Renal point-of-care testing: collaboration between biomedical scientists and community pharmacists

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ABSTRACT

The incidence of chronic kidney disease (CKD) is increasing with the prevalence of obesity, diabetes mellitus, elevated blood pressure and other cardiovascular-renal risk factors. Wider point-of-care testing (POCT) strategies in the community setting are needed to prevent CKD and delay progressive loss of renal function. Since publication of the Institute of Biomedical Science (IBMS) *Point of Care Testing (Near-Patient Testing) Guidance on the Involvement of the Clinical Laboratory*, the biomedical scientist can now provide enhanced services including tests for blood glucose, cholesterol, and monitor blood pressure. Under the current pharmacy contract, community pharmacies are now often equipped with sophisticated record access systems and interfaces to monitor drug interactions in suspect/high-risk CKD patients. Current facilities can be utilised further allowing pharmacists more clinical involvement based on community need. Further development of POCT in the community involving collaborations between biomedical scientists and community pharmacists would allow wider service availability in primary care and might be advantageous in suspect/high-risk patients.

KEY WORDS: Kidney disease.
Near-patient testing.
Pharmacy.
Point-of-care testing.
Renal insufficiency, chronic.

Introduction

Chronic kidney disease (CKD) has been described as the gradual and usually permanent loss of renal function over time. Early in the disease process, people with CKD often experience no symptoms and CKD has, for a long time, been an under-diagnosed condition, adding significantly to the incidence of cardiovascular disease (CVD) and ultimate death.[1]

In the 1970s renal diseases such as glomerulonephritis and pyelonephritis were the most prevalent causes for enrolment on to renal replacement therapy (RRT) programmes. In the past decade the prevalence of these diseases has diminished and increasingly CKD is linked to diabetes (predominantly type 2) and renal vascular diseases such as hypertension, where generalised renal function is brought close to the level where conservative renal protective treatments are ineffective and dialysis is required.[2] The National Health Service (NHS) currently provides diagnostic tests, medication and ongoing treatment for renal failure. Treatment costs, including haemodialysis, are around £20,000–£25,000 per patient per year.[3]

Proteinuria is an important parameter when considering point-of-care testing (POCT) of CKD in the wider community. Proteinuria originates from the kidney and occurs as a result of injury to the glomerulus, the renal tubule, or both. Chronic glomerular injury resulting in proteinuria may be secondary to prolonged diabetes or hypertension. A tubular origin of proteinuria may be associated with inflammation of renal tubules triggered by prescribed drugs or ingested toxins. In the absence of obvious clues to the cause of persistent proteinuria on history or clinical examination, it is worthwhile reviewing a patient's prescribed drugs to identify any potentially nephrotoxic agents (e.g., non-steroidal anti-inflammatory drugs [NSAIDs]).

The National Institute for Health and Care Excellence (NICE) guidelines[4] recommend POCT in patients at higher risk for CKD. These include patients with diabetes, hypertension, cardiovascular disease, connective tissue disorders, a family history of renal disease, and those prescribed potentially nephrotoxic drugs. Patients with sudden onset of lower limb oedema and associated proteinuria should have their serum albumin level measured to exclude nephrotic syndrome. As the guidelines also indicate, renal tract ultrasound can be used to measure kidney size, and to detect scarring associated with chronic pyelonephritis or prior renal stone disease, which can cause proteinuria.

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Prevalence of CKD in the UK

The prevalence of proteinuria is also an issue in the long-term management of patients with established CKD because it may also affect their blood albumin:creatinine ratio.[5–8] Analysis of patients with unidentified CKD suggests that their risk profile may be different to patients with identified CKD.[9] Given that CKD affects all age groups, there is significant variation in the management of CKD and in standards for prevention, early recognition and intervention. Data now emerging[10] point to the need for a global effort to improve CKD awareness and prevention, to improve treatment and healthcare outcomes. Renal function is determined by the glomerular filtration rate (GFR)/estimated GFR [eGFR]) and several reasons have been

put forward to explain the changes observed.[11] Table 1 lists the five stages of CKD based on GFR criteria in adults.

The measurement of prevalence of CKD in the UK is complicated by the fact that health professionals in primary and secondary healthcare employ different definitions for the stages of CKD based on eGFR, including either modification of diet in renal disease (MDRD) or creatinine clearance (CrCl). Measurement using CrCl has significant practical problems and is known to be inaccurate. An alternative is to measure serum creatinine (SCr) and/or eGFR using an equation that corrects for some of the more significant non-renal influences. Some health professionals take into account the patient's general clinical history before progressing to measure renal insufficiency.

