Screening for renal disease in a remote Aboriginal community using the Bayer DCA 2000

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Abstract
End-stage renal disease among Aboriginal Australians has reached alarming proportions during the past decade. The early identification of this disease through community screening programs is a key strategy in reducing the long-term financial and cultural burden of the disease. The small point-of-care Bayer DCA 2000 analyser, which tests for urine albumin:creatinine ratio (ACR), was used as a marker for early renal disease in an adult screening program in a remote South Australian Aboriginal community. Nineteen percent of 149 adults screened had previously undiagnosed persistent microalbuminuria (ACR between 3.4 and 33.9 mg/mmol), while a further 9% had persistent overt albuminuria (ACR greater than or equal to 34 mg/mmol). Aboriginal health workers were trained in the operation of the DCA 2000 to enable screening to be an on-going, sustainable activity within the community setting. The DCA exhibited excellent analytical performance characteristics and was robust and reliable throughout the study period.

Keywords - DCA 2000, point-of-care technology, screening, urine albumin:creatinine ratio, microalbuminuria, macroalbuminuria, sustainability

Introduction
During the 1990s there has been a rapid escalation in the number of Aboriginal Australians with end-stage renal disease. Recent age- and sex-adjusted figures indicate Aboriginal people have around nine-times greater risk of developing end-stage renal disease than all other Australians (1). In some parts of Australia, notably the Tiwi Islands, rates of this disease have now reached epidemic proportions and up to 500 new cases of end-stage renal disease among Aboriginal people are predicted by 2004 (2-5). Renal disease in Aboriginal people arises from a combination of metabolic and environmental factors including strong associations with diabetes, high blood pressure, maternal and infant malnutrition, high rates of obesity, low birthweight and recurrent

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Accepted for Publication: 21 August 2001
childhood infections (5). Many of these factors reflect poor socio-economic status and social disadvantage of Aboriginal people (6,7). The most common form of renal disease in Aboriginal people is glomerular in origin (8) and characterised by albuminuria, as measured by the urine albumin:creatinine ratio (ACR).

There is an urgent need to develop and implement community-controlled, self-sustainable screening programs for the early detection of renal disease in Aboriginal communities nationally, using simple, non-invasive and cost-effective tests, such as urine ACR.

Early detection is critical because albuminuria progresses as a continuum over time, with an increase in urine ACR of 15% per annum being reported in one Aboriginal cohort (9). Further, the magnitude of albuminuria predicts not only end-stage renal disease but also generalised cardiovascular disease and mortality (10,11). The earlier renal disease is detected, the greater the potential to modify the course of the disease through clinical intervention.

Treatment programs using the ACE inhibitor Coversyl (Servier Laboratories) have proven effective in slowing the progression of renal disease in Aboriginal people (12,13). Coversyl not only stabilises renal function but also reduces hypertension, itself a risk factor for renal disease progression. In addition to its value as a screening tool for early detection, the measurement of ACR levels are also important in monitoring the efficacy of treatment.

In the long-term, early intervention should lead to a reduction in the number of Aboriginal people requiring dialysis - at a conservative cost of $75,000 per patient per year (4) - and having to endure the considerable social and cultural trauma associated with family dislocation during this treatment (7).

The point-of-care DCA 2000 (Bayer Australia) is a small, portable instrument that can measure the albumin:creatinine ratio on 40 μL of urine in just 7 minutes. The analytical and diagnostic performance characteristics of the DCA have recently been validated (14) and the instrument was considered suitable for screening for renal disease in the Aboriginal community setting.

In mid 1997, the Renal Unit at Flinders Medical Centre in South Australia formed a partnership with a remote Aboriginal Community Controlled Health Service, 850 kilometres north of Adelaide, to conduct a renal disease screening program among the adult members of the local Aboriginal community.

The program followed a formal request from the Director and Board of this Aboriginal health service to the Flinders' Renal Unit. The screening program aimed to identify those adult members of the community who were at risk for developing end-stage renal disease, and to offer these people the opportunity to participate in tailored intervention programs at both clinical and community levels. The screening program was extended to include children from the community in late 1998, with the Renal Unit from the Women's and Children's Hospital in South Australia joining the partnership.

