Screening renal failure patients for tuberculosis

James Johnston, MD, FRCPC, Kevin Elwood, MB, BCh, MRCP, FRCP

Scope of problem

More than 60 years after the development of effective antimycobacterial therapy, tuberculosis (TB) remains a significant problem in British Columbia. Provincial TB rates exceed the Canadian average, attributable to the disproportionate burden in foreign-born and Aboriginal populations. Further reduction in the rates will require targeting populations at high risk of reactivation of latent TB with preventive treatment.

Patients with advanced chronic kidney disease (CKD) are susceptible to tuberculosis infection and disease. CKD is more common in foreign-born individuals—a population with high rates of latent tuberculosis infection (LTBI). More importantly, however, immunity is impaired in CKD patients through reduced function of T and B cells and neutrophils. Once infected with *Mycobacterium tuberculosis*, dialysis patients have a 20-fold increased risk of developing active disease. Renal transplant patients are at even higher risk due to added immunosuppressive therapy. The occurrence of an active infectious case of TB in a dialysis unit is highly disruptive, putting both staff and other patients at risk.

As of December 2009, there were 2720 patients enrolled in provincial dialysis programs, while 10 368 patients were registered in predialysis clinics. To date there is no provincial policy for LTBI screening in CKD patients, likely reflecting the uncertain value of current diagnostic strategies in this group.

Dr Johnston is a research fellow at the BC Centre for Disease Control. Dr Elwood is the director of TB Control at the BC Centre for Disease Control.

A diagnostic challenge

Diagnosis of LTBI traditionally relies on a combination of clinical history, tuberculin skin test (TST) and chest X-ray results. These traditional modalities, however, have their limitations in CKD populations. Half of dialysis patients have some degree of anergy to TST, so a negative TST cannot effectively rule out LTBI. These patients are often frail with thinning skin, making the test technically difficult. Chest X-rays are insensitive unless granulomatous abnormalities happen to be present.

The recently developed interferon gamma release whole blood assays (IGRAs) are a promising diagnostic addition in CKD populations. There are two commercially available tests in evaluation, the QuantiFERON-TB Gold (Cellestis, Australia) and T-SPOT TB assay (Oxford Immunotec, UK). These tests offer several advantages over the TST: they are highly specific in BCG vaccinated individuals, have inbuilt positive controls to detect anergy, and do not require 48-hour follow-up for reading. Both tests are available for limited indications through the BCCDC tuberculosis clinics and increasingly elsewhere in the province.

Early data support IGRA use in CKD populations. When compared with TST in cross-sectional studies and short-term cohorts, these assays appear to have improved sensitivity for LTBI. In particular, IGRAs appear to detect prior active disease and are associated with TB exposure history. Long-term follow-up is still required to demonstrate improved clinical outcomes associated with these assays.

Treatment of LTBI

Once the diagnosis of LTBI is established and active disease is ruled out, LTBI prophylaxis should be considered. The current standard of therapy for LTBI is 9 months of isoniazid (INH) monotherapy. INH is metabolized and cleared by the liver, and does not require dose adjustment in renal disease. Preventive regimens have been associated with neuropsychiatric, hepatic, and gastrointestinal side effects in CKD populations. However, the risk of side effects must be weighed against the high risk of active disease, so patients require individual assessments.

Guidelines and recommendations

The most recent guidelines addressing the issue were published by the British Thoracic Society. They stress that screening all CKD patients for LTBI is not supported by current evidence and would not likely be cost-effective. However, targeted testing for at-risk patients was recommended. Likewise, the Canadian Tuberculosis Committee recommends targeting testing for LTBI in CKD populations, specifically, all recent immigrants and high-risk populations with CKD requiring dialysis should be screened with TST (cutoff 10 mm or greater) followed by IGRA if available. If either TST or IGRA is positive, patients should be considered to have LTBI infection.

Improving the diagnosis of LTBI infection in CKD patients is challenging. The currently recommended strategy is TST followed by IGRA in patients with risk factors for LTBI infection. Alternatively initial screening with IGRA alone is an option. We recommend that clinicians consider

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Core-Plus Plan reminder

The open enrollment period for the Core-Plus Plan under the BCMA Health Benefits Trust Fund is underway. The deadline to enroll in this program, or to make changes to your coverage if you are already participating, is 31 October 2010. New coverage or changes to existing coverage for members who submit the required plan documents by the deadline will be effective 1 January 2011.

If you have any questions regarding the open enrollment period or the plans offered under the BCMA Health Benefits Trust Fund, please visit www.bcma.org/hbtf or contact an HBTF Administrator:

Cory St Jean
Toll free: 800 665-2262 ext. 2865
Direct: 604 638-2865
cstjean@bcma.bc.ca

Darlene Laird
Toll free: 800 665-2262 ext. 2818
Direct: 604 638-2818
dlaird@bcma.bc.ca

—Sandie Braid, CEBS
Assistant Director, BCMA Insurance

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and orthobiologics, especially the bone morphogenic protein (BMP)-7.

Full documents and other systematic reviews can be downloaded from www.worksafebc.com/evidence.

—Kukuh Noertjojo, MD, MHSc
—Craig Martin, MD, MHSc
WorkSafeBC Evidence-Based Practice Group

References

References are available by calling Carmen Prang at 604 244-6224 or toll-free 1 800 967-5377, extension 6224 or carmen.prang@worksafebc.com or online at www.bcmj.org.

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early screening in high-risk CKD patients, as anergy may be less of a confounder in those with less advanced disease. Once LTBI infection is established, prophylactic therapy should be considered in consultation with TB control and the patient's personal physicians. As always, an ounce of prevention trumps a pound of cure.

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Canada's Natural Health Products Directorate places Canadians in harm's way by failing to prevent exaggerated health claims and by exposing consumers to unnecessary health risks. Given that medical claims made on behalf of NHPs typically exceed the evidence of medical benefit, and that significant safety issues with various NHPs continue to be discovered upon proper scientific testing, many Canadians will wonder if a near-billion-dollar bonanza to industry is worth the price.

—Lloyd Oppel, MD
Chair, Allied Health Practices Committee

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2. Gavura S. Health Canada gets out a big rubber stamp. Science-based Pharmacy [blog] 15 July 2010. http://sciencebasedpharmacy.wordpress.com/2010/07/15/health-canada-gets-out-a-big-rubber-stamp/ (accessed 23 August 2010).

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