Early laboratory analysis has a positive effect on referral rates in a large adult population.[12] One study[2] estimated the prevalence of patients who have significantly reduced GFR using the Cockcroft-Gault (C-G) formula. This study included 2781 out-patients referred by community physicians to an urban laboratory network for SCr measurement. Patients were grouped according to the concordance of SCr level abnormalities (abnormal >130 μmol/L) with significantly abnormal C-G values (abnormal <50 mL/min). The C-G value ≤50 mL/min was chosen to reflect substantial renal impairment in all age groups. The study demonstrated that the prevalence of significantly abnormal renal function among patients identified by laboratories as having normal-range SCr may help to facilitate the early identification of patients with renal impairment.

Patients with elevated levels of urinary albumin are at increased risk for RRT and accelerated loss of renal function. Early detection of urine protein to slow progression of CKD and decrease mortality is not cost-effective unless selectively directed toward high-risk groups (i.e., older persons and persons with hypertension) or conducted at an infrequent interval of 10 years.[13] Point-of-care testing for albuminuria identifies patients at increased risk for progressive CKD, 40–50% of whom were previously undiagnosed or untreated.[14]

Renal guidelines

The number of patients taken into RRT programmes has gradually increased over the past decades. This may be due partly to improvements in dialysis techniques and a better availability of these programmes. However, the pattern of the cause of end-stage renal failure also has been changing over time.[15] In 2008, the Kidney Disease: Improving Global Outcomes (KDIGO) initiative[12] made recommendations that all countries should have a targeted POCT programme for CKD, focusing on patients known to have diabetes, hypertension and CVD.[15] One investigation suggested that measuring the serum albumin:creatinine ratio (ACR; preferably on a first-void morning specimen) by implementing POCT in all at-risk patients is important.[16]

Various tests can be used to screen for the early signs of disease or to assess the risk of a disease. For example, fasting glucose can be used to screen for diabetes mellitus (DM), and systolic blood pressure and the total serum cholesterol:high-density lipoprotein ratio can be measured to help assess the risk of coronary heart disease (CHD).[14] Service providers, policy-makers and payers should view CKD as a major public health problem and consider prompt, innovative POCT programmes to address this growing patient population.[17]

Table 1. Stages of chronic kidney disease.

Stage	Definition
1	Kidney damage with normal or raised GFR (≥90 mL/ min/1.73 m^2)
2	Kidney damage with normal or raised GFR (60–89 mL/min/1.73 m^2)
3	Moderately impaired GFR (30–59 mL/min/1.73 m^2)
4	Severely impaired GFR (15–29 mL/min/1.73 m^2)
5	End-stage renal failure (GFR <15 mL/min/1.73 m^2)

Table adapted from reference 1

Reducing CKD

An Australian investigation[18] explored the feasibility of early detection and treatment of renal disease by mass POCT. Twelve randomised trials of angiotensin-converting enzyme (ACE) inhibitors were undertaken in 1943 patients with varying degrees of renal impairment, hypertension and proteinuria. The results showed that the risk of developing CKD can be reduced by about 30% over a two- to three-year period.

In the POCT testing model, this finding supports the need to i) use a single dipstick test for proteinuria, ii) confirmatory 24-hour urine test for protein, and iii) commence administration of ACE inhibitors in suspect/high-risk renal patients. The study also showed that 20,000 people over 50 years of age would need to be screened to prevent one case of CKD. To achieve this, approximately 100 people would need to be treated with ACE inhibitors for two to three years, and 1000 would need to have a 24-hour urine protein test (of these, approximately 700 would be false positives).Given the lack of specific early detection data from POCT in middle-aged and older patients with proteinuria, preemptive treatment of at least some with ACE inhibitors is a promising primary prevention strategy for preventing CKD.[18]

In summary, large population-based cohort studies of the use of ACE inhibitors may help to answer questions such as i) What is an individual's risk of developing CKD, given measured values for proteinuria, blood pressure and renal function? ii) What is the benefit of ACE inhibitor administration in POCT-detected cases? iii) Is psychological and physical harm caused by POCT (including the specific renal investigations and treatments that follow proteinuria detection)?

Methods for CKD detection in POCT

Specific POCT initiatives should promote early detection of CKD and co-morbid conditions, along with the use of

appropriate outcome measures to clarify patient care, the implementation of strategies to delay disease progression and adequate preparation for timely initiation of RRT.[19] Suspect/high-risk patients for CKD can now also be offered POCT to help monitor microalbuminuria, haematuria, proteinuria and hyperlipidaemia. Future tests that could become available include serum cystatin C, ferritin and electrolyte levels.

Benefits of early CKD detection

Some conditions are functionally self-limiting, while others may progress so slowly that there is sufficient renal function for the patient to live out their normal lifespan. Even when the kidneys begin to fail, careful control of diet and blood pressure, and timely intervention to prevent complications, can enable a person to survive in good health for many years. To support more effective methods of monitoring CKD, biomedical scientists and community pharmacists should be encouraged to implement POCT in the community; Community pharmacists should also be encouraged to conduct Medicines Use Review (MUR) services to 'assess' the wider community.