The measurement of urine ACR on the Bayer DCA 2000 was the cornerstone of the adult screening program. This paper presents an assessment of the clinical, practical and sustainable use of the instrument in the adult renal screening program.

Methods

The Bayer DCA 2000

The DCA 2000 (Bayer Australia, Pymble, NSW) uses a reagent cartridge (DCA 2000 Microalbumin/Creatinine kit, catalogue number 0611, Bayer Australia) which provides a quantitative measurement of urine albumin (by immuno-turbidimetry, using a polyclonal goat antiserum) and urine creatinine (by spectrophotometry using 3,5-dinitro-benzoic acid at alkaline pH), as well as calculation of the urine ACR, all within a 7-minute turnaround time. There are 10 reagent cartridges per kit. The measuring range for urine albumin is 5 to 300 mg/L, and for creatinine 1 to 44 mmol/L. The DCA's lower limit of detection for urine albumin (5mg/L) is 60-times more sensitive than conventional dipsticks for this analyte.

Low and high control samples (DCA 2000 Microalbumin/Creatinine Low and High Control kit, Catalogue number 6012, Bayer Australia) were used to assess day to day precision with, in general, each control being used alternately to test the first cartridge of a new reagent kit.
Screening of adults

At the request of the community, adult screening was conducted in the health service clinic. Participation in the screening program was entirely voluntary, with each participant giving prior informed consent.

For the first 18 months of the program, a field team from Flinders Medical Centre comprising a nephrologist, scientist, nutritionist and information technologist visited the community at approximately six-week intervals and worked closely with the clinical nurse and Aboriginal health worker team from the Aboriginal health service to conduct adult screening sessions. During this period, the scientist performed the majority of the DCA testing on adults.

For the next 18 months, Aboriginal health workers conducted most of the adult screening, following a detailed skills transfer program (described later). Throughout the three-year study period, the Flinders Medical Centre renal team was responsible to the Director of the Aboriginal health service and its Board.

The adult screening program involved a full medical assessment including a family history, a height and weight measurement for calculation of body mass index, a blood glucose test by glucometer and a blood pressure measurement (both lying and standing). In addition, each participant brought with them a first-morning urine specimen, which was tested on-site for urine ACR on the Bayer DCA 2000 machine and for pH, protein, glucose, blood, leucocytes, nitrite, urobilinogen and bilirubin by qualitative dipstick urinalysis on the Clinitek 50 (Bayer Australia).

The first morning urine was the specimen of choice because it has greater sensitivity and specificity for microalbuminuria than the random spot urine (15). The latter is subject to a higher degree of variability due to postural factors such as physical activity or exercise and hence a higher rate of false positive test results (15). If the urine specimen was found to be dipstick positive for blood, nitrite or leucocytes (other conditions leading to false positive results), urine ACR analysis was not performed and the patient was asked to return with a fresh first-morning specimen in around two weeks.

Classification of albuminuria

The following levels of urine ACR were adopted in assessing risk for renal disease: ACR less than 3.4 mg/mmol, normal; ACR between 3.4 and 33.9 mg/mmol, microalbuminuria indicating early renal disease; and ACR greater than or equal to 34 mg/mmol, macroalbuminuria indicating overt renal disease (16).

If a raised urine ACR (greater than or equal to 3.4 mg/mmol) was found on initial assessment, then the participant was required to submit a further first morning urine specimen for repeat analysis of urine ACR. Both specimens needed to be between 3.4 and 33.9 mg/mmol before a subject was classified as microalbuminuric, and greater than or equal to 34 mg/mmol for being macroalbuminuric. The mean of the two values was used as the baseline ACR for each individual.

Towards the sustainable use of the DCA 2000 at the community level

A long-term goal of the renal screening program was to implement an education and training program for the community’s Aboriginal health workers, whereby they would have a sound understanding of kidney disease and be fully trained and competent in the use of the DCA 2000 point-of-care instrument.

