‘EXERCISE AS MEDICINE’ IN CHRONIC KIDNEY DISEASE

Running
Exercise in CKD

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Introduction

In medicine it is traditional to prescribe evidence-based treatment known to be the most effective with the least amount of side effects or risks (Salles, 2009). Over the past decade, there has been a changing paradigm in the role of ‘exercise as medicine’; and as such, physical activity and exercise are now seen to have a key role in the prevention and treatment of various medical conditions and chronic diseases (Pedersen & Saltin, 2006; Salles, 2009; Barcellos et al., 2015; Pedersen & Saltin, 2015).

A chronic condition that is largely overlooked as a potential target for exercise therapy is chronic kidney disease (CKD), where the delivery of rehabilitation programmes and exercise advice falls far behind that of pulmonary and cardiac services (Smith & Burton, 2012). In this short review, we aim to provide an evidence-based analysis for prescribing ‘exercise as medicine’ in CKD, which presents a unique pathophysiology, where the response to, and thus prescription of, exercise should be carefully considered.

Chronic kidney disease

Chronic kidney disease is a global health problem (Heiwe & Jacobson, 2014) affecting at least 1 in 10 Europeans (Brück et al., 2015). Patients with CKD present with a substantially increased risk of multi-morbidity including cardiovascular disease (Bansal et al., 2015), muscle wasting (Workeneh & Mitch, 2010), and endothelial dysfunction (Mustata et al., 2011). Further, patients have considerably poor physical functioning and exercise capacity (Heiwe et al., 2001; Mustata et al., 2011) which is strongly associated with all-cause mortality (Roshanravan et al., 2013), and can dramatically decrease quality of life, the ability to perform activities of daily living (ADLs), and independence.

Evidence-based physical training

Kidney disease can be divided into three approximate cohorts: pre-dialysis, dialysis, and transplant. Exercise has been successfully utilised within each, and whilst it is beyond the scope of this commentary to discuss the entire wealth of literature, we direct interested readers to several comprehensive reviews (Kosmadakis et al., 2010; Johansen & Painter, 2012; Smith & Burton, 2012; Gould et al., 2014; Heiwe & Jacobson, 2014; Barcellos et al., 2015).

Cardiovascular risk

In CKD, perhaps the most beneficial effect of exercise is improving cardiovascular health and vascular function. In pre-dialysis patients, reductions in systolic and diastolic blood pressure (BP) have been noted following 1 hour of aerobic exercise such as walking (Headley et al., 2008), and although Kosmadakis et al. (2012) found no change in BP following 30 minutes walking 5 times a week, they did observe a reduction in the number of anti-hypertensive medications required. Similar BP reductions have been noted in dialysis patients (Tsuyuki et al., 2003; Toussaint et al., 2008). Exercise can increase maximum (Tsuyuki et al., 2003) and reduce resting (Headley et al., 2012) heart rates in CKD. Three months supervised and home-based exercise for 1 hour also reduced arterial stiffness in pre-dialysis patients (Mustata et al., 2011), whilst Toussaint et al. (2008) reported improvements in arterial compliance during intradialytic cycling. Exercise, both an acute single bout (30 minutes) and regular walking (6 months, 5 days a week), may provide an anti-inflammatory response in pre-dialysis patients (Viana et al., 2014).

Exercise capacity, strength, and physical function

Exercise can improve exercise tolerance, aerobic-based fitness, and VO_{2MAX} (i.e. utilisation of oxygen) (Mustata et al., 2011; Kosmadakis et al., 2012; Watson et al., 2014; Headley et al., 2014). Leehey et al. (2009) found that walking 3 times a week for 24 weeks increased exercise tolerance (via a timed treadmill test) in pre-dialysis patients. Similar improvements were reported following 12 months twice weekly walking and cycling sessions (Mustata et al., 2011). Increases in physical performance tasks, such as the sit-to-stand test, have also been noted in pre-dialysis (Heiwe et al., 2001; Rossi et al., 2014; Watson et al., 2014) and dialysis (Mallamaci et al., 2014) patients following exercise. Resistance training (RT) can help increase muscular strength in pre-dialysis patients (Heiwe et al., 2001; Bohm et al., 2014; Rossi et al., 2014; Watson et al., 2014), with improvements also noted in dialysis (Mallamaci et al., 2014) and post-transplant (Painter et al., 2002) patients.

