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FILTRATION IS ABSENT IN THE RAT KIDNEY EARLY IN REPERFUSION

Chloe Johnson and Paul O'Connor

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Filtration is Absent in the Rat Kidney Early in Reperfusion

Presenter(s): Chloe Johnson

Author(s): Chloe Johnson and Paul O'Connor

Faculty Sponsor(s): Paul O'Connor, PhD

Affiliation(s): Department of Biological Sciences, Department of Physiology

ABSTRACT

Ischemic acute kidney injury (AKI) occurs following a period of ischemia and is a major clinical problem. In AKI, the cellular structure of the kidney often appears relatively normal, despite the almost complete loss of kidney function. Red blood cell (RBC) trapping occurs in AKI and is the trapping of RBC in the capillaries of the kidney medulla. As RBC trapping increases pressure in the kidney, this increased pressure may obstruct the tubules, limiting kidney filtration even when cellular injury is mild. In the rat ischemic reperfusion model of AKI, RBC trapping is most prominent early in kidney reperfusion (2-6 hours) before dissipating. As this is before most tubular injury is evident, if RBC trapping is responsible for the decline in kidney function, glomerular filtration rate (GFR) should be most reduced early in reperfusion. Therefore, the current study tested the hypothesis that 'the greatest reductions in glomerular filtration rate following ischemia occur early in reperfusion'. The rat warm bilateral arterial clamp model of ischemia reperfusion injury (IRI) was used. 4 male rats underwent IRI surgery and 3 rats were used as controls. GFR was determined early (2-4 hours) and late (24-25 hours) in the reperfusion period. The rats were anesthetized and the renal artery of each kidney was then clamped for a period of 45 minutes before removing the clamps and allowing the animals to recover. To measure GFR, sinistrin (20mg) was administered via the tail vein. Sinistrin is a molecule excreted by the kidney. The clearance of sinistrin from the blood can be used to estimate GFR. The clearance of fluorescent sinistrin from the blood was measured across the skin using a device stuck to the back of the rat (Medibeacon). As expected, glomerular filtration rate was markedly reduced following IRI compared to control rats with the ½ life of sinistrin in the blood of control rats being 23.6 minutes verses 2246 minutes for IRI rats. Importantly, the greatest reductions in GFR occurred

early in reperfusion with the ½ life of sinistrin in the blood being 3728 mins between 2-4 hours of reperfusion before falling to 765 mins by 24 hours of reperfusion ($P<0.001$ (Paired t-test). Our data are consistent with RBC trapping promoting the functional decline of the kidney following ischemia. Understanding the relationship between vascular congestion and renal functionality is essential for the development of clinically effective treatment options for acute kidney injury.

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Correspondence: Chloe Johnson, Augusta University, 1120 15th St. Augusta, GA 30912, chljohnson@augusta.edu