This training program was conducted from January to June 1999. Following completion of this program, the Aboriginal health workers were able to conduct community screening in their own time and space, independent of the Flinders Medical Centre renal team from September 1999 onwards.

Ethics approval

Approval to conduct the renal screening program was obtained from the Aboriginal Health Research Ethics Committee of South Australia and the Flinders Medical Centre’s Committee on Clinical Investigation.

Results

Analytical performance of the DCA 2000

Between-run coefficients of variation (CV%) (n=46) for each measurement on the DCA across the study period were: 6.9% and 3.6% for urine
albumin (at levels of 36 and 208 mg/L, respectively), 3.2% and 4.1% for urine creatinine (9 and 36 mmol/L) and 6.7% and 5.3% for urine ACR (for ratios of 4.1 and 5.8).

These levels of imprecision compare favourably with the median coefficients of variation obtained by laboratories participating in the Royal College of Pathologists of Australasia’s Quality Assurance Program Group’s Urine Chemistry Program (5.6% for urine albumin, 3.8% for urine creatinine, July to December 2000 testing cycle, J Gill personal communication).

Across 30 months of field use, no mechanical breakdowns were experienced, while the error rate for cartridge failure was less than 1%

**Screening for Renal disease using the DCA 2000**

We now report the results of urine ACR testing performed on the DCA during adult screening. The results of other screening parameters measured are not included in this paper.

From June 1998 when screening commenced until December 2000, 149 adult members of the Aboriginal community were investigated for their risk factors for renal disease, including urine ACR measurement on the DCA 2000. This number represented approximately 65% of the community’s adult population. Thirty-seven percent of those adults screened were males, and 63% were females. The mean age of adults screened was 41.7 years ± 1.1 (standard error of mean), with an age range from 18 to 78 years. In total, 232 urine ACR measurements were performed on adult subjects on-site in the community clinic across the screening period.

Twenty-eight (19%) and fourteen (9%) of adults were identified as having previously undiagnosed persistent microalbuminuria and macroalbuminuria respectively, following ACR measurement using the DCA (Table 1).

There was no significant difference between gender in the prevalence of microalbuminuria ($\chi^2=1.34; \text{df}=1; p=0.25$, NS) or macroalbuminuria ($\chi^2=0.010; \text{df}=1; p=0.92$, NS).

The mean and range of ACR values found in the micro- and macroalbuminuric groups are also shown in Table 1. There was no significant difference between gender in the mean ACR values observed in the microalbuminuric group (ANOVA, $p=0.56$, NS) or macroalbuminuria (ANOVA, $p=0.36$, NS).

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**Table 1.**

<table>
<thead>
<tr>
<th>Number of People Screened</th>
<th>Prevalence %</th>
<th>Mean ACR (mg/mmol)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Microalbuminuria</td>
<td>Macroalbuminuria</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SEM*</td>
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<tr>
<td><strong>Male</strong></td>
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<td></td>
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<tr>
<td><strong>Female</strong></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>All</strong></td>
<td>149</td>
<td>18.8</td>
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</tbody>
</table>

*SEM = standard error of the mean

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Figure 1 categorises the albumin:creatinine ratios found during screening by age group. Fifty percent of all adults over 45 years of age had either micro- or macroalbuminuria. Twenty-five percent of adults aged between 29 and 44 years exhibited albuminuria. A statistically significant association was observed between age and the progression of albuminuria ($\chi^2 = 16.2; df = 4, p=0.003$).

All subjects with microalbuminuria were either diabetic, diabetic with hypertension, or hypertensive alone. The high rate of microalbuminuria identified in this community is consistent with the findings from Aboriginal communities in other parts of Australia (12,17).

The number of people with previously unknown overt albuminuria was an unexpected and clearly disturbing finding, and further emphasises the need for screening and early detection of renal disease.