Implementing an enhanced POCT service that enables suspected or high-risk patients to be screened in the community in addition to an MUR service can help in i) early detection and prevention of CKD, ii) potentially spread the workload of GPs, iii) prevent late referrals to secondary care, iv) tighten control of medication with the implementation of an MUR service, v) allow wider service availability in primary care, and vi) strengthen renal care according to the NSF for Renal Services (National Kidney Foundation, 2008). Ultimately, early detection and proactive care/POCT in pre-dialysis patient communities will not only improve wellbeing, but also enable savings to the NHS.[19]

The community and POCT

Improved technology has enabled a range of POCT kits to be made available and accessible to patients. This should prompt biomedical scientists to become more active in community environments, increasing their role to monitor suspect/high-risk patients for specific long-term conditions such as CKD. This can include quality assurance and monitoring specific POCT initiatives. Equally, community pharmacists can have an increasingly clinical role to facilitate better self-care approaches or interventions for patients in their communities under the new Pharmacy Contract (2005) Advanced and Enhanced Services.

Point-of-care testing results can be expressed qualitatively, quantitatively or semi-quantitatively,[20,21] but reference values can vary from one laboratory to another and it is advisable for users to compare their results with reference values in which the sample has been taken (or with the laboratory to which a test has been sent for analysis).[20,21] Not all laboratory data are of direct relevance, but a general knowledge of them is recommended in order to understand a patient's medical background. Presently, community pharmacists do offer basic POCT services; however, services should be widened with the involvement of biomedical scientists to interpret results and advise on clinical parameters accordingly.[22,23]

With regard to CKD, biomedical scientists and community pharmacists should explore opportunities for collaboration to help increase patient and public knowledge, promote an understanding of a healthy lifestyle, and transmit public health messages so that they are empowered to take actions which will improve patient health. Biomedical scientists and community pharmacists should help to target the 'hard to reach' sectors of the population not frequently exposed to health promotional activities in other parts of the health or social care sector.[13,23]

Point-of-care testing in community can be used to fulfil three main objectives: i) to assess the risk of disease, ii) to screen for the presence of disease, and iii) to manage the disease. There is evidence of how POCT services are expanding and of environments where they could be implemented to serve wider communities.[18,21,24–27]

Clinical guidelines recommend regular monitoring of renal function in suspected and high-risk patients to ensure that drugs are prescribed in safe and effective doses.[28] Dosage adjustment or drug substitution is often necessary in patients with impaired renal function. Renal impairment is a patient-related risk factor for medication-related hospital admissions.[29–31] Both prescription interventions and MURs allow the community pharmacist to provide emphasis on drug formulations to help reduce nephrotoxicity in high-risk patients. Monitoring of renal function is recommended on labels of drugs, but biomedical scientists should emphasise that the kidneys are important in clearance[15] and the value of clinical guidelines.[32]

Community pharmacists can contribute to the safer use of medication as a result of their clinical pharmacological knowledge, their skills and ability to perform patient assessments and administer drugs, and monitor and, when relevant, adjust drug regimens. Biomedical scientists can contribute and prompt understanding of screen-specific parameters, conduct quality assurance and quality monitoring to ensure accuracy, validity and reliability in result reporting.[14,33] However, to do this they need up-to-date information about the patient's renal function.

Point-of-care testing methods have become more advanced and can offer the same clinical validity as central laboratory testing if quality issues are guaranteed by trained biomedical scientists.[34,35] It is also available in general practice and is considered both acceptable and satisfactory in an environment such as a community pharmacy.[23,36]

Conclusions

With POCT and disease prevention becoming increasingly important, biomedical scientists and community pharmacists can now play an active role. There are various costs to consider (e.g., human resource, POCT kits, clinical auditing, external quality assessment and quality control checks), but POCT and a collaborative referral service between primary care service providers would be more cost-effective than RRT. There has only been a single study that explores POCT in community pharmacies,[37] so there is a lack of robust evidence to identify how POCT would prove cost-effective; more immediately required are cost-benefit

studies, but initially POCT in high-risk patients is likely to be feasible, cost-effective and beneficial to patients.

In other parts of the world, biomedical scientists and community pharmacists have more clinical roles.[38] Collaborative screening, prescribing and referral services between biomedical scientists, community pharmacists and GPs will enhance patient access to care and medication management. With new healthcare initiatives on the horizon, many community pharmacies are equipped with sophisticated record access IT systems and interfaces to monitor drug interactions in suspect/high-risk CKD patients.[38] Current facilities can be utilised further, allowing biomedical scientists and community pharmacists to have more clinical involvement based on community need. Ultimately POCT collaborations to screen suspect/high-risk CKD patients in situations other than the traditional GP environment would allow wider service availability in primary care.[39–42] □

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