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Fractures in Parkinson's Disease

Meghana Anagani*, Terry Oroszi

Parkinson's Disease and Fractures, Department of Pharmacology & Toxicology, Boonshoft School of Medicine, Wright State University, Dayton, OH, USA
Email: *anagani.2@wright.edu

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Abstract

Parkinson's disease is a neurodegenerative disorder that is common in older people and is highly associated with depression, anxiety, apathy, psychosis, cognitive impairment, imbalance and sleep disturbances. These patients have an increased risk of fracture compared to the general population. Comprehensive searches of databases are performed to identify reviews about the risk of fractures in this disease. Parkinson's patients are at increased risk for low bone mineral density due to the effect of drugs, Parkinson's disease and age factor, leading to an increased risk of falling down and fractures, especially in the hip. So, improved and innovative treatments with the focus on minimizing inadvertent bone resorption with anti-Parkinson's disease medication will be highly effective in reducing fear of the disease and providing the patient with a better quality of life.

Keywords

Parkinson's Disease, Fractures, Antidepressants, Antipsychotics, Adverse Effects

1. Introduction

People with Parkinson's Disease are at increased risk for fractures. Non-vertebral fractures are also familiar with the disease, because Parkinson's Disease results in body balance problems, which result in poorer bone health. Parkinson's Disease also leads to higher falls and osteoporosis, the most common cause of fractures, especially in the hip. The Parkinson's disease research report states that Parkinson's Disease leads to a two-fold increased risk of hip fractures and non-vertebral fractures. The research report also points out that women are at higher risk of hip fracture due to the disease than men. However, Parkinson's disease in the US affects 1 million people. It is estimated that the common disability of people is hip fractures due to the balance problem associated with the disease. The gradual development of osteoporosis in the US is due to advanced stages of Parkinson's

Disease, low body mass index, inadequate sunlight exposure, and decreased vitamin D levels [1].

Furthermore, epidemiological studies suggest a relationship between Parkinson's disease and osteoporosis, vitamin D adequacy, and altered bone and mineral metabolism. Hence, the evidence suggests that patients with Parkinson's Disease are the victims of several types of fractures, especially hip. Parkinson's disease is highly associated with depression, anxiety, apathy, psychosis, cognitive impairment, and sleep disturbances. Neuropsychiatric disorders also lead to poor quality of life, increased disability, worse outcomes, and a more significant care burden. The antidepressants used in treating Parkinson's include citalopram, sertraline, paroxetine, fluoxetine, venlafaxine, amitriptyline, nortriptyline, and desipramine [2] [3] [4].

1.1. Metabolic Pathways Involved Parkinson's Treatment

1.1.1. Antidepressants

Antidepressants are the most effective way to treat depression. Furthermore, the use of antidepressant drugs helps in the effective treatment of Parkinson's Disease. It is also evident that selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase type B inhibitors (MAOIs), and tricyclic antidepressants are effective pharmacologic agents used in the treatment of depression in Parkinson's Disease. On the other hand, it is said that the strength of efficiencies of antidepressants in treating Parkinson's is highly controversial [5]. According to the meta-analysis, it is evident that the use of SSRIs and placebo for Parkinson's treatment is highly effective. Still, no level of efficacy was found in SSRI and placebo. In addition to the antidepressant drug in patients, the role of MAOBIs in treating motor symptoms of Parkinson's in a recent randomized, double-blind, placebo-controlled multicentre trial (ADAGIO study) states that the use of antidepressants in patients significantly reduces depression in patients who have Parkinson's Disease [6]. In addition to using dopamine agonists, pramipexole and ropinirole SSRI remain the best-used antidepressants for treating depression in Parkinson's patients.

1.1.2. Combination of Antidepressants and Antipsychotics

Parkinson's is caused by progressive damage to the brain that highly regulates the movement of body parts. It also leads to a decrease in nerve cells, which produces a signalling molecule called dopamine. It affects the patient, because it leads to excessive shakiness, slow movement, and stiffness. Dopamine release directly travels to the brain, known as the striatum. It is also released by spiny projection neurons (SPN) and is rich in the protein LRRK2 [5]. Therefore, protein-induced mutations lead to motor impairments associated with Parkinson's Disease. SPNs also send signals to other parts of the brain through a direct and indirect route.

