

KNOWN MSA TREATMENTS OVERVIEW 2020

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The purpose of this overview is to summarize known treatments for MSA. It is for informational purposes only. All readers are advised to consult with their health providers first before taking any steps. For any questions pertaining to diagnosis or treatment, please consult with your health provider.



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Known Treatments for Multiple System Atrophy

1) Orthostatic hypotension

Orthostatic hypotension (OH) is characterized by a drop in blood pressure upon standing, with accompanying symptoms including dizziness and lightheadedness. Usually, the autonomic nervous system regulates blood pressure (BP) and increases blood vessel constriction upon standing to keep BP constant. In MSA, disturbances in the autonomic nervous system leads to neurogenic orthostatic hypotension (nOH), defined as a drop in systolic BP ≥ 14 mmHg or in diastolic BP ≥ 6 mmHg.

Lying/sitting drops in blood pressure can also be used to diagnose OH in patients if standing is not feasible, with drops in sitting systolic BP ≥ 14 mmHg or diastolic BP ≥ 6 mmHg indicating the presence of nOH. (Sun 2016) These drops in blood pressure can lead to dizziness, problems maintaining balance, walking and an increased risk of falls. nOH occurs in anywhere from 54%-81% of patients with MSA¹.

1. Non-pharmaceutical treatments for OH include correcting aggravating factors and implementing other measures to decrease symptoms and risk of fall. OH has been found to be worse in the morning, in hot weather, after eating large meals (especially carbohydrate-heavy meals) and from lifting heavy objects. Avoiding exposure to these factors can decrease the frequency and severity of OH instances. Other non-pharmaceutical interventions include:
 - a. Expanding blood volume with **salt and water supplementation** may help minimize symptoms of OH, though the evidence for this is fairly weak². Patients may be encouraged to consume an additional 1-2 teaspoons of salt per day and increase their water consumption by their doctors³.
 - b. **Exercise**, when done in a safe environment, can improve symptoms of OH. Exercise can even be performed in a sitting or recumbent position, either on a recumbent stationary bike or rowing machine, for example. Exercise in a pool is also a safe option for those who have this option available.
 - c. **Compression stockings** have been shown to be an effective treatment for OH by increasing venous return. Waist-high stockings have been found to be most effective in preventing OH⁴.
 - d. The Valsalva maneuver that occurs during bowel movements can be a precipitating factor for OH, so the straining that occurs during constipation must be avoided. This can be avoided through **dietary changes** such as increasing fiber in diet and increasing water intake. Fermented milk products with probiotics, such as kefir, have been shown to prevent constipation in patients with Parkinson's disease and may be of use in MSA⁵. When dietary changes are not enough to avoid constipation, laxatives are sometimes needed.

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- e. Supplementation with **coenzyme Q10** has also shown promise to treat the symptoms of OH⁶.
 - f. **Raising the head of the bed** about 10 cm can also help decrease the symptoms of OH, especially those that occur in the morning⁷.
 - g. **Postural maneuvers** can also be used to combat the drop in blood pressure that defines OH. These include muscle tensing and swaying while standing, bending forward, leg crossing and squatting and have been found to have significant effects on blood pressure⁸.
2. Pharmaceutical treatments for nOH try to either increase plasma volume or to increase peripheral resistance through various mechanisms of action. Drugs used to treat MSA are described in Table 1.

Table 1: Medications to Treat Orthostatic Hypotension in MSA

Drug	How it Works	How it is Used	Side Effects
Fludrocortisone	Synthetic adrenal corticosteroid hormone that increases sodium and water absorption, increases blood volume, sensitivity to adrenaline, and causes contraction of blood vessels and increases in BP.	Commonly used in conjunction with a drug that increases blood vessel constriction, such as midodrine, droxidopa or other agents ³ .	Can lead to hypertension and end organ damage, leading to heart and renal failure and has been found to increase risk of hospitalization ⁹ . Side effects include ankle swelling, hypokalemia or low potassium levels, and headache.
Midodrine	Vasoconstrictive agent that leads to increased BP in laying down, sitting and standing positions.	It has been shown to be effective in the treatment of nOH among MSA patients, with an increase in	Found to cause an increase in supine hypertension, or dangerous increases in BP while lying down,
		standing systolic BP of nearly 22mg Hg ¹⁰ .	and should not be taken close to bedtime.

