

## Slowing the progression of chronic renal insufficiency

Marcello Tonelli, John Gill, Sanjaya Pandeya, Clara Bohm, Adeera Levin, Bryce A. Kiberd\*

The number of Canadians with end-stage renal disease will increase by approximately 6% annually through the year 2005.<sup>1</sup> Given that this condition is associated with substantial illness and death, high health care costs (more than \$1 billion annually) and poor quality of life, preservation of residual renal function in people with chronic renal insufficiency is an important public health objective.

Strategies that delay or prevent progression of chronic renal insufficiency to end-stage renal disease include aggressive control of blood pressure and use of angiotensin-converting enzyme (ACE) inhibitors.<sup>2-4</sup> Canadian guidelines recommend that the goal for mean arterial pressure be less than 92 mm Hg (125/75 mm Hg) in patients with greater than 1 g proteinuria daily (1 g protein in the urine for a 24-hour period) and less than 98 mm Hg (130/80 mm Hg) in patients with chronic renal insufficiency and non-proteinuric renal disease.<sup>5</sup> ACE inhibitors are recommended for almost all patients with chronic renal insufficiency, especially those with significant proteinuria or diabetes mellitus, because these drugs are known to slow the progression of renal disease.<sup>3</sup> A growing body of evidence suggests that angiotensin receptor blockers may have similar renal benefits.<sup>6</sup>

We recently conducted a cross-sectional study of 304 consecutive patients with chronic renal insufficiency, seen in 4 Canadian tertiary nephrology clinics, to investigate the use of these strategies. For only 128 (42%) of the patients was blood pressure at target levels. In 85 patients (28%) blood pressure was elevated, and in these patients antihypertensive medications were to be increased. The remaining 91 patients (30%) had suboptimal blood pressure control, but no changes in medications were made. According to responses to a questionnaire completed by the nephrologists at the study visit, most of the latter group were considered to be "at target," to have office hypertension or to have an unfavourable risk-benefit ratio. Although most patients in the study were taking or were to start taking ACE inhibitors or angiotensin receptor blockers, fully 25% of the entire cohort had never received such agents, in most cases because the treating nephrologist felt that additional benefit was unlikely. However, many of the patients who were not receiving these drugs were diabetic, had poorly controlled blood pressure or had known coronary artery disease, and it is possible that ACE inhibitors or angiotensin receptor blockers would in fact have reduced their cardiovascular and renal risk.

These data indicate considerable room for improvement in the care delivered by specialists. Surprisingly, the decision not to intensify antihypertensive regimens or prescribe ACE inhibitors or angiotensin receptor blockers was most commonly based on the perception that these interventions would not be beneficial. Although risk might outweigh expected benefit in some patients, it is likely that implementing these proven strategies would improve outcomes in a substantial proportion. In addition, for patients with chronic renal insufficiency, elevated blood pressure measurements obtained during clinic visits usually reflect true hypertension,<sup>7</sup> so "office hypertension" should be diagnosed with caution in these patients. Conversely, patients in this study who were seen at follow-up by nephrologists had better blood pressure control at that time than at referral. Furthermore, mean blood pressures achieved in this patient group were lower than those reported for a similar study conducted in 1997.<sup>8</sup> These findings suggest that improvement is possible in the care of patients with chronic renal insufficiency.

Patients with higher grades of proteinuria (more than 1 g daily) lose renal function more rapidly, perhaps because of a direct toxic effect of urinary protein. Reducing blood pressure to target levels, specifically through use of ACE inhibitors (and perhaps angiotensin receptor blockers), will reduce proteinuria and retard progressive renal dysfunction.<sup>2</sup> Consequently, current blood pressure targets for patients with chronic renal insufficiency are considerably lower than those for the general population and are based on quantitative proteinuria.<sup>5,9</sup> Physicians should be aware not only of the need to detect chronic renal insufficiency in patients with hypertension but also of the value of quantifying proteinuria to stratify renal risk and determine appropriate blood pressure targets.

We found that the number of antihypertensive medications prescribed was an important predictor of achievement of target blood pressure, which suggests that adding agents may improve control. For example, the use of  $\beta$ -blockers was relatively infrequent (103 patients [34%]). Given the high prevalence of coronary artery disease in association with chronic renal insufficiency and the efficacy of these agents in reducing cardiovascular mortality, physicians should consider using  $\beta$ -blockers as additional antihypertensives. Similarly, diuretics were used in fewer than half of the patients in this study, even though these medications are known to enhance the antihypertensive effect of ACE inhibitors.<sup>10</sup> While excessive diuresis may compromise re-

renal function, judicious use of diuretics is safe in chronic renal insufficiency.<sup>11</sup> Finally, salt-restricted diets are known to be synergistic with antihypertensive medications,<sup>12</sup> and restriction of dietary potassium may be appropriate for patients with chronic renal insufficiency and a history of intolerance of ACE inhibitors due to hyperkalemia.