Furthermore, LRRK2 genes influence both the direct and indirect pathways before completely losing dopamine activity. Two genetic mutations are found in

place of LRRK2 in the human body to improve dopamine activities, known as G2019S and R1441C [7]. The experiments with the gene declare that both mutations were disconnected between SPNs in the direct and indirect pathways, thus altering the activities of the nerve cell in the striatum. Therefore, the discoveries helped identify a new line of treatment and therapies in the early stages of Parkinson's Medicine before losing dopamine symptoms.

2. Factors Associated with Factures

2.1. Age

Parkinson's patients are at higher risk of falling, significantly increasing patient mortality rates. The studies on age-related falls state that hip fracture is prevalent in individuals between 60 and 79 years [8]. The post-fracture mortality of patients is significantly high with hip fracture than without it. On the other hand, some studies also claim that hip fractures are prevalent in patients between 70 and 75. Studies also report that fractures are more common among women than among men. The most common fracture was in the femur and forearm, apart men. Hence, the risk of fractures increases significantly with Parkinson's Disease and is partly preventable. Proper interventions and early diagnosis of Parkinson's are vital to preventing the adversities.

It is also analysed from the above discussion that the disease mainly affects older people. The condition is caused due to genetic and external factors. The disease also affects multiple parts of the body, especially the nerves, making the disease quite severe. The report also states that older adults with Parkinson's Disease have lost 60% to 80% of the neurons that produce dopamine and motor symptoms appear [9]. The increased death rate due to hip fractures is commonly found in patients below 75. The use of levodopa also reduced the ability of regular patients' life, leading to osteoporosis. Therefore, the severity of the disease is high and proper interventions lead to quality of life.

Furthermore, Ageing produces impairment of gait and postural control in Parkinson's Disease due to the combination of nondopaminergic and dopaminergic pathways [10]. Older patients are more likely to suffer from other side effects of anticholinergic drugs, such as confusion and hallucinations. It is due to the increasing cholinergic deficit in PD with age it results in severe side effects. Furthermore, Parkinson's drugs are not tried and tested on adults, so the efficacy of the treatments in older adults is not significantly noticed. Levodopa-induced dyskinesia also reduces with age because the younger patients highly suffer it. It results in a higher dopamine turnover rate relative to production than in older people [11]. Parkinson's patients also tend to have an increased risk of dementia with age and also their sedentary lifestyle [12]. Therefore, age is also another factor, as the impact of nonmotor symptoms gradually increases. The development of nonmotor symptoms leads to increased constipation, incontinence, falls, orthostatic hypotension, dribbling, and psychiatric disorders like dementia and hallucination. Therefore, apart from the increased risk of falls, it is also evident

that Parkinson's patients also suffer from other risk factors, making people vulnerable.

2.2. Symptoms of Parkinson's Disease

Parkinson's symptoms worsen with time. With the progression of the disease, people often face difficulty walking and talking. Behavioural changes, sleep disturbances, depression, memory difficulties, and fatigue are the most common symptoms of Parkinson's Disease. The disease significantly affects more than 50% of men than women. However, common symptoms of Parkinson's Disease include tremors in the hands, head, jaw, or legs, these tremors are highly variable [13]. It also provides the stiffness of the limbs and restricts or slows movement. On the other hand, it leads to impaired imbalance and coordination, leading to falls. Depression, emotional changes, and anxiety are some of the common symptoms of Parkinson's Disease.

2.3. Adverse effects of the Drugs Used in the Treatment

Parkinson's drugs are classified into anticholinergic drugs, levodopa alone or combined with carbidopa and/or catechol-O-methyl transferase (COMT) inhibitors, dopamine agonists, and monoamine oxidase B (MAO-B) inhibitors. Furthermore, according to peer-reviewed journals and articles, Parkinson's is highly associated with hip fractures but does not affect forearm and spine fractures. Parkinson's drugs which consist of anticholinergic drugs were associated with any fracture type. On the other hand, levodopa is highly associated with high hip fracture if the drug dose is moderate [14]. At the same time, the forearm is positively affected if the drug doses are significantly increased. It is also identified from the medical journals and articles that dopaminergic drugs are closely associated with the increased risk of hip fracture even at the middle dosage level.

On the other hand, MAO-B inhibitors are highly associated with the increased risk of hip factors with high doses. Neuroleptics are also associated with a higher hip fracture rate than other drugs [14]. It is also identified that recently, levodopa increased the tendency for hip fractures, while there have been no significant hip fracture results. Neuroleptics are also associated with an increased risk of hip fractures in both recent and past times. The effect of the drugs was associated with older adults under the age of 75 years, but the impact of the drugs is not restricted to this particular group. The effect of the drugs also affects the other age group. Particularly in the female or the women population, it is identified that risk factors greatly enhanced fracture rates among women. Excess fracture risk was identified in women 76 to 85 years of age [4].

