Poulter NR, Salvioli S, Speckmeier U, Taddei S, Webb DJ, Zanchetti A, Mancia G. Nitric oxide: role in vascular disease. PLoS One. 2015;10:e0117572.

7. Peng JF, Kimura B, Fregly MJ, Phillips MI. Reduction of cold-induced hypertension by antisense oligodeoxynucleotides to angiotensinogen mRNA and AT1-receptor mRNA in brain and blood. Hypertension. 1998;31:1317–1323.

8. Kunutsor SK, Apekey TA, Steur M. Vitamin D and risk of future hypertension: meta-analysis of 283,537 participants. Eur J Epidemiol. 2013;28:205–221.

9. Kunutsor SK, Burgess S, Munroe PB, Khan H. Vitamin D and high blood pressure: causal association or epiphenomenon? Eur J Epidemiol. 2014;29:1–14.

10. Weller RB, Wang Y, He J, Maddux FW, Usyutit L, Zhang H, Feilisch M, Kotanko P. Does incident solar ultraviolet radiation lower blood pressure? J Am Heart Assoc. 2020;9:e013837. DOI: 10.1161/JAHA.119.013837.

11. Moncada S, Palmer RM, Higgs EA. Nitric oxide: physiology, pathophysiology, and pharmacology. Pharmacol Rev. 1991;43:109–142.

12. Brunner H, Cockcroft JR, Deanfield J, Donald A, Ferrannini E, Halcox J, Kiowski W, Luscher TF, Mancia G, Natali A, Oliver JJ, Pessina AC, Rizzoni D, Rossy GP, Salvetti A, Speker LE, Taddei S, Webb DJ. Endothelial function and dysfunction, part II: association with cardiovascular risk factors and diseases: a statement by the Working Group on Endothelins and Endothelial Factors of the European Society of Hypertension. J Hypertens. 2005;23:233–246.

13. Lundberg JO, Weitzberg E, Gladwin MT. The nitrate-nitrite-nitric oxide pathway in physiology and therapeutics. Nat Rev Drug Discov. 2008;7:156–167.

14. Cosby K, Partovi KS, Crawford JH, Patel RP, Reiter CD, Martyr S, Yang BK, Waclawiw MA, Zalos G, Xu X, Huang KT, Shields H, Kim-Shapiro DB, Schechter AN, Cannon RO III, Gladwin MT. Nitrite reduction to nitric oxide by deoxymyoglobin vasodilates the human circulation. Nat Med. 2003;9:1498–1505.

15. Kapil V, Khambata RS, Robertson A, Caufield MJ, Ahluwalia A. Dietary nitrate provides sustained blood pressure lowering in hypertensive patients: a randomized, phase 2, double-blind, placebo-controlled study. Hypertension. 2015;65:320–327.

16. Kapil V, Millsom AB, Okorie M, Maleki-Toyserkani S, Akram F, Rehman F, Arghandawi S, Pearl V, Benjamin N, Loukogeorgakis S, Macallister R, Hobbs AJ, Webb AJ, Ahluwalia A. Inorganic nitrate supplementation lowers blood pressure in humans: role for nitrite-derived NO. Hypertension. 2010;56:274–281.

17. Mowbray M, McIntloch S, Weerakoon R, Lomatschinsky N, Jones S, Rossi AG, Weller RB. Enzyme-independent NO stores in human skin: quantification and influence of UV radiation. J Invest Dermatol. 2009;129:834–842.

18. Oplander C, Volkmar CM, Paunel-Gorgulu A, van Faassen EE, Heiss C, Kelm M, Halmer D, Murzt M, Pallua N, Suschek CV. Whole body UVA irradiation lowers systemic blood pressure by release of nitric oxide from intracutaneous photolabile nitric oxide derivates. Circ Res. 2009;105:1031–1040.

19. Liu D, Fernandez BO, Hamilton A, Lang NN, Gallagher JMC, Newby DE, Feelisch M, Weller RB. UVA irradiation of human skin vasodilates arterial vasculature and lowers blood pressure independently of nitric oxide synthase. J Invest Dermatol. 2014;134:1839–1846.

20. Saeki K, Oyabashi K, Iwamoto J, Tone N, Okamoto N, Tomioka K, Kurumatanri N. Stronger association of indoor temperature than outdoor temperature with blood pressure in colder months. J Hypertens. 2014;32:1582–1589.

Key Words: Editorials • environment • hypertension • risk factor • seasonal variation • solar radiation • UV radiation