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# MESENCHYMAL STROMAL CELLS (CYTO-MSC) ARE WELL-TOLERATED AND ASSOCIATED WITH RENAL FUNCTION IMPROVEMENT IN PATIENTS WITH CHRONIC KIDNEY DISEASE: AN OBSERVATIONAL RETROSPECTIVE STUDY

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**Background:** Microvascular disease and structural damage are hallmarks of chronic kidney disease (CKD). We have demonstrated previously that mesenchymal stromal cells (MSCs) could differentiate into mesangial cells in animal models of glomerular injury. We further demonstrated that MSCs promoted angiogenesis in diabetic patients with critical limb ischemia. Given the ability to improve vascularity and structure, MSCs may potentially improve renal function in CKD.

**Objective:** In this study, we evaluated the safety, tolerability and renal function of patients with CKD who had participated in MSC-related clinical trials.

**Methodology:** There were 4 clinical trials approved at the National University Malaysia in collaboration with Cytopeutics (Cyberjaya, Malaysia) which provided the mesenchymal stromal cells (Cyto-MSC) for treatment of acute stroke, heart failure, diabetes with critical limb ischemia and severe deforming osteoarthritis. All patients received 65-130x10 Cyto-MSC intravenously. Severity of chronic kidney disease is based on baseline estimated glomerular filtration rate (eGFR) and serum creatinine which are markers of renal dysfunction. These and other blood tests including fasting blood sugar (FBS) and Hba1c (marker of glycemic control) were measured at baseline and 12 months post infusion.

**Results:** 82 patients (53 men, 29 women; age 38-92 years) with different CKD stages (stage 3, n=65; stage 4, n=5; stage 5, n=12) were identified. 33 patients have type 2 diabetes. All patients tolerated the treatment well. There was significant improvement in serum creatinine (170±148 vs. 144±123 µmol/L; p=0.013) and eGFR values (37±17 vs. 41±18 mL/min/1.73m ; p=0.001). Patients with stage 3 CKD have the most significant eGFR value improvement (45±9 vs. 50±10 mL/min/1.73m ; p=0.006). Among diabetic patients, improvements were observed in creatinine (167±138 vs. 145±115 µmol/L, p=0.011), eGFR (37±15 vs. 41±16, p=0.05), HbA1c (7.4±2.1 vs. 6.2±1.4 %, p=0.011) and FBS (7.1±1.1 vs. 6.8±0.8 mmol/L %, p=0.021). There was also modest positive correlation between FBS with urea (p=0.001) and eGFR (p=0.016).

**Conclusion:** Cyto-MSC appears to be safe and well-tolerated by patients with moderate-severe CKD and associated with improvement in renal function particularly for moderate CKD patients. Further randomized prospective studies are warranted.