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Review Article

Management of Post Stroke Depression (PSD) Through Physical Exercise

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ABSTRACT

About one-third of patients with post-stroke depression (PSD), a common psychological disorder that impacts many stroke survivors, eventually experience depression. This depression may impair recovery and rehabilitation, lower quality of life, and raise mortality. The association between depression and stroke is complex and the underlying causes are still unclear, but there is evidence to support the possibility that both psychosocial and anatomical factors may play a role. PSD management is difficult and necessitates a multidisciplinary approach. Although some people respond well to conventional treatments like psychotherapy and medication, they may not be appropriate or available to everyone. On the other hand, a promising non-pharmacological intervention for the management of PSD is physical exercise. Physical exercise has emerged as a viable additional or substitute intervention for PSD control. There is mounting evidence that suggests physical activity can elevate mood and lessen depressive symptoms in PSD patients. Studies have shown that exercise interventions, such as aerobic exercise, resistance training, yoga, etc. can help stroke survivors with PSD who struggle with depression and anxiety as well as their general quality of life. Additionally, exercise has been linked to improvement in brain functions. This review intends to look at the evidence of physical exercise's value in treating PSD, its underlying causes, and considerable beneficial effect of exercise on depression, physical functions, and cognitive functions in stroke patients.

INTRODUCTION

Stroke is a condition that occurs when the blood supply to the brain suddenly stops, resulting in perpetual tissue damage. The risk of stroke increases with age. The majority of strokes are brought on by embolic, thrombotic, or hemorrhagic events, with 85% of ischemic strokes and 12% of hemorrhagic strokes [1]. Neuropsychiatric disorders like anxiety, psychosis, and depression are frequently experienced by stroke survivors, and these conditions can negatively affect their quality of life and ability to recover motor function. Post-stroke depression (PSD) refers to depression that occurs in individuals who have suffered a cerebrovascular accident. It is considered the most common psychiatric condition of stroke [2]. The average estimated prevalence of PSD is between 30 to 35%, although it can range from 20 to 60%. However, it is considered that high prevalence rates are due to methodological issues e.g., the use of different depression rating scales, varied timing of evaluation, diagnostic criteria variations, and various criteria for patient enrollment [3]. According to American Psychiatric Association, PSD is difficult to diagnose, and it often goes undetected and untreated [4]. A criterion that is used for PSD is DSM-IV criteria which are defined as "depression that occurs due to stroke with major depressive episodes."

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Although certain symptoms appear due to stroke at a somatic level such as fatigue, weight loss, energy loss, reduction in sleep and appetite, alterations in psychomotor functions & difficulty in concentration. These somatic symptoms, overrate the depression because, in these symptoms, some of the symptoms occur due to physical ailment. PSD's pathophysiology is still up for debate. Two main hypotheses are being considered: a biological hypothesis involving ischemic damage to neural circuits involved in mood regulation and a psychosocial hypothesis linking depression to stressors in the social and psychosocial environment related to stroke. However, neither of these hypotheses has concrete evidence to either prove or disprove it [5]. Timely and effective treatment of PSD is effective in both the rehabilitation of stroke and the management of depression. According to studies, it is necessary to treat PSD patients as they show improvement in symptoms if they are treated as compared to untreated patients. It is seen in clinical practice that patients with PSD show better results with antidepressants like nortriptyline and fluoxetine but if used within one month after stroke. However, due to the high rate of adverse drug reactions, drug interactions, and contraindications in elder patients, fewer patients with PSD are even diagnosed and treated [3]. According to studies, physical exercise is useful in improving post-stroke gait and mobility as well as lowering post-stroke depression (PSD). According to studies, exercise should be targeted to achieve a heart rate reserve of 60–80% to reduce PSD and enhance general well-being [6]. Physical activity is crucial for neurorehabilitation because it can alter the chemical and anatomical makeup of the brain. Even if a stroke does not physically damage the brain, modifications to the hippocampus' neuroplasticity may be a factor in post-stroke depression. Exercise raises the mBDNF/proBDNF ratio, which is a critical marker for fostering neuroplasticity in the hippocampus, according to research [7]. Regular exercise raises irisin (muscle cytokine) levels, improves cognitive function, and may contribute to the emergence of depression [8]. Eng and Reime, conducted 13 studies meta-analysis and found that exercise can significantly fewer depressive symptoms in people who have had strokes [9]. Acute and chronic stages of stroke recovery showed this effect, but only after four or more weeks of exercise. The study also showed that when the exercise was stopped, these beneficial effects did not persist.

Prevalence of Stroke

Stroke is a significant health issue. It is the second major cause of disability & death after coronary artery disease. And ranking third in causing long-term disability [10]. In the United States, stroke is a frequent occurrence, with an estimated 795,000 people experiencing it annually. It indicates that on average stroke occurs every 40 seconds and death due to stroke in every 4 minutes [11].