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Droxidopa	Converted to norepinephrine, a hormone that increases BP and has shown significant reductions in BP in several small clinical trials, while results from larger clinical trials have been mixed ¹¹ .	Patients with a lower level of norepinephrine while lying down tend to have better success with droxidopa and may be used to predict success ¹² .	The most commonly observed adverse reactions were headache, dizziness, nausea, and hypertension ⁴⁸ .
Pyridostigmine	Stops the breakdown of acetylcholine, the main neurotransmitter of the autonomic nervous system, increases the release of adrenalin.	Has been shown to cause an increase of an average of 4mm HG in systolic BP ¹³ .	Side effects can include stomach pain, nausea, vomiting, diarrhea, blurred vision, muscle cramps and twitching.
Epoetin alfa	Recombinant erythropoietin that increases the sensitivity of the blood vessels to the hormone angiotensin, which increases vasoconstriction and consequently BP.	The use of this to treat nOH is not widely recommend as the evidence to support it is weak ² .	
Non-steroidal antiinflammatory drugs	Blocks prostaglandinmediated vasodilation and has been hypothesized as using this mechanism to prevent OH.	Results haven't been validated in large trials.	Possible gastrointestinal irritation.
Yohimbine	Leads to increases in the activity of the autonomic nervous system through increases in norepinephrine.	Clinical evidence of effective control of OH is scarce ² .	Side effects can include anxiety, palpitation, tremor and confusion.

Desmopressin (DDAVP)	Helps to contract blood vessels and may combat OH by mimicking the action of the hormone vasopressin.	Helps to prevent nocturnal urination thereby improving BP control in the morning. Limited data on this agent make recommendations for the use of this agent weak ² .	Alternations in blood chemistry, specifically low sodium levels.
Atomoxetine	Short acting norepinephrine transport inhibitor, increases BP in nOH.	Especially effective in patients with high levels of norepinephrine ¹⁴ .	Side effects can include gastrointestinal and urinary symptoms.

2) Parkinson-like symptoms

There are symptoms of MSA that mimic Parkinson's disease, including stiffness and rigid muscles, tremors, slow movement, balance issues, trouble walking, and dystonia. These are especially prevalent in MSA-predominant Parkinsonism (MSA-P), which is the more common type of MSA.

1. Non-pharmacologic treatment of Parkinson-like symptoms of MSA include:
 - a. A regular schedule of **physical and occupational therapies** can help to control the parkinsonian symptoms of MSA. These can help to maintain balance and flexibility as the disease progresses and can prevent falls and additional injury. Research has shown that inpatient, combined with at-home, physical therapy improves gait disturbances in patients with MSA¹⁵. Tai-chi has also been shown to have positive effects in patients with Parkinson's disease, and may have a similar effect on patients with MSA¹⁶.
 - b. The **Alexander Technique**, an educational technique taught to patients to improve balance, posture and mobility, has demonstrated modest benefits to patients with Parkinson's in small studies, although recommendations are mixed.
 - c. The most common type of speech therapy for Parkinson's patients is the **Lee Silverman Voice Treatment**, in which speech therapists focus patients on speaking loudly as a way to target vocal cords and improve speech fluency. An off shoot of this method can be used to improve motor control in Parkinson's patients, with a focus on big, expansive movements as a way to control muscles.

