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Treadmill Exercise and its Effect on Rehabilitation of Patients after Ischemic strok: A Narrative Study

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ABSTRACT

Aim: Stroke is the third leading cause of death after cardiovascular disease and cancer. Stroke causes disability in various forms in sufferers. It has been suggested that various pathological mechanisms are involved in causing this injury. Articles show that regular exercise is a way to treat stroke patients. One of the most common exercise therapy models is treadmill exercise. However, there is still controversy about when to start treadmill workouts, the intensity of the workout, the type of treadmill workout, and how it has positive effects. This article offers an overview of treadmill exercise and its' effects on post-ischemic stroke rehabilitation. In this study, the effect of exercise time, exercise intensity, exercise style, and the positive effects of this type of exercise on rehabilitation of patients after ischemic stroke were briefly examined.

Keywords: Ischemic , Rehabilitation , Stroke , Exercise , Treadmill.

Introduction

Stroke is the third leading cause of death after cardiovascular disease and cancer in most developed countries [1]. Studies have shown that 20% of stroke survivors need medical attention 3 months after the stroke, and approximately 15 to 30% of them suffer from long-term disability [2]. The main pathological mechanisms of ischemic brain injury include inflammatory response, oxidative activation, protease activation, stimulation of intracellular toxicity, and impaired Ca2 + homeostasis [3]. There is virtually no effective treatment other than thrombolysis to facilitate neurorehabilitation in the post-stroke stage [4]. Exercise and rehabilitation after ischemic stroke may provide significant neuroprotection against ischemic stroke by reducing cerebral edema, proinflammatory reactions, dysfunction of the blood brain barrier, and behavioral and cognitive impairments [5] which rapidly improve movement quality, increase motor and cognitive function, and play a role in memory formation and learning following ischemia [7, 6]. Exercise can improve cerebral blood flow [8] and be effective in facilitating the improvement of nerve function and reducing the volume of cerebral infarction (compared to spontaneous healing) [9]. Starting rehabilitation exercises at an appropriate stage after a stroke can have a greater impact and improve performance in patients [10]. Among these, performing forced aerobic exercises compared to voluntary aerobic exercises have a better effect on promoting improved post-stroke performance [11]. Among the many examples of exercise which are available , treadmill exercise, wheel training, and involuntary muscle contraction due to electrical stimulation are more common. Doing these exercises improves cognitive function and neural rehabilitation, and have a point of good physical effects following brain injury [12]. Treadmill

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training is a type of voluntary, purposeful, and endurance training that can be done with or without body weight supported in or out of the water. There are differing and sometimes conflicting opinions about treadmill exercise and its various effects on ischemic stroke rehabilitation, andthe available documentation sometimes does not support a single view. Therefore, the aim of this study was to investigate treadmill exercise and its effect on rehabilitation of patients after ischemic stroke and the factors affecting it.

Treadmill Exercise: Regarding treadmill exercise (like other exercises), it seems necessary to pay attention to a few points, such as: exercise time, intensity of exercise, style of exercise which are discussed as following.