Unlike men, the effect is restricted to 76 to 85 years of age, and other age groups are not affected by Parkinson's drugs. The increased risk of hip fracture is highly associated with anticholinergic drugs and tricyclic antidepressants that are also anticholinergic [15]. Patients suffer significantly as anticholinergic drugs

increase the risk of falling as the postural balance is completely lost due to the effect of drugs. It also affects the sufferer, just like the effect of tricyclic antidepressants, because this mechanism is independent of Parkinson's. The use of all Parkinson's drugs is often associated with fractures in high, medium, and low doses. It is also estimated that past and current users suffered mercilessly due to fracture problems. Drugs also affect the postural balance, leading to increased fracture risk. The increased risk of fracture is also very evident in the case of low doses. However, patients' tolerance level of the drugs increases with prolonged use, diminishing the risk of fractures [16].

Neuroleptics additionally deal with mental issues related to an expanded gamble of breaks. The other medication, levodopa, is likewise connected with an expanded crack gamble because the drugs don't standardize the development designs, prompting abrupt falls and breaks [17]. Although development designs are worked on yet not standardized, they lead to break takes chance by falls or unpredictable developments. It is additionally straightforward that dopamine agonists likewise have an associated fracture risk. The propensity is fundamentally low due to the everyday use of the medications and is utilized for a more limited period. Parkinson's is exceptionally connected with expanded risk factors, particularly among men, yet the dangers were essentially diminished by changing the prime supporters [18]. Levodopa and neuroleptics lead to an expanded gamble of cracks among victims. Dissimilar to antidepressants, SSRIs didn't impact break risk among a partner of moderately aged and more established adults. It was also hypothesized that SSRIs have a defensive impact against dead myocardial tissue (MI) [19].

3. Research and Treatment of Parkinson's Disease

Presently there is no treatment for Parkinson's disease, but with time, several therapies are evolving continuously, which leads to the efficient management of the disease. Furthermore, levodopa is the most commonly used drug to produce dopamine in the brain. The first line of treatment includes medication, but if the patients are resistant to the medicines, the physicians opt for other methods, including surgery and deep brain stimulation. Furthermore, surgeries are often risky leading to brain bleeding and death of the patients. The genetic inheritance of the disease usually involves autosomal recessive and dominant patterns of inheritance, but the molecular mechanisms of the disease are still not deciphered by researchers [8]. Moreover, the complexity of the genetic mutations of the disease is also unknown. Thereby for effective treatment options, CRISPR-Cas9 is implemented to identify the various models of Parkinson's phenotype.

It is also evident from peer-reviewed journals and articles that CRISPR screening is one of the most highly effective tools to determine the genetic sequences and physiological and morphological effects of Parkinson's Disease. The screening tool is highly effective in analysing the genes associated with the disease, thus providing an effective solution for future therapy [2]. The researchers

also state that neuronal cells in the human body are affected due to Ageing and neurodegeneration. So CRISPR tools are used to detect positive and negative regulators of Parkinson's disease significantly [20]. The tool effectively determines the generation of Parkin protein that leads to the development of the disease. The abundance of protein secretion in the human brain leads to the development of the disease. The screening tool effectively determines the pathways of the disease with efficiency.

The screening tool is highly efficient in detecting therapeutic aspects of Parkinson's Disease. The instrument acquired the potential to detect the SNCA gene with a bioluminescent tag and for accurate measurement of the α-synuclein protein generation field [21]. Furthermore, the tool generated a luminescent signal with the expression of α-synuclein. Hence, the tool effectively determines endogenous α-synuclein (with no external reporters). The tool is also beneficial because it produces accurate results of the Disease through Parkinson's screening tool. The screening tool is also effective in the epigenetic regulation of the SNCA gene. As mutations in SNCA gene are associated with pathological features of the disease [22].

The histone demethylase also works as the epigenetic eraser, thereby helping to regulate the SNCA gene [22]. The effectiveness of the process is because it is derived from neurons in the human body and is derived from stem cells produced in the human body. Therefore, the epigenetic regulators and the CRISPR screening tool are highly effective in developing therapeutic target treatments for Parkinson's Disease.