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- d. **Deep brain stimulation** is not an approved therapy for MSA, but there have been anecdotal reports and small case studies reporting the benefits of this treatment. Recently, a review of studies that examined deep brain stimulation concluded that it is not a recommended therapy in MSA¹⁷.
 - e. **Dietary modifications** can enhance the effects of certain classes of medication used to treat Parkinson-like symptoms in MSA. In patients taking levodopa, a low-protein diet has been tied to increase effectiveness of the drug and a longer time period where the drug works¹⁸. Patients on monoamine oxidase inhibitors also have been found to benefit from avoiding foods high in the amino acid tyramine, including fermented foods such as aged cheeses, pickled fish, tofu, soy sauce and sauerkraut. Excessive tyramine consumption in patients on these drugs can lead to dangerous spikes in blood pressure.
2. Drugs used for Parkinson's disease may provide relief of motor symptoms for some MSA patients, though primarily in the earlier stages of the disease. Parkinson's drugs also can lower blood pressure and may worsen OH symptoms, dizziness, and fainting episodes. Pharmacologic options include:
- a. **Levodopa** is a medication that mimics the effect of dopamine in the brain. It was originally used as a treatment for Parkinson's disease, and a poor response to levodopa therapy is one of the hallmarks of diagnosis of MSA. Only about one-third of MSA patients may experience a benefit, and a response is more likely in the MSA-P subtype than in MSA-C¹⁹. The benefits of levodopa therapy diminishes over time and has been shown to be useful for MSA-P individuals for about 2 to 3 years. A side effect of levodopa is an abnormal increase in body movement, called dyskinesia, as well as an increase in the symptoms of orthostatic hypotension.
 - b. Other **dopamine agonists** increase the level of dopamine receptors in the brain, allowing dopamine to have a greater effect. Examples bromocriptine, pramipexole, apomorphine, and ropinirole. Pramipexole has shown promise with some preliminary improvements in Parkinson-like symptoms. Apomorphine helps to treat muscle stiffness and loss of muscle control. As dopamine agonists can exacerbate orthostatic hypotension, they should not be considered first-line drugs in MSA. Potential side effects of this class of medication include daytime sleepiness, dizziness, fainting, nausea, difficulty sleeping, hallucinations, behavioral changes and uncontrolled movements.
 - c. **Monoamine oxidase inhibitors** block the enzyme monoamine oxidase, which normally breaks down neurotransmitters like dopamine and norepinephrine. As a result, level of these chemicals increase and can alleviate Parkinson-like symptoms. Recently, safinamide has been shown to improve symptoms in MSA patients. This class of medication are commonly used in conjunction with other medications.
 - d. **Anticholinergic medications**, including trihexyphenidyl and benztropine mesylate, have been used to treat these symptoms in MSA. This class of drugs block the activity of the neurotransmitter acetylcholine, which cause muscles to contract.

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- e. One **glutamate antagonist**, amantadine, is used to treat Parkinson-like symptoms in MSA. It works by increasing dopamine release and blocking the reuptake of dopamine, leading to mild symptom improvement. Amantadine, which is also an antiviral medication, helps to alleviate tiredness and stiffness in MSA.
- f. Research has indicated that certain **selective serotonin reuptake inhibitors (SSRIs)** can help to decrease Parkinson-like symptoms. Specifically, paroxetine has shown benefits to MSA patients²⁰.

3) Dystonia

Dystonia is a neurological condition where muscles contract involuntarily. It can occur anywhere in the body, including the muscles of the arms, legs, trunk, or face, and appears as repetitive, twisting movements and unnatural posture. Nearly half of patients with MSA experience dystonia. Dystonia in MSA predominantly affects the head and neck area in a form called antecollis, which accounts for one-quarter of all dystonia in MSA patients, with dystonia in one limb being present in over 20% of patients studied²¹. Both of these types of dystonia, when present, can affect balance and walking in MSA patients. Dystonia can also affect the face and mouth, affecting speech. If dystonia affects the vocal cords, obstructive sleep apnea can result.

1. Non-pharmacologic treatment of dystonia in MSA include:
 - a. **Speech therapy** can be beneficial for patients whose dystonia affects their speech. Speech therapy has been shown to be a very effective treatment option in patients with Parkinson's Disease, and may be especially effective as patients with MSA have more trouble with speech than those with Parkinson's Disease²².
 - b. **Physical and occupational therapy** can assist patients with dystonia. Physical therapy helps to maintain mobility and to reduce the risk of contracture, spasm and further loss of function. Occupational therapy has been shown to minimize the risk of fall, assist patients in completing their activities of daily living with the use of assistive devices or modifications around the home²³.
 - c. **Geste antagoniste** is a sensory 'trick' that involves moving an arm to the face or head to alleviate abnormal posture associated with cervical dystonia. This maneuver has proven quite effective at reduction in head deviation in patients with cervical dystonia²⁴.
 - d. **Electromyographic (EMG) biofeedback** has been found to be an effective therapeutic technique for decreasing decrease dystonia in patients with movement disorders²⁵.
 - e. **Continuous positive airway pressure devices** can be used when dystonia affects vocal cords and breathing, resulting in sleep apnea.

