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MANAGEMENT & PRACTICE

THE OFFICIAL MANAGEMENT JOURNAL OF ISICEM

VOLUME 16 - ISSUE 2 - SUMMER 2016

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EARLY DIAGNOSIS AND PREDICTION OF ACUTE KIDNEY INJURY

PENKID – A DYNAMIC INFLAMMATION-INDEPENDENT BIOMARKER OF KIDNEY (DYS)FUNCTION

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Early recognition and close monitoring of acute kidney injury (AKI) is vital in the ICU, given AKI's high prevalence and effect on length of stay and risk of re-hospitalisation and death (McCullough et al. 2013). As more becomes known about biomarkers, intensivists need to be well-informed about the benefits of currently available kidney biomarkers. While serum creatinine is still the standard method to determine kidney dysfunction, it has major limitations. It increases too slowly to detect worsening of kidney function in a timely manner and it decreases too slowly when kidney function is improving. In addition, it largely depends on other variables (McIlroy et al. 2010; Mårtensson et al. 2010). Most other biomarkers for acute kidney injury are affected by inflammation, and most AKI patients have inflammation, as sepsis and septic shock are the primary cause of AKI (Zarjou and Agarwal 2011). Hence, these biomarkers have failed to reliably predict AKI in ICU patients (Bell et al. 2015).

The sphingotest® penKid immunoassay measures the plasma level of penKid, a stable surrogate marker for the instable Enkephalins (Ernst et al. 2006). Enkephalins are endogenous peptide hormones that are highly expressed in the kidney and regulate renal excretion (Denning et al. 2008; Sezen et al. 1998). penKid is an inflammation-independent functional marker that indicates the actual kidney status by predicting the future change in serum creatinine. The highly dynamic nature of penKid enables close monitoring of the changes in kidney status, thereby supporting early clinical decision-making, e.g. regarding the use of nephrotoxic drugs, initiation of renal replacement therapy or discharge.

Clinical Studies

Inflammation-Independent Plasma Biomarker for Sepsis-Induced AKI

In a retrospective observational study, physicians from the Emergency Department (ED) Sant'Andrea Hospital, University of Rome Sapienza, analysed the blood of 101 patients admitted to the ED with sepsis (Marino et al. 2015). sphingotest® penKid was used to evaluate plasma levels of penKid and the results were compared to concentration levels of neutrophil gelatinase-associated lipocalin (NGAL). The results showed that penKid correlates with the severity of AKI in septic patients, as determined by RIFLE criteria, while sepsis patients without kidney failure display essentially normal penKid levels. NGAL is elevated above normal in patients with systemic inflammation, even without kidney injury.

Diagnosis of Kidney Dysfunction and Prediction of Adverse Cardiac Events

A UK study assessed the prognostic value of penKid levels in acute myocardial infarction (AMI) patients at admission for major adverse cardiac events (MACE) and death during follow-up of 2 years (Ng et al. 2014). N-terminal pro-B-type natriuretic peptide (NT-proBNP) and Global Registry of Acute Coronary Events (GRACE) scores were used as comparators. 1,141 AMI patients admitted to the University Hospitals of Leicester NHS Trust between August 2004 and April 2007 were included in the study. MACE is defined as a composite endpoint of all-cause mortality, heart failure, hospitalisation or recurrent acute myocardial infarction. Using a simple cut-off (99th percentile of normal range) penKid confirmed its significant predictive power for short-term mortality and MACE, as expected for a functional kidney marker. Univariate as well as multivariate models adjusted for ST elevation, age, sex, past history of hypertension, diabetes, IHD, eGFR, Killip class show that penKid predicts short-term (2 years) mortality and MACE stronger than NT-proBNP and Troponin. ■

penKid Key Points

- Plasma marker – in contrast to urine, plasma is easily available on ED/ICU;
- Functional kidney marker – indicates worsening or improvement of kidney function much earlier than mere markers of kidney damage;
- Indicates actual kidney status by predicting the future change in serum creatinine;
- Dynamic nature enables close monitoring;
- Unaffected by systemic inflammation;
- Simple cut-off for unambiguous results;
- Supports very early clinical decisions on nephrotoxic drugs, renal replacement therapy and discharge.

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