

Voluntary Wheel Running Augments Vascular Function in Rats with Chronic Kidney Disease

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Purpose: Reduced nitric oxide (NO) bioavailability contributes to endothelial dysfunction in chronic kidney disease (CKD) and is associated with an elevated risk of cardiovascular disease (CVD). Vascular uptake of the NO precursor L-arginine is attenuated in CKD, resulting in reduced substrate bioavailability for NO synthesis. We sought to determine if 4 weeks of voluntary wheel running alone or in combination with L-arginine could improve impaired vascular function in animals with CKD. **Methods:** Twelve week old, male Sprague-Dawley rats underwent either 5/6 ablation/infarction surgery to induce CKD or a similar SHAM surgery as a control. CKD animals were randomly assigned to either remain sedentary (SED) or receive a 4 week intervention consisting of voluntary wheel running (RUN) or wheel running + L-arginine (RUN+ARG). Interventions began 4 weeks after surgery to allow time for the disease to progress. Animals were sacrificed 8 weeks after surgery and endothelial-dependent relaxation (EDR) in response to acetylcholine (Ach; 10^{-9} - 10^{-5} M) was assessed in isolated aortic rings. **Results:** EDR was significantly impaired in SED vs. SHAM animals after 8 weeks, demonstrated by an attenuated maximal relaxation ($58.47\% \pm 6.1$ vs. $97.28\% \pm 1.6$, $p < 0.001$) and a rightward shift in LogEC50 (-6.54 ± 0.09 vs. -7.74 ± 0.12 , $p < 0.05$). Max EDR was significantly improved above SED in both RUN ($80.39\% \pm 5.3$, $p < 0.05$) and RUN+ARG ($89.34\% \pm 3.0$, $p < 0.01$). LogEC50 was also improved significantly above SED in RUN (-7.072 ± 0.10 , $p < 0.05$) and RUN+ARG (-7.198 ± 0.08 , $p < 0.05$). **Conclusion:** 4 weeks of voluntary wheel running with or without L-arginine supplementation significantly improved endothelial function in rats with CKD. These results suggest that exercise is a potentially beneficial therapy to reduce CVD risk in CKD.

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