Received: 1 January 2022 | Revised: 1 January 2022 | Accepted: 4 January 2022

DOI: 10.1111/jch.14434

COMMENTARY

WILEY

The role of tadalafil in treated hypertensive patients with erectile dysfunction

Ehud Grossman MD[1,2]

[1] Internal Medicine Wing, The Chaim Sheba Medical Center, Tel-Hashomer, Israel

[2] Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel

Correspondence
Ehud Grossman, MD, The Chaim Sheba Medical Center, Floor-1, Room 132, Tel-Hashomer, 526601 Ramat-Gan, Israel.
Email: grosse@tauex.tau.ac.il

Editorial to manuscript # JCH- 21-0330R1 entitled "Analysis of integrated clinical safety data of tadalafil in patients receiving concomitant antihypertensive medications"

In this issue, Kloner and colleagues showed in a pooled safety analysis that tadalafil—a phosphodiesterase type 5 (PDE-5) inhibitor—is safe in treated hypertensive patients and is not associated with increased hypotension-related treatment adverse events and major cardiovascular (CV) events.[1] The safety data were extracted from 72 Phase II–IV clinical studies of tadalafil used for erectile dysfunction (ED) or benign prostate hypertrophy. PDE-5 inhibitors are vasodilating drugs that work by blocking the degradation of cyclic GMP by PDE-5 in the smooth muscle cells lining the blood vessels supplying various tissues. The increase of the intracellular cyclic GMP prolongs its duration of action resulting in increase in nitric oxide bioavailability, smooth muscle relaxation, vasodilation and increased blood flow in the corpora cavernosa, and penile erection. The main PDE-5 inhibitors are sildenafil, vardenafil, avanafil, and tadalafil. They differ in their pharmacodynamic and pharmacokinetic properties allowing targeting the treatment to the patients' needs. Avanafil has the fastest onset of action and tadalafil has the longest duration of action (half-life of 17.5 h and duration of action up to 36 h).[2]

ED impairs the quality of life of affected individuals and may be a prognostic marker for the development of CV disease.[3] The prevalence of ED in the general population is around 15–20% and it is significantly higher in patients with hypertension,[2,4] probably due to vascular changes. Hypertension is a major modifiable risk factor for CV disease and lowering blood pressure is beneficial. Lowering blood pressure may cause or aggravate ED and it is not clear whether it is a side effect of the antihypertensive treatment or a result of the blood pressure decrease. The development of ED is one of the major reasons to withdraw antihypertensive treatment leading to inadequate blood pressure control. PDE-5 inhibitors improve ED and improve adherence to antihypertensive therapy, improve blood pressure control, and thereby may reduce CV risk in hypertensive patients with ED.

The effect of PDE-5 inhibitors is not limited to the corpora cavernosa and they also vasodilate other vascular beds thereby reducing blood pressure. There was a concern that blood pressure decrease may cause CV side effects particularly in patients with CV risk factors. Kloner and colleagues in this issue showed that in subjects not receiving antihypertensive medications the incidence of hypotension related treatment emergent adverse events was low, but it was significantly higher in the tadalafil group than in the placebo group.[1] Most subjects (>90%) not receiving antihypertensive medications were normotensives, and in this group, lowering blood pressure by tadalafil may increase the incidence of hypotension-related events. However, in hypertensive patients on antihypertensive medications tadalafil does not increase the hypotension related events.

The co-administration of tadalafil with doxazosin, a blood pressure lowering alpha blocker is associated with a remarkable blood pressure decrease that maybe deleterious.[5] However, with other antihypertensive agents tadalafil is not associated with hypotensive related side effects.

The co-administration of PDE-5 inhibitors with various antihypertensive drugs, except alpha blockers, is safe. This was observed even in those who used several antihypertensive agents.[1]

It has been shown that all PDE-5 inhibitors are safe in treated hypertensive patients.[2]

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.
© 2022 The Authors. *The Journal of Clinical Hypertension* published by Wiley Periodicals LLC

The hypotensive effect of PDE-5 inhibitors should be exploit to treat resistant hypertension, particularly in those with ED. Since tadalafil has the longest duration of action it will probably be the best PDE-5 inhibitor to use for lowering blood pressure. Low dose tadalafil (5 mg daily) can improve blood pressure control and erectile function. The fact that PDE-5 inhibitors can lower blood pressure and improve erectile function suggests that lowering blood pressure by itself does not cause ED and it is probably related to the antihypertensive medications.

The safety profile of tadalafil presented by Kloner in this issue may justify wider use of the drug in hypertensive patients. Wide use of tadalafil in hypertensive patients may improve erectile function and blood pressure control leading to a decrease in CV events. Further long term studies should be done to prove this concept.

CONFLICT OF INTEREST

The author has no competing interests.

ORCID

Ehud Grossman MD https://orcid.org/0000-0001-8353-0661

REFERENCES

1. Kloner RA, Kostis JB, McGraw T, Qiu C, Gupta A. Analysis of integrated clinical safety data of tadalafil in patients receiving concomitant antihypertensive medications. *J Clin Hypertens (Greenwich)*. 2022;244:167-178.
2. Viigimaa M, Vlachopoulos C, Doumas M, et al. Update of the position paper on arterial hypertension and erectile dysfunction. *J Hypertens*. 2020;38:1220-1234.
3. Litwin MS, Nied RJ, Dhanani N. Health-related quality of life in men with erectile dysfunction. *J Gen Intern Med*. 1998;13:159-166.
4. Wang T-D, Lee C-K, Chia Y-C, et al. Hypertension and erectile dysfunction: the role of endovascular therapy in Asia. *J Clin Hypertens (Greenwich)*. 2021;23:481-488.
5. Kloner RA, Jackson G, Emmick JT, et al. Interaction between the phosphodiesterase 5 inhibitor, tadalafil and 2 alpha-blockers, doxazosin and tamsulosin in healthy normotensive men. *J Urol*. 2004;172:1935-1940.

How to cite this article: Grossman E. The role of tadalafil in treated hypertensive patients with erectile dysfunction. *J Clin Hypertens*. 2022;24:182–183.
https://doi.org/10.1111/jch.14434