Exercise time: There are different points of view about exercise time. Bernhardt et al. have stated that early mobility and exercise (24 hours after stroke) seem safe for patients with acute stroke [13]. Morreale [14], Nielsen [10], Buiatti [15] stated that the beginning of early rehabilitation exercises (compared to delayed rehabilitation) is useful in the process of improving motor function after stroke (especially for lower limb healing). Zhang et al. stated that early exercise (within 24 to 72 hours after the onset of stroke) may increase mitochondrial biogenesis. This may play an important role in the initial motor mechanisms and exercise-induced neuroprotection in the ischemic brain [16]. In another study, Zhang et al. found that neuronal apoptosis could be reduced by early exercise (24 hours after ischemia) by inhibiting nerve cell apoptosis [17]. Yang also stated that starting exercise early (within 24 hours after ischemia) is more effective in facilitating improved nerve function and reducing the volume of cerebral infarction (compared to spontaneous healing) [9] and can clearly enhance spatial memory and improve movement, but cannot improve balance function and sense [18]. Hubbard et al. also argued that early and intensive training of the upper limbs can activate the brain more areas related to accuracy (anterior cingulate) and hypothetical movements (cerebellum and complementary motor area) because the activation of these functions and areas plays a role in the early stages of the recovery process [19]. Contrary to the above views, some following studies do not recommend doing exercises too early within 6 hours and early within 24 hours: Risedal [20], Li [21] stated that starting too early (within 6 hours) or early exercise (within 24 hours) after local ischemia of the brain may lead to increased production of proinflammatory cytokines, and cellular stress. The occurrence of this kind of exercise may exacerbate the tissue damage caused by cerebral ischemia / reperfusion injury. Li et al. also stated that starting exercise too early (within 6 hours after cerebral ischemia) triggers the production of proapoptotic factors (caspase-3 and BAX), which may be associated with cellular apoptosis. While starting training between 24 hours and 3 days after a stroke may increase the beneficial effects of exercise and prevent harmful effects to achieve better performance [22]. Ying et al. also stated in their paper that starting exercise too early (less than 24 hours after the onset of stroke) may play an adverse role in the recovery process. While starting exercises later in the stroke (24 to 72 hours after the onset of the stroke) may have positive effects. Therefore, the start time of exercises is an important factor in determining their positive or negative effect [23].

Intensity of exercise: There are also different points of view regarding the intensity of exercise. s sexplained as
and rapidly facilitate the regeneration of new neural pathways and the formation of synapses, and accelerate the healing process of post-ischemic motor activity [29].

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Contrary to the above views, some studies like the following studies recommended moderate to light exercise. Dromerick et al. stated that the intensity of exercise should be controlled during exercise therapy. Higher-intensity movement exercises do not necessarily have a more beneficial effect, especially in the early stages of stroke [30]. Deplanque et al. stated that regular physical exercise reduced the risk of stroke injury so that engaging in strenuous physical activity may be harmful. While both normal and moderate exercise can lead to potential neuroprotection [31].Lee et al. stated that light to moderate intensity exercise started early in ischemic stroke could facilitate improved mobility, and that the presence of astrocytes could also have positive effects on improving motor rehabilitation [32]. Zhang et al. stated that low-intensity exercise may significantly reduce body weight, cerebral infarction volume, and phospho-NR2B expression more than the moderate-intensity exercise group [33]. Better spatial memory function and synaptic ductility may be improved through light-intensity training compared to high-intensity exercise after ischemic stroke. In the meantime, the intensity factor is a key factor in the training process [34]. Ying et al. also stated in their article that any mild, moderate and high-intensity exercise can have benefits by protecting the brain from stroke injuries. However, light and moderate intensity exercise compared to high-intensity exercise provides better neuroprotection [23].

Exercise Style: Stinear stated that initiating bilateral upper limb rehabilitation exercises in the early stages -active and passive- can accelerate upper limb function in the early stages of stroke [35].Silver et al. stated that treadmill training accelerates the performance of functional activities on the ground in patients with chronic stroke with stable hemiparesis [36]. Linder stated that forced aerobic exercise can be used as an intervention to improve the sustainable and safe promotion of rehabilitation, motor and non-motor activities, and to improve aerobic fitness in patients with chronic stroke. [37]. Platz et al. stated that specific active and hard upper extremity exercises are vital for improving motor function, and can accelerate recovery in patients with mild or severe upper extremity paralysis [38]. Ke et al. stated that voluntary exercise compared to involuntary and forced exercise showed the best effect on improving motor function, increasing hippocampal BDNF gene expression, and reducing the corticosterone stress response in people with ischemic stroke [39].

Effects of Treadmill Exercise after Stroke

Various studies have expressed the effects of various exercises in this regard, some of which are mentioned as following.

