Antihypertensive medication prior to nocturnal sleep reduces the risk of new-onset type 2 diabetes in hypertensive patients: a role for slow-wave sleep?

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Abbreviations

SNS Sympathetic nervous system
SWS Slow-wave sleep

To the Editor: I read with great interest the study by Hermida et al [1]. In their study involving 2,012 hypertensive patients without type 2 diabetes, it was found that regular bedtime vs morning intake of antihypertensive medication reduced the risk of new-onset type 2 diabetes, with the strongest risk reduction associated with the use of ACE inhibitors. Moreover, compared with the morning-treatment group, patients on the bedtime medication schedule exhibited a larger relative blood pressure decline across sleep. These findings provide novel evidence as they suggest that circadian timing of antihypertensive medication can alter patients' type 2 diabetes risk. The question is: why do ACE inhibitors have such a protective effect

against diabetes when intake is scheduled prior to nocturnal sleep?

Following enzymatic conversion of angiotensin 1 into angiotensin 2 (inhibited by ACE inhibitors), the latter exerts complex cardiovascular actions, including sympathoexcitation [2]. Studies have shown that increased activity of the sympathetic nervous system (SNS) can alter human sleep. For example, in response to peripheral infusions of the α -adrenergic agonist phenylephrine which does not pass the blood–brain barrier, during first hours of nocturnal sleep, healthy normotensive volunteers are more prone to intermittent wakefulness and spend less time in slow-wave sleep (SWS) [3]. Experimental reductions of SWS and interruptions of sleep have recently been linked to impaired morning insulin sensitivity in healthy humans [4, 5]. With these results in mind, it could be speculated that intake of ACE inhibitors close to sleep onset dampens nocturnal activity of the SNS, and thereby reduces frequency of awakenings after sleep onset and increases time in SWS (Fig. 1). Such promotion of sleep consolidation could therefore offer an alternative mechanism through which bedtime ingestion of ACE inhibitors reduces the risk of new-onset type 2 diabetes in hypertensive patients [1]. Importantly, there are also other sympatholytic antihypertensive drugs that have been shown to affect human sleep, e.g. the centrally acting α_2 -adrenergic receptor agonist clonidine [6]. It could therefore be hypothesised that sympatholytic antihypertensive drugs other than ACE inhibitors, if regularly ingested near to bedtime, may also reduce the type 2 diabetes risk in hypertensive patients. Finally, there are also other functions that benefit from SWS, e.g. formation of long-term memories [7]

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Fig. 1 Proposed scheme through which regular intake of sympatholytic antihypertensive drugs (e.g. ACE inhibitors) prior to nocturnal sleep reduces risk of new-onset type 2 diabetes in hypertensive patients

and initiation of adaptive immune responses [8]. Thus, scheduling the intake of sympatholytic antihypertensive drugs near to intended bedtime may offer additional health benefits for hypertensive patients.

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