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- f. In refractory cases of dystonia, **surgical intervention** can be considered. Surgical interventions can either be focused on the brain or peripherally, but the goal for both is to interrupt the communication between nerve and muscle that causes the involuntary contraction seen in dystonia.
2. Pharmacologic treatment of dystonia in MSA include:
- a. **Botulinum toxin** has been found to relieve many types of focal dystonias and is widely used in MSA. Localized injections, especially for facial and cervical dystonias, have proven effective²⁶.
 - b. The symptoms of dystonia can also be treated with **anticholinergic medications**, blocking the muscle-contracting effect of acetylcholine. Drugs in this class include benztropine, biperiden, procyclidine, and scopolamine.
 - c. Drugs that cause **muscle relaxation** have also been used in treating dystonia in MSA. These include those that increase levels of the neurotransmitter gamma-aminobutyric acid (GABA) which has the effect of reducing activity of the neurons it binds to, thereby causing muscle relaxing effect (e.g. baclofen, benzodiazepines and zolpidem) as well as traditional muscle relaxants, such as carisoprodol, cyclobenzaprine, metaxalone and methocarbamol. These medications must be used with caution, as dependency is a side effect of some.

4) Cerebellar Ataxia

Cerebellar ataxia, seen primarily in patients with subtype MSA-C, arises from problems with the cerebellum, which helps to coordinate and synchronize movements. As a result, patients with cerebellar ataxia have difficulty controlling voluntary movements, including walking, speech, hand movements and other motor functions. Although no cure exists for cerebellar ataxia, treatment of symptoms can improve quality of life and prevent complications.

1. Non-pharmacologic treatment of cerebellar ataxia relies most on **physical and occupational therapy**. Occupational therapy has been found to improve ability to perform activities of daily living and decrease disease symptomology²³. Aspects of treatment also includes speech and swallowing therapy and the use of adaptive equipment.
2. While there are no medications that have proven completely efficacious in the treatment of cerebellar ataxia, there are medications that can help control symptoms. (Table 2)

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Table 2: Pharmacologic Treatment of Cerebellar Ataxia Symptoms

Imbalance and Speech Symptoms	Tremor	Nystagmus
<ul style="list-style-type: none"> • amatadine • buspirone • acetazolamide 	<ul style="list-style-type: none"> • propranolol • clonazepam 	<ul style="list-style-type: none"> • gabapentin • baclofen • clonazepam

5) Neurogenic Bladder

Urinary symptoms are experienced by nearly all MSA patients and can be one of the earliest signs of the disease²⁷. Symptoms include trouble voiding, incontinence, increased frequency and urgency and leakage. In MSA, urinary tract problems are thought to occur due to a decline of neuronal control from the cerebellum. These problems can lead to a lack of control of the urinary sphincter and a change in activity of the detrusor muscle found in the wall of the bladder, leading to incontinence and an inability to fully empty the bladder. These problems can lead to repeated urinary tract infections and kidney infection if not properly treated.

1. Non-pharmacologic treatments of neurogenic bladder include:
 - a. **Catheterization** can help to control the symptoms of neurogenic bladder. Intermittent catheterization can be used when residual urine volume is >100ml. This can be performed by the patient or caregiver at regular intervals during the day to drain excess urine from the bladder to prevent infection. When urinary symptoms progress, a permanent catheter may need to be placed.
 - b. **Surgery** is an option when catheterization doesn't work or is not feasible. A permanent suprapubic catheter can be surgically placed to drain urine. In men, surgery may remove the external sphincter to prevent urinary retention. Stents can also be placed into the urethra to maintain a patent pathway for voiding and to prevent urine retention.
 - c. There are **lifestyle modifications** that can also help with urinary symptoms of MSA. Avoidance of diuretics, including caffeine and alcohol, can limit the frequency of urination. Adequate exercise and the use of compression stockings can also decrease edema, which can lead to increased urination, especially at night.
 - d. A **bladder diary** is an important way to discern symptoms and the progression of symptoms in MSA patients. A bladder diary can track urinary tract symptoms, fluid intake, urine output, and time to voids.

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2. Medications used to control neurogenic bladder include:
 - a. Anticholinergic agents are used when post-void urine volume is <100ml. These medications block the neurotransmitter acetylcholine and the muscle contraction it causes, and can ameliorate symptoms of urgency, frequency and incontinence, but increase the risk of urine retention. Drugs in this class include **propiverine**, which can increase bladder capacity, **oxybutynin**, which not only increases bladder capacity, but

can also decrease the activity of the detrusor muscle. Oxybutynin has the added benefit of being available as an extended release capsule or a transdermal patch. **Tolterodine**, **solifenacin** and **darifenacin** are other drugs in this class that have been shown to decrease symptoms of neurogenic bladder.