Improved Gait: Patients after stroke mainly suffer from abnormal gait and the resulting disability [40]. Gait and coordination are the result of complex sensory-motor function controlled by integrated cortical, subcortical, and spinal networks [41]. The goal of rehabilitation is to improve gait recovery in these people. Treadmill training is a valuable and effective way to retrain walking that can be used in various periods after a stroke, which mainly leads to improved walking speed and capacity [40]. Findings from functional MRI after treadmill exercise showed changes in some areas of patients with ischemic stroke including primary motor cortex, complementary motor area, and cingulate motor area. These findings suggest that treadmill exercise improves lower limb function and gait in these patients and improves stroke by altering the plasticity of patients' brains. [42]. Exercising with a treadmill is helpful in improving gait performance after a stroke. In treadmill training, the intensity of the exercise may be a more important factor than the specificity

of the exercise, and may further improve posture control and balance parameters even beyond gait performance [43]. It has also been shown that performing progressive task-repetitive Treadmill Exercise (T-Ex) improves limb adaptation and gait function through the use of cerebellar-midbrain circuits and stimulation of the neuroplasticity process [41]. There are articles on the methods of using treadmill -use alone or in combination with other devices- and its results in patients with stroke, some of which are mentioned here.

Treadmill exercise -with or without body weight support and using harness- is a physiotherapy intervention used to improve the ability to walk after a stroke [44]. Some studies suggest that weight training on a treadmill may be more effective than exercise on a treadmill alone, and that exercise on a treadmill with task-oriented exercise may be more effective than sham exercises. [45]. In subacute patients with stroke, doing Body Weight Support Treadmill Training (BWSTT) can improve gait quality compared to normal gait training. Of course, both methods -doing treadmill exercises with body weight support, and regular walking exercises- can improve balance and motor function [46].Treadmill training may be more effective than conventional walking training in improving some gait parameters such as functional ambulation , stride length, percentage of paretic single stance period, and gastrocnemius muscle activity [47]. Exercising with a treadmill usually results in a higher number of steps, faster walking speed, and a higher heart rate than walking on the ground. Adding challenging motor skills exercises to treadmill exercises may create more opportunities to improve walking and balance skills [48]. These exercises may not lead to the ability to walk independently in sufferers, but it can improve their walking speed and endurance slightly in the short term. [49]. Partial Body Weight Support Treadmill Training (PBWSTT) is a task-specific approach that is often used to improve gait during the acute period of stroke recovery (less than one month post infarct). The speed of training in such activities affects the activation of paralyzed and non-paralyzed leg muscles, gait characteristics, and ranking of activity observed during acute stroke rehabilitation.During the acute phase of stroke recovery, PBWSTT at the fastest speed promoted practice of a more optimal gait pattern with greater intensity of effort as evidenced by the longer stride length, increased between-limb symmetry, greater muscle activation, and higher Borg Ratings of Perceived Exertion (RPE) compared to training at the slowest speeds.[50].Stroke causes gait defects in several joints, so the main goal of post-stroke rehabilitation is to restore normal gait function. Applying two-way Functional Electrical Stimulation (FES) along with walking on a treadmill significantly improves walking speed, functional mobility, functional ambulation, range of motion, and stride length in post-stroke survivors. But it does not play a significant role in reducing the spasticity of the flexor muscles of the sole of the foot and the extensor muscles of the knee [51]. People with stroke are often at higher risk of falling. Therefore, the implementation of a combined protocol -including treadmill use and strength training- has long-term beneficial effects on gait activity after chronic stroke especially in patients who initially have low balance ability [52]. Research has also shown that walking with acoustically paced on the treadmill is an effective means of immediately correcting the frequency of steps and improving gait coordination in people after a stroke [53].

Improving Muscle Strength: Performing water-based aerobic exercise on a motorized water treadmill has a beneficial effect on the isometric muscle strength of the lower

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extremities [54].

Improving Balance: Treadmill exercise and using Thera-Band is beneficial and effective in improving lower limb motor function, gait, and balance ability in stroke patients [55]. Using virtual reality -using video games and accompanying visual feedback- and practicing treadmill walking can also help stroke patients adjust their center of gravity, balance, and gait directly.[56].Treadmill exercise does not significantly improve the stabilometrically evaluated balance, but it does improve the symmetry of the load of the lower limbs and improves the dynamic balance of people with stroke [57].

