

Major study enhances diagnosis of acute kidney injury

A major New Zealand kidney study, the largest of its kind in the world, is expected to cause a re-think in terms of the early detection and treatment of acute kidney injury (AKI).

The HRC funded research, carried out by the University of Otago's Kidney Research Group, combined several studies including a trial of erythropoietin in the treatment of AKI, a modern term for kidney failure.

Professor Zoltán Endre says animal model studies by his and other groups had shown that erythropoietin protects the kidney against ischemic injury if given within six hours. His group has now published the first study in humans on the role of erythropoietin in AKI and is one of seven published papers, two commentaries and two reviews to have come out of the study so far.

Professor Endre says this was part of a two-pronged investigation of 529 patients, which also looked at many biomarkers, including urinary Y-glutamyltranspeptidase and alkaline phosphatase, in the early detection of AKI. They found high dose erythropoietin was safe, but didn't ameliorate AKI in the trial. However Professor Endre says it is the first trial in the world where a urinary biomarker has been used to triage patients to treatment, and so it is quite important from that perspective. He clarified that the biomarker didn't detect all the patients expected, because it remained detectable for a much shorter time than anticipated. That was complicated by finding that many of the 162 patients randomised to treatment had suffered their AKI up to 29 hours earlier.

"While we recruited successfully, and randomised nearly all of 162 patients

with an increased urinary biomarker concentration within the planned six hours of ICU admission, the time after actual kidney injury was often much longer, which we discovered when we went back and reviewed all the patients' charts."

That meant that rather than having patients triaged and treated within six hours of AKI, the median time after injury was 12.9 hours, well beyond the effective treatment window for erythropoietin. While this failed to show erythropoietin had a benefit, Professor Endre says that being able to triage patients using a urinary biomarker is a major advance that others around the world are racing to emulate.

"Our study clarifies the rules of triaging. It highlights that we need to be careful about the time after injury in selecting patients with particular biomarkers, and demonstrates ways of increasing the chance of future successful intervention in AKI."

Professor Endre says they have learnt a lot about biomarker combinations and are submitting a major paper on three other novel biomarkers investigated in collaboration with the groups in the United States. This will provide the first head-to-head comparison on six urinary biomarkers collected simultaneously and will shed light on how these should be used in triaging patients to treatment.

"We're going to end up with panels of biomarkers. Some will detect initiation of injury, others will monitor progression of injury, and others still will allow us to assess treatment by monitoring inflammation and healing," he says. "Ideally, we need to be able to



Professor Zoltan Endre

Key words:

- Kidney injury, erythropoietin, biomarkers

Aims of this research:

- To generate a review of early detection and treatment of acute kidney injury

treat people within a six hour timeframe from injury, rather than use a treatment 24 or 48 hours later when we've already shown that it is then ineffective."

The paper, *Early intervention with erythropoietin does not affect the outcome of acute kidney injury – the EARLYARF trial*, was published in 'Kidney International' the official journal of the International Society of Nephrology. It was accompanied by a glowing editorial entitled *Timed and targeted therapy for acute kidney injury: a glimpse of the future*.

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