Spironolactone for Survivors of Critical Illness (SSCILL)

Mansoor Bangash

For many patients, surviving critical illness does not equate to a return to baseline health. Instead, the end of a life-threatening phase of illness becomes a phase of chronic illness. Through the follow-up of both paediatric and adult survivors of critical illnesses such as sepsis, severe trauma, burns and acute respiratory distress syndrome (ARDS) we know that patients from all these groups are at increased risk of developing cardiovascular diseases such as atherosclerosis, heart attack and heart failure in the ensuing years. Furthermore the risk of developing new diseases like chronic kidney disease and diabetes, both of which contribute to cardiovascular disease, is also increased. Importantly, cardiovascular illnesses are suggested to be a leading cause of death and re-hospitalisation in the months and years following critical illness. Why is this so?

During critical illness, in order to restore health, the body’s tissues and immune system frenziedly communicate with one another to signpost and respond to tissue damage and pathogens. This inflammatory activity is detected by blood tests, and is used to gauge treatment response during illness. One might expect that when patients are no longer critically ill inflammation levels are low – however this is only true for some patients. Studies show that patients with persistently elevated levels of inflammation have the highest risks of cardiovascular and all-cause mortality after critical illness. Blood tests which usually indicate cardiac stress correlate with inflammation and also identify these high risk patients.

Spironolactone is a drug with proven efficacy in reducing cardiovascular deaths in heart failure and after myocardial infarction. Spironolactone also reduces urinary protein loss (an important risk marker for cardiovascular death) in chronic kidney disease and diabetes. In both cardiac and kidney diseases spironolactone acts on inflammatory immune cells to reduce abnormal immune-repair behaviours (remodelling) that result in fibrosis and reduce organ function. Similarly in the walls and lining of blood vessels spironolactone targets the same remodelling abnormalities to improve vascular health. We believe that spironolactone could analogously target inflammation-driven cardiac and renal remodelling to reduce cardiovascular morbidity and mortality during critical illness survival.

Through SSCILL we aim to improve the understanding of survivor cardiovascular disease processes so that we improve the short-term and long-term health of critical illness survivors. SSCILL is a phase II randomised controlled trial that will recruit sepsis, major trauma and ARDS patients at high risk of chronic cardiovascular disease (defined by an ICU admission stay of at least 7 days AND high levels of the cardiovascular biomarker NT-proBNP) and randomise them to receive 6-months of spironolactone or a placebo. We will follow-up these patients at ICU and hospital
discharge and 6-months after randomisation and assess changes in their hearts, blood vessels, kidneys and immune systems. This will provide the opportunity to better understand the natural history of chronic cardiovascular and renal disease in critical illness survivors, and will simultaneously provide crucial safety, feasibility and efficacy data required to design a larger definitive study of spironolactone in this patient group.