- b. Alpha-adrenergic blockers, such as **alfuzosine chlorhydrate** and **tamsulosine chlorhydrate**, can be used to reduce post-void urine residuals when there is an impaired urinary sphincter muscle. Given the worsening of orthostatic hypotension that may occur with this class of medication, care must be taken using these²⁸.
- c. Nitrous oxide induces vasodilation and has been shown to relax the muscles of the bladder and increase bladder capacity²⁹. Drugs that mimic the mechanism of action of nitrous oxide include **sildenafil**, **tadalafil** and **vardenafil** and have been shown to be effective both for neurogenic bladder and erectile dysfunction.
- d. **Tamsulosin** can be used in conjunction with tadalafil to assist with voiding, decreasing residual urine volume and increase bladder storage capacity.
- e. **Botulinum injection** into either the detrusor muscle or urethral sphincter can be used when medications don't work. This can decrease overactivity in the detrusor muscle and increase bladder capacity and can be used in the urethral sphincter to assist in bladder emptying.
- f. **Desmopressin** can be used to decrease urine volume and is especially useful in treating excessive nighttime urination, while having the additional benefit of improving orthostatic hypotension, but given its high rate of hyponatremia and cognitive impairment, it is not recommended¹².

6) Sexual Dysfunction

Sexual dysfunction is a frequent and early symptom of MSA and can include erectile dysfunction, decreased libido, vaginal dryness and difficulties achieving orgasm. Erectile dysfunction (ED) is often the first symptom of MSA and is reported by 100% of patients with MSA.

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1. Non-pharmacologic treatment of sexual dysfunction include:
 - a. **Cognitive therapy** to treat underlying depression and anxiety that is common among MSA patients.
 - b. **Moderation of alcohol and tobacco use**, as excess use has been tied to ED.
 - c. Use of **vacuum pumps** to increase blood flow to the penis and allow an erection to be attained and maintained.
 - d. **Avoidance of medications** known to interfere with sexual function, including beta blockers, SSRIs and finasteride.
 - e. Surgical placement of a **penile implant** can also treat the symptom of ED.
 - f. **Vaginal lubricants** can be useful to combat the vaginal dryness often seen in women with MSA.

2. Medications used to treat sexual dysfunction include:
 - a. PDE-5 inhibitors, including **sildenafil**, increase blood flow to the penis and have been proven to treat ED in patients with MSA. Drops in blood pressure are an important side effect of this class of medication and in patients with OH, this may not be recommended²⁸.
 - b. Intracavernosal or intraurethral injections of the prostaglandin **alprostadil** and the vasodilator **papaverine** are also effective in achieving and maintaining erection.
 - c. Other drugs that have proven effective in the treatment of ED include **apomorphine**, which can be given either by under the tongue or as an injection into the penis.
 - d. Female sexual dysfunction can be treated with **hormonal therapy**.

7) REM Behavior Disorder

REM Behavior Disorder (RBD) is a condition that involves violent movements and nightmares during REM sleep. RBD has been reported in a vast majority of MSA patients, with a prevalence ranging from in 69% to 100% of MSA patients²⁸. RBD symptoms can often precede other MSA symptoms by years.

1. Non-pharmacologic treatment of REM behavior disorder include:

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- a. Ensuring **bedroom safety** to prevent injury includes lowering the bed, padding bedside furniture and removing firearms is an important aspect to managing RBD.
 - b. A **bed alarm** can also alert patients and caregivers when RBD causes patients to get out of bed.
2. Medications used to help with REM behavior disorder include:
- a. **Clonazepam**, a benzodiazepine, has been shown to reduce frequency and severity and prevent injury in RBD³⁰. Residual daytime sleepiness and headache are two side effects of clonazepam therapy, as well as possible worsening of sleep apnea.
 - b. **Melatonin**, a naturally occurring hormone secreted by the pineal gland, has been shown to improve REM sleep and decrease RBD-associated injuries with few side effects.
 - c. **Zopiclone** is a benzodiazepine that decreases sleep disturbances and has been used to treat RBD.
 - d. **Rivastigmine** and **donepezil**, cholinesterase inhibitors, has proven effective among patients who have not had improvement with either clonazepam or melatonin³¹.
 - e. **Pramipexole**, a dopamine agonist, has also been shown to improve RBD symptoms, although some studies have produced mixed results.

8) Psychiatric Issues

Many patients with MSA experience depression, anxiety, panic attacks, and cognitive impairment over the course of their disease. Depression has been found in over half (60%) of MSA patients and anxiety has been found in over 75%. Both are more common in patients with MSA-P and are tied to lower quality of life³². Cognitive impairment may also occur in up to 75% of patients.