Improving Motor Activity: Treadmill exercise improves movement activity after ischemia -except 12 hours after surgery- [15]. Treadmill training improves motor function and short-term memory by increasing synaptic flexibility and neurogenesis in stroke mice, and can be used as an effective therapeutic strategy to improve stroke-related brain function [58]. Stroke rehabilitation is often associated with the concept of motor re-learning, which requires patients to engage in active practice of skill-specific training and receive feedback. Treadmill exercise with real-time visualization feedback and functional electrical stimulation feedback can have a beneficial synergistic effect on improving motor activity [59].

Improving Functional Activities: Treadmill training, skilled reach training and improving functional activities can affect the production of neurotrophic factors. Neurotrophic agents are defined as endogenous soluble proteins that regulate survival, growth, morphological plasticity, and the synthesis, or synthesis, of proteins for different neuronal functions [60]. Treadmill exercise increases the therapeutic efficiency of brain stromal cells by potentially inhibiting neuronal apoptosis and improving nerve function and transplantation of brain stromal (Stromal cells are cells of the connective tissue of any organ that support the function of the parenchymal cells of that organ). In the brain, neurons make up the functional tissue of the brain. The rest of the brain tissue that is structurally or connectively called the stroma [61].Treadmill exercise can reduce apoptotic cell death and accelerate the recovery of central nervous system dysfunction after stroke [62].Treadmill exercise speeds up functional overground mobility in patients with chronic stroke with persistent hemiparesis [36].

Neuroprotective Effect: Exercising with a treadmill may reduce cerebral edema, and dysfunction of the Blood-Brain Barrier (BBB) during ischemic injury / cerebral reperfusion by reducing AQP4 setting [63]. Furthermore, by doing these exercises, the amount of pro-inflammatory factors can be reduced to protect against cerebral ischemia-reperfusion injury [64]. It can also reduce ischemic brain damage by enhancing microvascular integrity after cerebral ischemia [65]. Prolonged exercise on a treadmill can also cause molecular neuroprotective changes in the rat brain [66].

Improving Cardiopulmonary Function Most people with stroke suffer from heart disease, are immobile, and therefore have little endurance for exercise. Their aerobic capacity decreases severely, and they do not reach adequate levels after regular rehabilitation programs. Their cardiovascular readiness decreases sharply after a stroke [67]. Early exercise on a treadmill with the help of robotics and with feedback significantly increases the intensity of exercise and improves cardiovascular compatibility after a stroke [68]. Progressive treadmill therapy compared to conventional stroke rehabilitation therapy may alter blood flow during exercise and rest to healthy and paralyzed legs [40]. Doing endurance exercises with a treadmill -lightly for six months- may

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lead to a gradual and obvious reduction in cardiovascular needs, and energy expenditure in walking in elderly patients with chronic stroke [69]. The limit to doing a treadmill exercise is the ability to do it before general fatigue in the hemipartic organs of stroke patients [70].Cardiovascular exercise is useful for improving aerobic capacity in mild to moderate strokes. Treadmill training with the help of robots and with feedback control is a relatively new intervention method that can be used to train and evaluate aerobic capacity in patients [67]. People with outpatient stroke can benefit from walking-based cardiovascular adaptive exercise after the stroke. High intensity Treadmill Aerobic Exercise (T-AEX) effectively improves cardiovascular fitness and gait in people with chronic stroke.[71]. (T-AEX) improves both functional and ambulatory function and cardiovascular fitness in patients with chronic stroke, and is more effective than conventional rehabilitation [72]. High energy intake while walking helps to aggravate functional disability after stroke especially in older patients who are physically disabled. Performing task-oriented aerobic exercise with low intensity on the treadmill causes a significant and progressive reduction in energy expenditure and cardiovascular needs of patients with chronic stroke while walking [69]. It has been suggested that having a 6-week aquatic treadmill exercise program can improve maximal aerobic capacity, gait endurance, and improve O2 peak in patients with subacute stroke, and significantly effective cardiopulmonary preparation in these patients [73]. Immersion and walking on a treadmill in water can reduce the workload of the cardiovascular system -although the cardiovascular responses of people with stroke may vary- [74].