Furthermore, the future possibilities of the screening tool are vast, leading to massive success. The tool has significantly led to identifying several types of Parkinson's disorder and created immense scope for correctly identifying neurodegenerative disease. The therapeutic approaches to eliminating disease are highly significant for future treatment development. Furthermore, to decipher more about the disease, the Alliance for Therapies in Neuroscience (ATN) collaborated with CRISPR technology to decipher more about the treatments. The collaboration helps identify the complex genetic mutations and molecular mechanisms leading to neurodegenerative disorders such as Parkinson's [23]. Due to the efficiencies of the CRISPR tools and technology, there is a growing chance for clinical advancements in the disease. Therefore, the tool is proven effective in treating the disease, thereby providing better treatment options in the future.

4. Contemporary Therapies for Parkinson's Disease

4.1. Gene Therapy

Despite the Covid 19 pandemic, the evolution of Parkinson's disease drug therapies is pervasive. The impact of Covid 19 was huge on the development of Parkinson's drug therapies. The closure of academic research institutes created a havoc impact on research and development activities. Parkinsonism is a major

concern that affects the world population equally. Furthermore, even in the pandemic, research is growing continuously to find alternative ways to reduce the disease. According to peer-reviewed articles, there have been new developments in Parkinson's treatment that restrict the spread of the disease. Currently, cell and gene therapies are the most effective treatment for Parkinson's Disease. However, the evolution of new therapies is possible with the innovation and creativity of technical developments. Cell and gene therapies have proven to be the most effective therapies because they use powerful molecular and genetic tools and techniques. It significantly led to robust developments in the neurodegenerative disease field [1]. The wide-scale development of cell and gene therapies would not have been possible without the support of the biotech industry and large pharmaceutical companies.

It is exceptionally clear from peer-investigated clinical research and articles that Parkinson's isn't acquired from a hereditary transformation from the guardians. In any case, hereditary treatment is exceptionally compelling in decreasing the illness. The articles in clinical diaries state that individual qualities are investigated to be profoundly viable in treating disease, giving new light on the movement of the treatment. With quality treatment, dopamine-delivering cells are not impacted in the mind and help bite the dust cells in the cerebrum to rejuvenate with treatment that is most terribly impacted because of the Disease [24]. Gene treatment additionally helps increment protein and dopamine creation in the cerebrum. It is profoundly compelling because it educates synapses not regularly harmed in that frame of mind to create dopamine to assist with recuperating lost capability. This approach has been profoundly fruitful, and specialists guarantee it could decrease levodopa admission because of its unfriendly incidental effects. It is also guaranteed that this approach helps make levodopa's working more effective later [25]. The analysts additionally pronounce that keeping up with adjusted levodopa levels without changes prompts powerful and effective treatment.

Gene therapy is also effective in restoring nerve cell activities in the brain. The nerve cells become hyperactive in the basal ganglia area of the brain. The basal ganglia of the brain also help control the brain's movement. Changes in the function of the brain also affect movement. So, the hyperactive responses of the brain tissues are controlled by increasing the level of enzymes used to produce GABA (neurotransmitter produced in the brain) [2]. This approach is presently induced and is highly effective and efficient in controlling the abnormal activities of the brain. The use of light-responsive genes and proteins is proven effective in treating the disease. Gene therapy also leads to the growth of cells and tissues in the brain, which helps to protect individuals from further damage. The growth of the cells and tissues of the brain helps increase human beings' rejuvenation and survival rate because it helps protect the neurons [26]. It is proven to be a highly effective treatment, and soon, more advances in technology and medical sciences will lead to effective treatment of the disease.

Gene therapy is highly effective in people with Parkinson's Disease with any condition. As gene therapy continues to improve towards betterment, the suitability of the treatment for everyone is of concern. If the treatment does not suit the individuals, it leads to adverse risks. Furthermore, there is a long-term impact on the central nervous system and increased exposure to therapeutic genes. Currently, the research and development team is working proactively to reduce the risks of contemporary treatment. Therefore, gene therapy aims to enhance the production of dopamine levels in the human body through neural cells [6]. This contemporary therapy has great potential for the robust management and effectiveness of the disease. The advancement in therapies is significant to the future generation as effective treatment is successfully devised from the recent advances.

Moreover, this therapy also leads to the death of AAV vector patients with arthritis. However, this situation also requires proactive vigilance for patients who have undergone gene therapy. Although AAV is highly safe as per the present reports from clinical trials, in some cases, it is fatal, which remains a major concern of the treatment. However, constant gene regulation systems and constant developments will lead to effective results in the future [27].

