

EDITORIAL

Interaction between antihypertensives and NSAIDs in primary care:

A controlled trial

High blood pressure is the leading risk for death in the world.¹ In North American society it is estimated that over 90% of adults will develop hypertension if they live an average life span.² Lowering blood pressure with antihypertensive therapy can reverse much of the risk associated with hypertension.³ Nevertheless, even in developed countries poor blood pressure control is the norm rather than the exception.⁴ For this reason commonly used drugs that increase blood pressure or interfere with blood pressure lowering therapies are of great importance.

Approximately 25% of the elderly Albertan population are prescribed a non-steroidal anti-inflammatory drug (NSAID) during a six month time frame.⁵ Regular use of non-steroidal anti-inflammatories has been documented to increase blood pressure and to interfere with the blood pressure lowering of many classes of antihypertensive drugs.⁶ Several trials have suggested that calcium channel blockers may retain their antihypertensive effectiveness during non-steroidal anti-inflammatory therapy. In this issue of the Canadian Journal of Clinical Pharmacology Pavličević et al describe a single blind randomized trial (http://www.cjcp.ca/pdf/CJCP08016_Rumboldt_e372-e382.pdf) examining the effects of two non-steroidal anti-inflammatory drugs and acetaminophen on the antihypertensive effectiveness of amlodipine, a calcium channel blocker and on a combination of an ACE inhibitor and diuretic (lisinopril/hydrochlorothiazide). In general, their findings are consistent with those in the literature; non-steroidal anti-inflammatory drugs increased blood pressure in patients taking the combination of lisinopril and

hydrochlorothiazide and did not in patients taking amlodipine. Acetaminophen did not appear to affect blood pressure. The trial adds to current literature that shows non-steroidal anti-inflammatory drugs interfere with antihypertensive treatment.

The study however, does have a number of limitations. It was a single blind trial and awareness of treatment assignment by the patient may have influenced the blood pressure results. The authors have provided the data on standing blood pressure as the primary outcome and did not provide data on seated blood pressure. This is important, as it is seated blood pressure that is used to establish the diagnosis of hypertension and control of hypertension clinically and in research. The relevance of standing blood pressure is largely to assess postural hypotension. Further, the findings based on automated measures only achieved statistical significance on one comparison. Finally, the manuscript does not describe which blood pressure measure (seated vs. standing) is used to assess blood pressure control. Typically, this should be the seated blood pressure. The findings based on automated measures in this protocol using 5 minute intervals would substantially underestimate usual blood pressure and hence should not be used to assess blood pressure control.⁷

Despite the limitations, the article by Rumboldt et al is an important reminder to clinicians of the adverse consequences of NSAIDs which are commonly used in our elderly population. It is likely that a part of the adverse cardiovascular consequences of NSAIDs are based on their blood pressure raising effects. Additionally, clinicians should be alert to an uncommon but serious drug

interaction between NSAIDs, diuretics and ACE inhibitors where patients present in renal failure with hyperkalemia. That specific adverse effect was not seen in this study population.

Yours sincerely,

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REFERENCES

1. Lawes CM, Vander HS, Rodgers A. Global burden of blood-pressure-related disease, 2001. *Lancet* 2008;371:1513-18.
2. Vasan RS, Beiser A, Seshadri S, Larson MG, Kannel WB, D'Agostino RB, et al. Residual lifetime risk for developing hypertension in middle-aged women and men. *JAMA*. 2002;287:1003-10.
3. Smith SC Jr, Blair SN, Criqui MH, Fletcher GF, Fuster V, Gersh BJ, et al. Preventing heart attack and death in patients with coronary disease. *Circulation*. 1995;92:2-4.
4. Wolf-Maier K, Cooper RS, Banegas JR, Giampaoli S, Hense H-W, Joffres M, et al. Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States. *JAMA* 2003;289:2363-69.
5. Hogan DB, Campbell NRC, Crutcher R, Jennett P, MacLeod N. Prescription of nonsteroidal anti-inflammatory drugs for elderly people in Alberta. *CMAJ* 1994;151:315-22.
6. Gyamlani G, Geraci SA. Secondary hypertension due to drugs and toxins. *South Med J* 2007;100:692-99.
7. Culleton BF, McKay DW, Campbell NR. Performance of the automated BpTRU measurement device in the assessment of white-coat hypertension and white-coat effect. *Blood Press Monit* 2006;11:37-42.