There is evidence that even patients with advanced chronic renal insufficiency may benefit from these agents. However, when creatinine clearance is less than 30 mL/min, treatment with ACE inhibitors and angiotensin receptor blockers should be combined with careful follow-up monitoring. In addition, guidelines from the Canadian Society of Nephrology suggest that these patients should be referred for nephrological assessment.<sup>13</sup>

The attitude of physicians about the likelihood that a given patient will derive benefit appear to be an important determinant of the use of ACE inhibitors and angiotensin receptor blockers and resultant blood pressure control. If we are going to change the management of chronic renal insufficiency for the better, we will have to start by changing our own approach to this problem.

## References

- Schaubel DE, Morrison HI, Desmeules M, Parsons DA, Fenton SSA. End-stage renal disease in Canada: prevalence projections to 2005. *CMAJ* 1999;160:1557-63. Available: [www.cma.ca/cmaj/vol-160/issue-11/1557.htm](http://www.cma.ca/cmaj/vol-160/issue-11/1557.htm)
- Jafar TH, Schmid CH, Landa M, Giatras I, Toto R, Remuzzi G, et al. Angiotensin-converting enzyme inhibitors and progression of nondiabetic renal disease. A meta-analysis of patient-level data. *Ann Intern Med* 2001;135:73-87.
- Lewis EJ, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. *N Engl J Med* 1993;329:1456-62.
- Klahr S, Levey AS, Beck GJ, Caggiula AW, Hunsicker L, Kusek JW, et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group. *N Engl J Med* 1994;330:877-84.
- Feldman RD, Campbell N, Larochelle P, Bolli P, Burgess ED, Carruthers G, et al. 1999 Canadian recommendations for the management of hypertension. *CMAJ* 1999;161(12 Suppl):S1-17. Available: [www.cma.ca/cmaj/vol-161/issue-12/hypertension/hyper-e.htm](http://www.cma.ca/cmaj/vol-161/issue-12/hypertension/hyper-e.htm)
- Parving HH, Lehnert H, Brochner-Mortensen J, Gomis R, Andersen S, Arner P. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. *N Engl J Med* 2001;345:870-8.
- Schwenger V, Ritz E. Audit of antihypertensive treatment in patients with renal failure. *Nephrol Dial Transplant* 1998;13:3091-5.
- Tonelli M, Djurdjev O, Carlisle EFJ, Ethier J, Mendelssohn D, Burgess E. Factors affecting rate of progressive renal decline: observations in a non-clinical trial setting [abstract]. *J Am Soc Nephrol* 1998;9:80A
- The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch Intern Med* 1997;157:2413-46.
- Townsend RR, Holland OB. Combination of converting enzyme inhibitor with diuretic for the treatment of hypertension. *Arch Intern Med* 1990;150:1175-83.
- Pahor M, Shorr RI, Somes GW, Cushman WC, Ferrucci L, Bailey JE, et al. Diuretic-based treatment and cardiovascular events in patients with mild renal dysfunction enrolled in the Systolic Hypertension in the Elderly Program. *Arch Intern Med* 1998;158:1340-5.
- Wing LM, Arnolda LF, Harvey PJ, Upton J, Molloy D, Gabb GM, et al. Low-dose diuretic and/or dietary sodium restriction when blood pressure is resistant to ACE inhibitor. *Blood Press* 1998;7:299-307.
- Churchill DN, Blake PG, Jindal KK, Toffelmire EB, Goldstein MB. Clinical practice guidelines for initiation of dialysis. Canadian Society of Nephrology. *J Am Soc Nephrol* 1999;10(Suppl 13):S289-91.

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Drs. Tonelli and Kiberd are with the Department of Medicine, Dalhousie University, Halifax, NS. At the time of writing, Dr. Gill was with the Department of Medicine, University of British Columbia, Vancouver, BC. Dr. Levin is with the Department of Medicine, University of British Columbia, Vancouver, BC. At the time of writing, Dr. Pandeya was with the Department of Medicine, University of Western Ontario, London, Ont. At the time of writing, Dr. Bohm was with the Department of Medicine, University of Saskatchewan, Saskatoon, Sask.

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Correspondence to: Dr. Bryce A. Kiberd, Room 5077, Dickson Building, 5820 University Ave., Halifax NS B3H 1V8; fax 902 473-2675; [bkiberd@is.dal.ca](mailto:bkiberd@is.dal.ca)

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