4.2. Stem Cell Therapy

On the other hand, stem cell therapy is also proven to manage the disease better effectively. Furthermore, in combination with gene therapy, cell therapy is also beneficial for treating Parkinson's Disease [3]. Cell therapy has also been shown to effectively control damage and repair of brain cells, which significantly produces dopamine [28]. Furthermore, a single dose of cell therapy was used in a pilot study among patients aged twenty-two to sixty-two. Positive results were derived from the pilot study in which therapy is highly effective in treating and managing the disease. Recent developments in Parkinson's disease therapies have become critical because levodopa is effective in treating the disease but is induced by multiple side effects ranging from physiological and psychological effects, which worsen the condition of people who have Parkinson's [7] [29]. From the recent developments in the treatment of Parkinson's Disease, it has been identified that the benefits of the drugs have become limited, and the patient's conditions are continuously evolving with time. So, current drugs are highly incompetent in producing the best results for the disease, thereby developing alternative treatment methods.

It is also identified from peer-reviewed journals and articles that Cord Tissue-derived mesenchymal stem cells have led to robust efficiencies and treatment efficiencies yield [13]. The reliability and viability of the therapy increased significantly, making the treatment more effective. On the other hand cell therapies, such as bone marrow treatment, did not show valid results in treating the disease. Hence the other cell therapies are highly beneficial in the robust management of the disease. Some peer-reviewed studies portray that cell therapy led

to improvements in Parkinson-affected patients.

It was likewise seen that look, stride, and freezing episodes had worked essentially in the patients in the cell treatment [30]. Thus, the utilization is exceptionally viable and ok for later use to treat patients with neurodegenerative illness. Also, direct cell treatment works in dopamine-delivering cells, accordingly prompting legitimate treatment of the illness and essentially further developing the patient's satisfaction. These contemporary medicines and surgeries produce a lot of dopamine for the illness yet, in addition, cause extreme complexities, prompting the development and improvement of elective treatments. The performances of gene therapy and cell therapy for the effective treatment of Parkinson's Disease are emerging significantly [31]. Therapies are also continuously developing to produce reliable results for future generations. Hence, these therapies emerge slowly and create more comprehensive treatment options for the future generation [32]. The peer-reviewed journals also state that gene therapy is the most effective therapy as per the present reports. Future clinical trials will decipher more information about the study area and eventually lead to further advancement in treatment.

5. Treatment for Fractures

5.1. Use of Painkillers to Treat Pain

The various pain management options are the best for bone fractures. The treatment includes ibuprofen, codeine-containing acetaminophen, and Vicodin, immobilization and stabilization. Reducing the pain by using these mediations leads to short and long-term treatment measures. Furthermore, the use of pain management options by using medications also leads to long-term and short-term treatment measures so that it does not intervene in any surgical methods in the future. The pain management options also rely on the severity and location of the fractures.

5.2. Replacement Surgery

Surgery is essential in the case of hip fracture or any other fracture. It is the best treatment option because it involves surgery as the primary procedure to repair the fracture. Metal rods, screws, or plates are used frequently in repairing the fracture area which may lead to complications but Pain relief and sustained walking ability were observed in patients after surgery field [33] [34] [35]. This procedure is highly applicable and recommended in the case of complicated fracture cases where the long-term use of casts is not feasible.

Open reduction and external fixation surgery also help to repair fractures. The surgery process also leads to the placement of an external fixation device on the limb in case of fracture. The external device is helpful because it supports the bone externally to lead to healing by maintaining the correct position. Henceforth this technique is generally applied to a complex fracture that cannot be cured with open reduction and internal fixation.

6. Discussion

Fall-related fracture is one of the most disabling causes of Parkinson's Disease. Some of the factors responsible for falling are the duration of the disease, restrictions in everyday activities, severe motor symptoms, abnormal posture, gait freezing, frontal impairment, impaired balance, and reduced knee strength. It is also identified that osteoporosis and osteopenia are the prevalent factors resulting in falls and are the most common findings in patients with Parkinson's. The development of osteoporosis due to Parkinson's also leads to a reduction in mobility, endocrine problems that are vitamin D deficiency, nutritional and iatrogenic factors, duration of the disease, and severity. Some studies state that fractures are prevalent in Parkinson's Disease, but severity and duration vary significantly.

Research in the study area states that 90% of fractures among older people result from falling due to disease. It is also identified from peer-reviewed medical reports that certain people who cannot dress up or wash independently are at higher risk of extreme conditions [36]. Moreover, vertebral fractures are very common such as fractures in the femur, forearm, vertebra, ankle tibia, rib, and pelvis.