Overall Physical Activity Improvement: Stroke often results in sensory, motor, and cognitive impairments. Exercise therapy is the most common strategy for rehabilitating stroke patients through enhanced neurogenesis, angiogenesis, neurotrophic factors expression, and synaptogenesis. Neurogenesis plays an important role in improving sensory-motor and cognitive function that can be enhanced by exercise. Treadmill training facilitates the improvement of sensory-motor and cognitive function after Transient Middle Cerebral Artery Occlusion (TMCAO). Increases the proliferation of ipsilateral stem cells / precursors, and significantly increases CD200 and CD200 (CD200R) receptor levels in the hippocampus and ipsilateral cortex. Simultaneously with the effect of exercise on the treadmill, CD200Fc (a CD200R agonist) significantly enhances the process of neurogenesis, improves function, and improves the inflammatory environment after stroke [75]. Intensive and early treadmill exercise also significantly helps to improve the overall physical activity of patients with acute ischemic stroke [76].

Other Benefits of Treadmill Exercise: Designing and performing a specific and targeted intervention with using treadmill exercise in addition to improving walking speed, can have other secondary benefits such as a positive effect on depression, mobility, and social participation in people with Stroke [77]. Treadmill exercise with a moderate level of controlled fatigue is more effective in reversing movement than doing forced exercise, and has positive effects on striatum neuroplasticity. Therefore, for better rehabilitation of stroke, it is recommended to use a protocol that has individual exercises with fatigue control [78]. Treadmill training stimulates the physiological fitness reserve in elderly patients with mild to moderate chronic gait disturbance by increasing maximal training capacity and reducing energy expenditure in the hemipartic region [79] increases

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the expression level of Basic Fibroblast-based Growth Factors (bFGF), enhances neurorehabilitation, reduces infarct volume compared to non-exercise cases, and increases the expression level of 2 Vascular Endothelial Growth Factor (VEGF) receptors [80]. High-Intensity Treadmill Training (HITT) has a positive effect on walking ability, quality of life, cardiorespiratory fitness, compared to Low-Intensity Treadmill Training (LITT) , increased maximal VO2, and the cost of walking in people with chronic stroke [81]. Doing high-intensity exercise on a treadmill as a self-management approach during inpatient rehabilitation can lead to sustained improvement in physical activity, walking ability, fitness, and quality of life [82]. Treadmill exercise with a focus on intensive task-specific training is also a way to facilitate neural plastic brain changes and to strengthen associated motor behavior gains following nerve damage [50].

Clinical Messages: 1-In terms of training time, starting training too early -less than 24 hours after the onset of stroke- may play a detrimental role in the recovery process of patients, while starting training early in the onset of stroke -24 to 72 hours after stroke- may have positive effects. Therefore, exercise timing is a critical factor in determining their impact, good or bad after a stroke.

2-In terms of intensity training, light, moderate and high intensity exercise can have benefits by protecting the brain from stroke injuries. In addition, light and moderate intensity exercise compared to high-intensity exercise can provide better nerve protection.

3-Regarding the style of training, it has been stated that the point of effect of active, voluntary, and purposeful training based on a specific task compared to resistance training is better in promoting and improving functional activities after a stroke.

4-Training and performing various forms of exercise on a treadmill early in the onset of stroke has a variety of positive effects. Doing these exercises can regulate the process of cerebral edema, cell apoptosis, oxidative damage, stem cells and other mechanisms to apply neuroprotection in the brain. It can also improve gait, lower limb muscle strength, stable balance, motor activity, functional activity, cardiopulmonary status, general physical activity, and prevent falls.

Conclusion

Doing different forms of exercise on a treadmill especially in the early occurrence of stroke has various positive effects. Doing these exercises can cause improvement in various dimensions. Therefore, it is recommended to do them at the right time and right intensity and also in accordance with the clinical condition of patients with ischemic stroke.

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