Of a total of 232 urine samples tested during the study, 11% had albumin concentrations greater than the upper limit of the DCA’s measuring range (300 mg/L) and therefore an on-site quantitative albumin result could not be obtained on these samples at the time of analysis. None of the urine samples had a creatinine concentration greater than 44 mmol/L. A simple dilution technique to enable on-site quantitation of over-range albumin concentrations has subsequently been developed, the results of which will be published elsewhere.

Towards the sustainable use of the DCA 2000 at the community level

Figure 2 shows the number of urine ACR tests performed on-site by the service’s Aboriginal health workers since education and training initiatives were completed in June 1999. This number is compared with the number of urine ACR tests performed by the field team during visits to the community. The crossover of responsibility for urine ACR testing on the DCA occurred in September 1999. During 2000, there was a 165% increase in the number of urine ACR tests performed by the Aboriginal health workers.

Discussion

Screening programs for the early detection of renal disease can be effective in making in-roads into
the current epidemic of renal disease among Aboriginal Australians provided they are community controlled and sustainable at the community level. The point-of-care DCA 2000 meets these requirements because testing for renal disease can be done in the community setting by a trained health worker, the result is immediately available to both the local medical officer and patient, and ownership of the screening information remains in the community.

The large number of adults detected with albuminuria during this screening program confirms a high prevalence of incipient renal disease in this community, while illustrating the clinical and practical usefulness of the DCA 2000.

Common blood markers of renal disease such as urea and creatinine may only begin to rise significantly when 30% to 50% of nephron function has been lost (18). However microalbuminuria may be evident with as little as 10% damage to kidney function (18). The earlier the disease process is detected the greater the chance of retarding the progression of disease through appropriate intervention.

All people identified as at risk for renal disease in this study were given the opportunity to participate voluntarily in both clinical and community-based intervention programs (the results of which will be published later).

The ACE inhibitor Coversyl was offered to those at risk to reduce blood pressure and stabilise renal function. Those persons with macroalbuminuria are now under specialist nephrological care. Information about nutrition, the value of exercise, and alcohol and tobacco consumption reduction strategies has been given to both individuals at risk and to the community in general.

The role of the DCA 2000 in identifying those people with albuminuria has been pivotal to the screening program. The DCA’s small, portable nature and its simplicity of operation given appropriate training have resulted in the machine being well accepted by the Aboriginal health worker team. In performing urine ACR tests themselves, health workers have been empowered to take greater responsibility for renal screening in their community.

During the study period, the DCA has continued to demonstrate sound analytical performance and proved robust and reliable in the remote health setting. The only minor deficiency in using the machine in the field was that just over 10% of the urine samples tested were unable to be quantified on-site due to their high urine albumin concentrations. However, as mentioned earlier, this problem has been addressed by the development of a suitable on-site dilution technique.

At the end of 2000, the renal screening program was formally handed over to the Aboriginal health service as a self-sustaining activity.

The Australian Government has noted the successful use of the DCA in the Aboriginal health setting and the full potential of the machine’s analytical capability is now being realised. The Bayer DCA 2000 instrument can also measure Haemoglobin A1c (HbA1c) on a finger prick of blood in six minutes.

HbA1c is an established marker for monitoring control of diabetes. In 1999, the Office for Aboriginal and Torres Strait Islander Health within the Commonwealth Department of Health and Aged Care, in partnership with the National Aboriginal Community Controlled Health Organisation, initiated a program for community-based HbA1c testing using the DCA 2000 in 47 Aboriginal Community Controlled Health Services around Australia (19).

Opportunities for the broader application of point-of-care instrumentation for screening and management of chronic diseases in Aboriginal communities seem considerable.

Acknowledgments

The authors wish to thank Bayer Australia for their generous support of this study. The authors also wish to acknowledge the commitment and enthusiasm of the Aboriginal health worker team and the Director and Board of the Aboriginal Health Service, and the support of the community members throughout this project. The expert technical assistance of Sandra Harris, Senior Technical Officer, Women’s and Children’s Hospital, in performing on-site DCA analyses during field team visits is particularly acknowledged.
References


