Exercise is Medicine: Treatment and Prevention of Chronic Disease

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Introduction

Health–enhancing benefits of exercise have long been known—Hippocrates encouraged exercise for the maintenance of optimal health and for prevention and treatment of disease.[1] More recently, noncommunicable chronic diseases are now responsible for more than 68% of deaths globally, with 75% of deaths in low– and middle–income countries.[2] Many chronic diseases are influenced by physical inactivity (PIA). Worldwide, PIA is the fourth leading risk factor for all–cause mortality.[3-5] PIA, with its associated low cardiorespiratory fitness, increases the risk of dying at least as much as smoking, obesity, hypertension, and high cholesterol combined.[6,7]

The concept of exercise as medicine has evolved with the expanded understanding of exercise physiology and molecular biology. Exercise is a potent stimulus for important signaling pathways at the cellular and molecular level.[8,9] It can modify inflammatory processes, which are often associated with chronic disease, and can initiate anatomical remodelling resulting in improved function in both health and chronic disease.[8,10-12]

Prescribing Exercise as a Medicine

Exercise is structured physical activity that improves health and fitness by stimulating physiological and morphological adaptations in the body. Similar to other medicines, the response to exercise is specific and predictable. The prescription of exercise includes a dosage generated from dose–response curves for optimal treatment. A single dose can often initiate small but measurable benefits, with greater impact attained with regular use. Like most medicines, exercise also has a half–life: its positive benefits will dissipate if exercise is not continued regularly.

Optimizing the therapeutic potential of an exercise prescription involves following the FITT principle of **F**requency (number of sessions per week), **I**ntensity (level of effort), **T**ime (duration per session), and **T**ype (mode of exercise) within the well–established principles of exercise training. These include exercise progression, specificity, overload, and rest. Prescribed properly, physical exercise is an essential, first–line form of prevention and treatment of over 30 chronic diseases.[9]

Canadian Physical Activity Guidelines of 150 minutes of moderate–to–vigorous physical activity (MVPA) plus two muscle– and bone–strengthening activities per week help to optimize exercise prescription for the greatest health benefit.[13] Evidence indicates that by achieving these guidelines, risk of all–cause mortality can be reduced by at least 30%, as can the risk for cardiovascular disease (30%), osteoporosis (25%), stroke (25%), hypertension (20%), diabetes (20%), colon cancer (20%), and breast cancer (14%).[14] Understanding how exercise protects against and/or provides treatment for specific chronic diseases is critical to the prescription of exercise as a medicine. The following sections provide examples and evidence of how exercise imparts its effect on chronic disease.

Type 2 Diabetes: Management and Treatment with Exercise

Type 2 diabetes (T2D) provides an excellent model of exercise as medicine. Skeletal muscle plays a critical role in glycemic control through the actions of glucose transporters (GLUT4) responsible for glucose uptake. A single bout of exercise enhances GLUT4 translocation to the sarcolemma, even in insulin–resistant skeletal muscle fibers.[15,16] Contraction–induced increases in the activity of calcium/calmodulin–dependent protein kinases, AMP–activated protein kinase, nitric oxide synthase, and reactive oxygen species have all been linked to enhanced GLUT4 translocation independent of insulin. Additionally, GLUT4 expression is elevated following exercise, providing enhanced glycemic control post–exercise.[15] Exercise also effectively reduces hemoglobin A1c (HbA1c).[17-19]

While aerobic and resistance training each independently improve glycemic control in T2D, improvements are greatest with combined aerobic and resistance training.[9,20] Notably, there is growing interest in high intensity interval training (HIIT) to reduce risk of chronic disease, particularly T2D. A benefit of HIIT is that it requires less time commitment, though greater exercise effort, than MVPA. Because adherence to exercise prescriptions is often poor, typically due to perceived lack of time, this time–efficient exercise intervention can result in excellent benefits.[21,22] HIIT exercise has been reported to effectively increase GLUT4 expression and reduce HbA1c.[18-22]

The distinct signalling pathways of insulin and muscle contraction characterize just how important exercise is to the management and treatment of T2D. However, like most medicines, there is potential for deleterious drug interactions when prescribing exercise to those dependent on exogenous insulin. With the enhanced insulin–like effect of exercise, a careful, informed manipulation of insulin dose is often required. If prescribed effectively, and with due caution, exercise may be as efficient as glucose–lowering medications.[22] There is good reason to believe that, with appropriate exercise prescription, T2D may be a reversible chronic disease.[9]

Anti–Inflammatory Response of Exercise

Many chronic diseases are associated with persistent, low–grade inflammation. Inflammatory cytokines have been associated with insulin resistance, initiation and progression of tumours, atherosclerosis, and several neurodegenerative diseases, including Parkinson's disease, Alzheimer's disease, and depression.[24,25] The anti–inflammatory role of exercise exists due to the ability of contracting muscle to release the myokine interleukin–6 (IL–6).[9,25-28] Through a cascade of cellular events, IL–6 initiates the inhibition of pro–inflammatory cytokines including tumor necrosis factor alpha (TNF–α). Exercise–induced IL–6 response is proportional to contracting muscle mass, exercise intensity, and exercise duration.[9,27] As a result, the prescription of exercise may

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effectively reduce the risk and progression of many chronic diseases by attenuating inflammation.

Exercise for Mental Health

Individuals who engage in regular exercise experience fewer days of poor mental health compared to those who are inactive.[25,28] The benefits of exercise on depression are comparable to the effects of cognitive behavioural therapy and occur with all types of exercise when performed regularly.[25,29] With mental illness comes a high risk of PIA, a factor identified as contributing to a 15-25 year difference in life expectancy relative to those with good mental health.[30] Exercise, therefore, should be considered when treating mental illness, as it has the potential to reduce this gap and increase quality of life of those experiencing mental health challenges.

Summary

Evidence from epidemiological studies and clinical research demonstrates that exercise attenuates the risk of many health challenges. As a medicine, exercise has a role to play in the maintenance of optimal health, as well as in the prevention, management, and even adjuvant treatment of chronic diseases. Perhaps exercise should be viewed as a chronic disease vaccine.

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