Hyperkalemia is a common and life-threatening complication frequently seen in patients with end-stage renal disease (ESRD), advanced chronic kidney disease (CKD) and acute kidney injury. Indeed, acute hyperkalemia is one of the most common reasons for patients requiring emergency dialysis [1]. However, hyperkalemia does not affect all patients in the same manner. Some of them persistently exhibit chronic hyperkalemia without ostensible signs or symptoms, whereas others are clearly symptomatic with the same plasma potassium concentration (\([K^+]_p\)). The former group appears to develop an undefined compensatory mechanism to mitigate the effects of long-term hyperkalemia. Thus, a significant variation appears to exist in the tolerance to hyperkalemia. A \([K^+]_p\) that causes no signs, symptoms or changes on the electrocardiogram (ECG) for one patient with chronic hyperkalemia may subject another patient to significant risk, presumably due to greater cell membrane depolarization.

To date, there is no predictor of the degree of hyperkalemia a patient can tolerate without an adverse event, except for the ECG and even this direct assessment of electrical cardiac conduction has its limitations (see below). Thus, there is no diagnostic test that can determine what \([K^+]_p\) is acceptable for that particular patient. This knowledge would be particularly useful for the treatment of various diseases. For example, in CKD, certain drugs (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and mineralocorticoid receptors blocker) often cause hyperkalemia. Despite this, each of these drug classes has been shown to be beneficial for cardiac and renal protection. Thus, their potential to cause hyperkalemia can be significant and may outweigh the potential benefit for an individual patient. Indeed, hyperkalemia is a frequent end-point that requires discontinuation of these beneficial medicines. If there was a way to determine what degree of hyperkalemia was acceptable in an individual patient, then a more aggressive treatment plan could be enacted for that patient. As of now, most physicians feel obliged to treat hyperkalemia, particularly significant hyperkalemia (\([K^+]_p > 6.0\) mEq/L) as potentially dangerous. This is based on epidemiological data that demonstrate an association of hyperkalemia with morbidity and mortality in different patient populations. Until a test is developed which would allow a physician to deem an elevated \([K^+]_p\) as tolerable for a particular patient, this practice should continue.

All this is not to say that hyperkalemia never affects diagnostic tests. Hyperkalemia is manifested on an ECG, but the correlation between ECG changes and \([K^+]_p\) is imprecise: only in 50% of patients with \([K^+]_p > 6.5\) mEq/L changes will be seen on an ECG. A common manifestation of mild hyperkalemia (5.5–7.0 mmol/L) in ECG is the ‘tented T-waves,’ which are characterized as tall, peaked and narrow-based [2]. Unfortunately, not all patients with mild hyperkalemia exhibit tented T-waves. If there was another accurate ECG measurement that could predict whether the hyperkalemia was life-threatening, this would be a major advance to direct therapy. An ECG is a relatively noninvasive procedure that is widely available, which makes it an excellent candidate for this use.

The article by Green et al. [3] from Manchester in this issue of *Nephrology, Dialysis, and Transplantation* aims to do just this. The authors propose a possible predictive tool based on ECG reading for hyperkalemia in ESRD and CKD stage 5. In this study, the authors examine the utility of the ratio of the T-wave to the R-wave (T:R) and whether it is more useful than the presence of tented T-waves as a predictor of hyperkalemia in patients with ESRD. The authors report that tenting was no more common in cases of hyperkalemia compared with normal serum potassium and was less common than left ventricular hypertrophy. T:R was less sensitive, but more specifically identified hyperkalemia with a serum potassium >6.0 mmol/L. They also noted that no clinical feature exhibited a correlation with the likelihood of developing abnormal T-waves in hyperkalemia. Finally, they report that abnormal T-waves in patients with hyperkalemia had greater all-cause mortality in their patient population with a mean follow-up of 3.5 years compared with those with normal T-waves.

Unfortunately, this study did not provide us with a tool for guiding management of hyperkalemia within an individual patient. Neither T-wave shape or T:R ratio offered a good, predictive method for the management of hyperkalemia in ESRD. The authors remarked that younger individuals have a higher rate of ‘tented’ T-waves and that older patients naturally have lower T-waves. Because the majority of patients in the ESRD population are older...
individuals, using T:R ratio of 0.75 can potentially miss a significant amount of T-wave changes from the baseline.

An understandable shortcoming of this paper was the lack of a baseline ECG in the absence of hyperkalemia which could be used for comparison. This left the authors unable to determine if the effects on the ECG were from hyperkalemia or from intrinsic heart disease. Immediate short-term reversibility of ‘tented’ T-wave or other signs of hyperkalemia (P–R interval, QRS duration, QTc interval, etc.) with intravenous infusion of calcium, in a patient with true hyperkalemia-related ECG changes, is used at our institution as a diagnostic tool to evaluate the effect of hyperkalemia on cardiac conduction. This physiological approach can be used to assess the risk of hyperkalemia for the patient in the acute clinical setting and also warrants systematic study.

Importantly, this study emphasizes how essential it is for clinicians to be competent in the interpretation of an ECG using the clinical content rather than solely relying on a computer’s interpretation. While a formal curriculum on ECG interpretation is required in internal and emergent medicine programs, proof of competency is not assessed by the majority of them. Furthermore, this paper provides a framework for further study into the management of hyperkalemia. The authors have made a significant start to systematically study the predictive tools for adverse events in hyperkalemia. Clearly, this is an area that deserves further study and innovation.

Conflict of interest statement. None declared.


References

Received for publication: 3.5.2012; Accepted in revised form: 1.8.2012

Increased prevalence of acute interstitial nephritis: more disease or simply more detection?

Andrew S. Bomback1 and Glen S. Markowitz2

1Department of Medicine, Division of Nephrology, Columbia University Medical Center and the New York Presbyterian Hospital, New York, NY, USA and 2Department of Pathology and Cell Biology, Columbia University Medical Center and the New York Presbyterian Hospital, New York, NY, USA

Correspondence and offprint requests to: Glen S. Markowitz; Email: gsm17@columbia.edu

Acute interstitial nephritis (AIN) is the second leading cause of acute, intrinsic kidney disease [1]. Unlike acute tubular necrosis, the most common cause of intrinsic kidney injury, AIN is known to have a high potential for reversibility if identified early [2]. The diagnosis of AIN is often made empirically based on the clinical presentation (e.g. a case of acute kidney injury (AKI) accompanied by a history of rash and fever, peripheral eosinophilia and a urine devoid of protein), yet a true diagnosis of AIN can only be established by a renal biopsy. Indeed, because AIN most commonly occurs in the absence of supportive clinical or laboratory findings, the importance of kidney biopsy to firmly diagnose AIN as the cause of AKI cannot be understated. A biopsy not only confirms the pathologic diagnosis but can also provide information on the severity of the injury, activity versus chronicity of the lesion, and the presence of other significant glomerular or vascular abnormalities that may influence treatment decisions [3].

In this issue of ‘Nephrology Dialysis Transplantation’, Goicoechea et al. report findings from kidney biopsies in the Spanish Registry of Glomerulonephritis over a 16-year period (1994–2009) [4]. Of the total 17 680 native kidney biopsies cataloged in the registry, 468 (or 3%) met the histopathologic criteria for the diagnosis of AIN. In the subgroup of 3059 biopsies performed for the indication of AKI, 392 cases (or 13%) were diagnosed with AIN. As the authors note, these findings are not particularly novel, as the 3% prevalence of AIN has been shown in other biopsy series, as has the higher prevalence in patients presenting with AKI [5]. The intriguing features of their report, however, emerge in the analysis of