Post-stroke depression (PSD)

PSD occurs in 31% of stroke patients within 5 years after the stroke. It is the most prevalent complication of stroke [12]. Post-stroke depression occurs in different forms i.e., impaired thought processes, diseases of the autonomic nervous system, depression, and even physical dysfunctions. PSD has many negative effects on a patient`s recovery and rehabilitation leads to mortality [13]. The prevalence of PSD is generally around 30-35%, with a range of 20-60%. And this high prevalence rate is due to different methodological issues like various rating scales used for depression, different diagnostic criteria, variation in time for patient evaluation, and criteria for patient enrollment. Due to all these variations and factors, it is difficult to accurately determine the prevalence rate of patients affected with post-stroke depression (PSD) [3].

Pathophysiology of post stroke depression (PSD)

The pathophysiology of PSD is not exactly known. Generally, two hypotheses biological and psychosocial are proposed. According to the biological hypothesis, neural circuits affected by ischemic insults that regulate mood, results in low mood and depression. And psychosocial hypothesis proposed that social and psychosocial environmental stressors can be a major cause of depression. But still, there is no clear evidence present to approve or disapprove of these hypotheses [5]. However, some conflicts are present in the biological mechanism of PSD. According to studies, there is an association between the size of the lesion and the severity of post-stroke depression with a correlation of post-stroke depression with left frontal pole lesions [14].

Causes of PSD

The exact cause of PSD is still a topic of debate. According to research, inflammation can be a major cause of post-stroke depression. And it is proved by evidence of pathways & markers of inflammation in post-stroke depression patients and animal models. It shows that PSD occurs due to complex networks of different inflammatory mechanisms. However, research has shown that post-stroke depression symptoms can be reduced by rehabilitation and exercise training. It is not only effective treatment of PSD but also improves the quality of life of patients [15]. Research on the animal model showed that exercise can inhibit the pathway of nuclear factor kappa B (NF-kB) in this way reducing depression and promoting neuron repairing and immune functions [16]. Studies have shown that the inflammatory molecule Interleukin-1β (IL-1β) and inflammasome NLRP3 level raises in the blood of depressed patients. However, its level maintains to normal

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level by taking anti-depressants [17]. Accumulation of inflammasome NLRP3 in the brain results in cognitive dysfunction, especially in patients already affected with neurodegenerative disorders. It shows that inflammasome NLRP3 has a significant role in causing post-stroke depression [18].

Conventional Treatment of PSD

Treatment for PSD traditionally includes a combination of medication and psychological therapy. Published reviews have shown that both drug therapy and psychological therapy are effective in reducing the symptoms of depression in patients affected with physical diseases or older individuals [19]. Antidepressants can be effective in treating PSD, it is necessary to consider their numerous side effects such as effects on CNS, adverse effects on CVS, bleeding, and metabolic enzyme inhibition. These potential side effects should be considered when determining the appropriate treatment plan for PSD patients [20]. PSD can effectively be treated by antidepressants such as selective serotonin reuptake inhibitors and tricyclics. However, SSRIs may be a better option for stroke patients due to their faster action and fewer side effects. Among SSRIs, citalopram and fluoxetine are preferred first-line treatment options for PSD due to their efficacy and minimal side effects [21]. Research shows that selective serotonin reuptake inhibitors (SSRIs) usually inhibit thrombocyte aggregation. And it reduces the risk of hemorrhagic stroke. However, no evidence is present that shows that SSRI is equally effective for ischemic stroke. But still, accurate evidence is not present that prove that conventional intervention such as psychotherapy and antidepressants should be used for the prevention of post- stroke depression [22].