Parkinson's patients have a two-fold increased risk of fracture. The tendency to hip fracture increases three or four times. Furthermore, Parkinson's Disease is increasing, so hip fractures are rising. The incidence of hip fractures is considerably more in patients with Parkinson's than in the general population. It is also estimated that fracture risk is more common in males than females, while the latter suffer from dementia-related risk factors. Second, contralateral and no contemporaneous hip fracture is commonly found to be highly evident in patients [37]. Parkinson's disease patients also report collateral hip fracture, while 3.2 times increased second hip fracture.

Clinical diagnosis of Parkinson's Disease depends on bradykinesia in the mix with a resting tremor/rigidity. For the most part, early symptoms present asymmetrically, with the shortfall of atypical symptoms like vertical supranuclear palsies or cortical sensory loss, early severe autonomic dysfunction, and cerebellar signs would be demonstrative of an elective analysis. An asymmetric outset of signs also a decent reaction to levodopa are steady for a diagnosis of Parkinson's Disease and also are one of the 2 most essential elements to separate Parkinson's Disease from the different types of Parkinsonism. As the infection advancements, so do the sincerity of engine and non-engine symptoms. Parkinson's disease is a highly heterogeneous infection, and there have been endeavours to subgroup the sickness further. Albeit congruence still can't be fulfilled, 1 sub-classification founded on clinical qualities suggests 2 subtypes: a prevailing tremor Parkinson's disease & a non-tremor predominant Parkinson's Disease. A patient with persistent tremor Parkinson's disease requires other engine symptoms and answers more useful to dopamine substitution therapy. Then again, a patient with a non-tremor prevalent Parkinson's disease might have an aki-

netic-unbending state, a postural insecurity issue, and an expanded occurrence of non-engine highlights. The course of the illness and forecast contrasts have been hypothesized that the various subtypes have precise pathogenesis and etiologist.

Drugs are used to treat the disease, which increases the level of dopamine, and some drugs are also used that affect brain chemicals in the body [14]. Some specific drugs also help to control the non-motor symptoms. The primary therapy for the disease includes levodopa, and the subordinate Medicine is carbidopa, which treats side effects such as nausea, vomiting, restlessness, and low blood pressure of levodopa therapy.

Deep brain stimulation is also another way of treating Parkinson's Disease. Patients irresponsive to medication are treated with deep brain stimulation. It is a surgical procedure that implants electrodes in the brain and connects with the chest, where a small electrical device is implemented [1]. The device makes sure that the movements or difficulties related to Parkinson's are restricted significantly. Other therapies include occupational therapies and physical and speech therapies as well. Hence, these interventions reduce the associated difficulties with the disease. The goal of the interventions is to improve the level of activity of elderly patients and to provide a quality of life.

7. Conclusion and Recommendation

It is estimated that Parkinson's is the cause of falls and other imbalances in the human body, which leads to fractures. Therefore, the effect of the disease is severe, leading to broken bones or fractures that cause restrictions in movement and other disabilities for quality of life. It is highly evident from the above discussion that drugs, disease, and age factors significantly contribute to hip fractures. Maybe, in the future scope of the research, it is imperative to focus on minimizing inadvertent bone resorption with anti-Parkinson's disease medication. It is also important to ensure compliance with bone protection and medication.

It is vital to explore how to accelerate safe surgery and perioperative anaesthesia in sustained fractures in patients. So, from the above discussion, it is quite evident that the disease affects the quality of life of the people with the disease. The role of caregivers is vital in this case as they will help the patient get out of the problem and lead to a better life in the future. Caregivers need to have a proper understanding of the symptoms, needs, and demands of the patients to improve their lives of the people. The location and proper knowledge about the progression and treatment of the disease are vital, because they lead to the effective and efficient management of the disease in case of urgency. It is also vital to keep track of scheduled appointments and involve patients in regular exercise so that the situation does not worsen. The love and support of caregivers also help eliminate the critical scene in the patient's life.

The above discussion also identified that patients with non-motor symptoms are highly affected by the disease. The increase in levodopa intake resulted in

hampering personal relations, work, and leisure activities due to the drug's adverse side effects, which resulted in gene and cell therapy, which is proven effective in most cases. As discussed in some cases, therapies are fearful of costing the life of the patients. Therefore, it is evident that improved and innovative treatments are highly effective in reducing fear of the disease and providing the patient with a better quality of life.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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