1. Non-pharmacologic treatment of psychiatric issues include:
 - a. **Cognitive therapy** can not only help manage the mental health symptoms associated with MSA, it has also been shown to increase memory, help slow down cognitive decline, and decrease fall risk in patients with MSA³³.
 - b. **Exercise** has been shown to promote positive effects on cognitive function in patients with Parkinson's Disease and may promote positive cognitive effects in MSA patients, as well³⁴.
 - c. **Electroconvulsive therapy** is an option for patients with depression who have not responded to other treatment.
 - d. **Repetitive transcranial magnetic stimulation (TMS)** has been studied in patients with Parkinson's and has shown a positive effect on depression³⁵.

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2. Medications used to help with psychiatric issues include:
 - a. **Selective serotonin reuptake inhibitors** are effective anti-depressants and may have a lower risk of orthostatic hypotension than other drugs to treat depression.
 - b. **L-dopa or dopamine agonists** may also help mood disorders in MSA.

9) Breathing Problems

Patients with MSA can develop breathing problems as their disease progresses. These can include obstructive sleep apnea, low oxygenation, breathlessness and stridor. Stridor, or a high-pitched wheezing sound heard on inspiration, occurs in up to 40% of MSA patients and may be a predictor of poor disease outcome³⁶. Stridor occurs as a result of overactive vocal cord muscles that fail to relax normally during inspiration. It can occur any time of the day, but when it occurs during sleep can result in obstructive sleep apnea, which involves frequent periods during sleep when breathing stops. Breathing problems during sleep has been reported in 15%-37% of MSA patients³⁷.

1. Non-Pharmaceutical treatment of breathing problems

- a. The primary treatment of sleep apnea is the use of **continuous positive airway pressure (CPAP)** for patients with mild to moderate stridor and can be useful for symptomatic control, although its impact on survival is unclear³⁶. CPAP does not have good adherence by patients as MSA progresses due to discomfort³⁸.
- b. **Tracheostomy** is the recommended treatment for persistent and severe stridor and can be used in patients with advanced disease for stridor during wakefulness³⁶.



2. Medications for the treatment of breathing problems

- a. **Botulinum toxin** injected into the vocal cords has been studied as a treatment of stridor in MSA patients, but there is not enough evidence to be recommended³⁶.
- b. **Selective serotonin reuptake inhibitors (SSRIs)** have been thought to improve sleep disturbances in MSA, as serotonin induces sleep and throat relaxation during sleep. The combination of ondansetron and fluoxetine has been shown to reduce the severity of sleep apnea, but recent studies have found no difference in survival in MSA patients on an SSRI but was associated with higher rates of Parkinsonism and falls³⁹.

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10) Pain

Pain is an often-overlooked aspect of MSA, but it is very common. Studies have found that pain is reported anywhere from 50% to 80% in patients with MSA⁴⁰. Pain tended to be more common among MSA-P, as compared to MSA-C subtype.

1. Non-pharmacologic treatment for pain include:
 - a. **Exercise** and **physical therapy** are ways to help deal with the pain associated with MSA⁴⁰.
2. Medication for the treatment of pain include:
 - a. Dopaminergic medication, including **levodopa** and **pramipexole**, have shown promise for pain relief⁴⁰.

11) Neuroprotective Diet

Dietary modifications have been shown to provide neuroprotective effects and may hold promise for patients with MSA⁴¹. There have been connections between dietary patterns and risk of Parkinson's disease, but no large studies have been conducted in relation to MSA⁴². A neuroprotective diet is recommended by some physicians, including calorie restriction, which may increase an amino acid, glutamate, which is connected to motor control. Calorie-restricted diets have shown promise in Parkinson's disease, and may hold hope for MSA patients, as well⁴³.

Diets rich in foods that fight inflammation may also have a role in MSA treatment. Curcumin, the main component of turmeric spice with proven anti-inflammatory effects, has been found to improve symptoms in mice with similar molecular changes as seen in MSA, but has yet to be proven in humans⁴⁴. Other anti-inflammatory dietary patterns, including diets high in fruits and vegetables, have been tied to regression in many diseases. A Mediterranean diet has been connected to a decreased risk of Parkinson's disease, and may also confer protective effects in MSA^{42,45}. Recently, an association between decreased coenzyme Q10 and the severity of motor symptoms in MSA has been found. This may provide further support of a diet rich in antioxidants may prevent or slow the progression of this disease^{46,47}.

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