Treatment of PSD through physical exercise

Recently exercise is suggested as a corresponding treatment option not only for depression but also for post-stroke depression by some studies [23]. Exercise reduces depression by affecting various mechanisms in the body. For example, depression may lead to maladjustment in various immune functions and the HPA axis, leading to high levels of cortisol in the body. However, exercise improves immune functions and also regulates the HPA axis (a system where the hypothalamus, pituitary gland, and adrenal glands interact and control stress and also regulate other systems of the body) [24]. Research shows that post-stroke depression can be treated by exercise of high intensity, but low-intensity exercise is not that effective [9]. Some guidelines are recommended by different organizations for the performance of physical exercises. Higher intensity exercises should be performed for at least 30 minutes and 3 to 5 days a week to reduce depressive symptoms [25], and a combination of various physical activities, resistance exercises, neuromotor and cardio exercises for 150 minutes in a week [26]. A reason for post-stroke depression is the reduction in a neurotransmitter, 5HT. Due to stroke, the pathway of 5-hydroxytryptamine (5HT) is damaged in the brain so, a 5HT level decrease leads to depressive symptoms in stroke patients. Some drugs help in the reduction of depressive symptoms by increasing the level of 5HT such as selective 5-HT reuptake inhibitors and monoamine oxidase inhibitors [27]. It is described that inflammatory factors raised in the brain due to stroke regulate the NF-kB pathway and activates NLRP3 in the brain leading to the development of depressive symptoms. It is also proposed that irisin also has a significant role in the regulation of pathways and in this way acts like an antidepressant. And exercise effectively reduces these depressive symptoms by reducing inflammation [28]. Usually, exercise raises irisin level and helps in the reduction of depressive symptoms, and improves cognition [8]. research on mice models, it is inferred that exercise decreases inflammation causing neurochemicals like in the NF-kB pathway, NLRP3 inflammasomes, TLR4, and also PTEN (protein that acts as a tumor suppressor) levels leading to a reduction in PSD symptoms [29]. In a meta-analysis, it is reported that exercise has a positive impact on the reduction of PSD especially structured exercises such as aerobic exercise, strength training, and cardiorespiratory exercise programs performed for at least 150 minutes. In this meta-analysis, 1700 stroke survivors were taken from 13 studies and specific exercise protocols were followed. Along with these, high- intensity exercise was also found beneficial and positive impacts can be seen in the first 6 months after stroke [9]. In another study, it was described that aquatic exercise is also beneficial for mood elevation after stroke. If proper exercise protocol is followed, it can cause a reduction in post-stroke depressive symptoms such as 2 sessions a week for at least 45 or 60 minutes until 12 weeks. And author summarized it as the mood has a correlation with mobility, if a patient`s mobility improves, the mood will also improve [30]. Tai Chi a type of aquatic therapy in which body coordination is combined with breathing exercises leading to improved mood and better life quality [31]. Chan & colleagues conducted an RCT study on PSD patients in Australia and first describe the significant role of yoga (a mind & body therapy) on PSD. It was suggested that patients that performed yoga along with other PSD rehab exercises showed significant improvement in depressive symptoms [32]. Physical exercise may influence mood in multiple ways, such as through the release of neurotransmitters like endorphins, enhanced physical function, and improved psychological factors affecting mood. However, there is less research available to

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determine the role of exercise on the level of neurotransmitters. But it is observed that exercise reduces endorphin levels in heart patients as compared to normal individuals [33]. There is a need for a well- designed, prospective study to determine the efficacy of aerobic exercise on depression in stroke survivors, especially after 6 months of injury. It is suggested that aerobic exercise should be performed with the proper protocol of at least 30 minutes, 3 days a week for 12 weeks. It will be beneficial in reducing depression and improving quality of life. The program was found to be highly satisfactory and feasible for future trials, adding to the limited existing research on the benefits of aerobic exercise on stroke [34]. In this way, another study found exercise effectiveness in the reduction of depression over time and it is in line with other studies that suggest non-conventional methods of intervention effective in depression that mostly occurs in neurological disorders [35].

Summary of Review Findings

Title	Main Findings	Authors
Stroke Prevalence	2nd leading cause of death & disability In US almost 8 lakh people affected annually	[10, 11]
Post Stroke Depression	31% stroke survivors experience PSD Affect patients in different ways	[3, 12, 13]
PSD Pathophysiology	Biological and psychosocial hypotheses Correlation of PSD with size, severity of lesion of anatomical structures	[5, 14]
PSD Causes	Inflammatory mechanisms NF-kB, Inflammasome NLRP3, Interleukin -1β (IL-1β)	[15-18]
PSD conventional treatment	Drug and psychological therapy Antidepressants and it`s side effects i.e., SSRIs, (citalopram and fluoxetine)	[19-22]
PSD treatment through physical exercise	Exercise reduces PSD by different mechanismsImproves immune functions and also regulates the HPA axis, raises irisin level, increases the level of 5HT Exercise decreases inflammation by reducing neurochemicals like in the NF-kB pathway, NLRP3 inflammasomes, TLR4, and PTEN levels.High intensity exercise more effective Impact of yoga, aquatic, Tai Chi, aerobic exercises	[8, 9, 23-35]

CONCLUSIONS

In conclusion, the evidence reviewed in this article suggests the effectiveness of physical exercise as an intervention for PSD. In stroke patients, physical exercise has been found to improve depression, and cognitive & physical functions. The enhancement of cardiovascular fitness, neuroplasticity, and the release of brain-derived neurotrophic factors are the mechanisms underlying these advantages. The review's findings are in favor of PSD rehabilitation programs including physical exercise as a viable therapy. To further know the benefits of physical exercise in the management of PSD and to establish the ideal exercise prescription, additional well- designed, controlled trials are required.

Authors Contribution

Conceptualization: AK
Writing-review and editing: DENB, MZ, SA, TG, AA
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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