Cachexia

Patients with CKD often suffer from muscle wasting or cachexia (Workeneh & Mitch, 2010). Resistance training is highly effective in reversing this atrophy. For example, in pre-dialysis patients, an 8-week progressive RT programme (3 times a week) increased muscle mass (Watson et al., 2014) with similar findings reported in dialysis (Mallamaci et al., 2014; Bohm et al., 2014) and transplant patients (Painter et al., 2002).

CKD progression

A key aim in the treatment of CKD is slowing disease progression, and ultimately preventing treatment via dialysis. Whilst higher levels of leisure-time physical activity are associated with slower declines in kidney function (Robinson-Cohen et al., 2014), evidence regarding exercise-based interventions remains equivocal (Baria et al., 2014; Gould et al., 2014; Viana et al., 2014) and further well-conducted study is required (Johansen & Painter, 2012).

Possible mechanisms

As discussed above, exercise has many different health-related parameters in CKD. Pertinently, these include favourable effects on the multiple risk factors that underlie CKD aetiology such as hypertension and diabetes (Headley et al., 2014; Bansal et al., 2015). Exercise also has beneficial effects on endothelial health (Mustata et al., 2011) and body composition (Kosmadakis et al., 2012; Baria et al., 2014). Chronic inflammation is highly predictive of mortality and cardiac disease development in CKD (Meuwese et al., 2011), as well as cachexia (Workeneh & Mitch, 2010). Regular exercise may promote an anti-inflammatory environment. Viana et al. (2014) found that an acute 30 minute exercise bout increased plasma IL-10 levels, whilst regular walking resulted in a reduction in plasma IL-6:IL10 ratio, and the down regulation of T-lymphocyte and monocyte activation. Exercise training is effective in combating muscle atrophy associated with CKD through up-regulation of protein synthesis, increasing muscle mitochondrial content, and reducing muscle catabolism (Watson et al., 2013).

Type of training

The optimal recommendations for exercise for patients with CKD have not been determined (Johansen, 2005; Johansen & Painter, 2012); however an extensive systematic review (Heiwe & Jacobson, 2014) concluded that regular exercise, regardless of type, duration, or intensity, is beneficial in CKD patients. Physical activities that utilises large muscle groups that can be maintained continuously such as walking are most effective, although RT should be used to significantly improve muscular mass and strength, which can consequently improve functional capacity (e.g., walking). Our group is currently investigating the combined effect of a 12 week aerobic and RT programme in pre-dialysis CKD patients. Intradialytic exercise, generally using a specially designed cycle ergometer, is available in some renal units and offers opportunity for supervised exercise (Smith & Burton, 2012). Further study into the effectiveness of intradialytic exercise on cardiovascular function, particularly left ventricular mass, is currently being investigated by our group.

Contraindications to exercise

Fluid and electrolyte imbalances are frequent in CKD, and may contribute to reduced exercise tolerance. Hypertension is also common in CKD and, as such, a BP measure of ≥180/105 is a contraindication to undertaking exercise. Although minimal data exists on the risk of cardiovascular events during exercise in CKD, given the high prevalence of heart disease risk factors, it is likely the risk is greater than the general population. Patients with known or suspected cardiac disease should undergo prior testing to participation in exercise (American College of Sports Medicine, 2012).

Musculoskeletal risk may be increased in CKD patients due to renal bone disease and hyperparathyroidism. Fragility fractures (Alem et al., 2000) and spontaneous quadriceps tendon rupture (Shah, 2002) has been reported in the CKD population. Special considerations need to be given to dialysis patients who may experience frequent fluid and electrolyte balance shifts. Whilst exercise may be safer on non-dialysis days, studies have shown that intradialytic exercise is safe and effective (Tsuyuki et al., 2003; Bohm et al., 2014), and does not exacerbate systemic inflammation or immune dysfunction (Dungey et al., 2015). Patients can exercise their fistula arm, but should not apply weight to that area (Johansen, 2005).

Conclusion

Exercise has favourable effects on a range of health related outcomes in CKD, and should be used as an adjunct treatment to help improve many of the disease-related morbidities such as hypertension, cachexia, and poor functional capacity. Whilst the provision of rehabilitation programs is considerably behind that of cardiology and respiratory services, CKD patients should be encouraged to exercise and increase their physical activity. As Pedersen and Saltin (2015) state, "it is now time that the health systems create the necessary infrastructure to ensure that supervised exercise can be prescribed as medicine".

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