CONVENTIONAL AND HERBAL APPROACH IN MANAGEMENT OF MULTIPLE SCLEROSIS – AN OVERVIEW

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ABSTRACT

Multiple sclerosis (MS) is an auto- immune, neuro- inflammatory disease which interfere with the central nervous system and damage the myelin sheath and axons. It is interceded via auto-receptive lymphocytes that cross the blood cerebrum obstruction cause aggravation, demyelination and axonal misfortune upset the interchanges between the neurons.The exact cause of the MS is not known but it is reported that it may be due to the genetic, environmental factors, viral infections (Epstein Barr virus). There are various approaches for the management of Multiple sclerosis like disease modifying agents are mainly used. Some of the monoclonal antibodies (Ocrelizumab) are approved recently for the management of MS. Due to various unwanted side effects with conventional medicines people are eager to use cost effective medicines with no or less side effects; therefore herbal medicines are best choice for them, they works by different pharmacological actions like reduce oxidative stress, anti-inflammatory, antioxidant effects and others. Mainly used herbal plants like Ginkgobiloba, Salvia officinalis, Nigella sativa.

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Keywords: Multiple sclerosis, autoimmune, DMTs, Herbal plants

INTRODUCTION

Numerous sclerosis is an ongoing and reformist immune system, incendiary, neurologicaldisease of the CNS.It destroysthe myelin sheath and axons to the varying degrees[1]. It is characterized by inflammation, selective demyelination and gliosis.It focuses on the Focal sensory system and it is interceded via auto-responsive lymphocytes that cross the blood mind obstruction. These lymphocytes enter the Central Nervous System and cause nearby irritation bringing about demyelination and axonal misfortune; by harming the defensive covering of the nerve axons (myelin sheath)cause correspondence issue between your mind & rest of your body [2]. According to World Health Organization Multiple Sclerosis affects approximately 2.8 million people worldwide, and multiple sclerosis affects the people age between 20-50 years old & it is investigated that females are more prone to the multiple sclerosis than males[3]. The multiple sclerosis characteristic features are common vision loss, pain, fatigue, and impaired coordination, low close to home movement related self-viability, limit of self-administrative ideas, socio-segment factors limitations, decay work state, and decline instructive level[4].Individuals with different sclerosis may likewise create; muscle solidness or fit, loss of motion ordinarily in the legs, issues with bladder, inside, sexual capacities, mental changes discouragement epilepsy.The reason is obscure, however, it seems to include a blend of hereditary elements and non-hereditary factors like ecological components, infection, Digestion that together outcome in a self-supporting immune system problem that prompts intermittent safe

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framework assaults on the focal sensory system[5]. All the Various Sclerosis medicines attempt to endeavor to improve the neuronal capacity following Different Sclerosis happens and stop any movement of the illness. The utilization of Numerous Sclerosis medicines in the beginning phase of Various Sclerosis can prompt antagonistic results and can be incapable by any means. The medicines with great outcomes are seen in young person ladies where Various Sclerosis shows up right on time with backsliding type with not many neurons harmed. Numerous Sclerosis diminishes existence with a normal 5–10 years than other solid ones. There are numerous medicines and symptomatic strategies of Various Sclerosis are presently improvement[3].

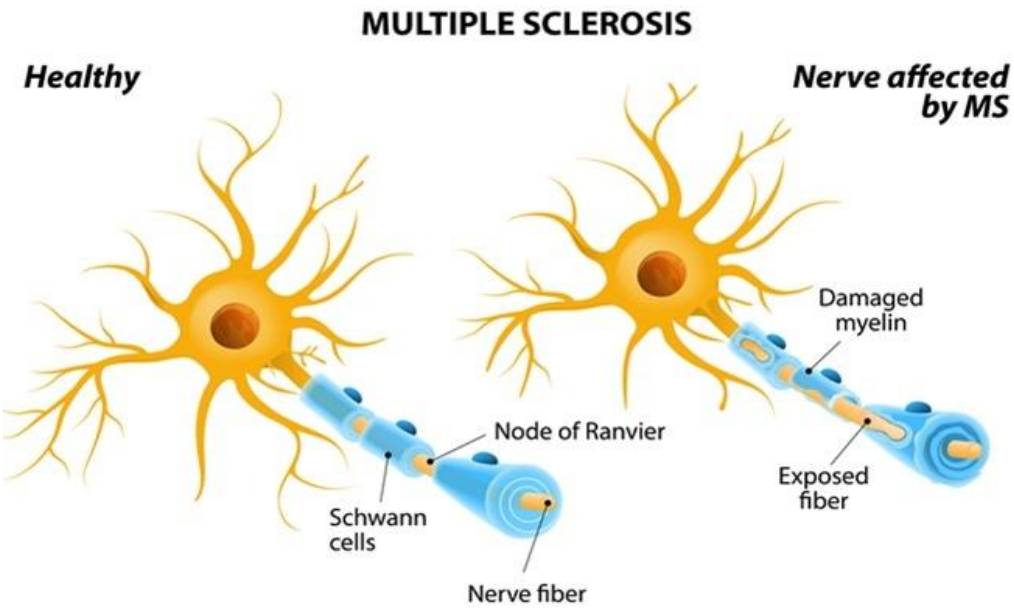

Fig. 1. Image of multiple sclerosis

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Neurologists agree thatpatients might be assembled into four significant classes dependent on the course of disease; the

Table 1: following table shows the categories of Multiple Sclerosis [6].

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Types	Clinical features
Relapsing/Remitting Multiple Sclerosis (RRMS)	Relapses followed by incomplete remissions, during relapses, symptoms can get more severe

Secondary Progressive Multiple Sclerosis (SPMS)	Gradual progression of symptoms and disability over time following a period of RRMS
Types	**Clinical features**
Primary Progressive Multiple Sclerosis (PPMS)	Gradual, progression of symptoms from initial presentation
Progressive Relapsing Multiple Sclerosis (PRMS)	Gradual symptoms progression over time accompanied by acute attacks of undesired effects

CAUSES

The exact cause of the multiple sclerosis is unknown but some of the investigations shows that it may be due to the genetic and environmental factors some other cause are such as viral infections. Most of the studies suggest that multiple sclerosis is immune-genetic viral disease with Epstein Barr Virus[7].

Risk factors are age (most of the time between 20-50 years old), sex (females are more prone to multiple sclerosis than males), family history (genetic susceptibility), certain viral infections like EBV, vitamin D deficiency[8].

Some other risk factors like climate (more in cold areas), autoimmune diseases (higher risks with thyroid diseases, type 1 DM, and IBS), smoking, stress, fatigue, physical injury.

PATHOPHYSIOLOGY

Because of etiological elements enacted Lymphocytes (perceive self-antigen) acquire section into the mind by means of disturbance in the blood cerebrum obstruction and macrophages (B cells) goes into the mind from fringe course, creation of fiery cytokines and free extreme species than actuated B cells and White blood cells causes demyelination and annihilation of oligodendrocytes and harm the resistant framework; oligodendrocytes are the phones which are liable for myelination of axonal nerves now without oligodendrocytes there's no more myelination to the axon. Development of plaque cause scarring and annihilation of sheath it further interfere with the transmission of motivations. Demyelinated axons dispersed sporadically all through the CNS. The most habitually influenced territories are the optic nerves, frontal cortex, cerebrum stem, cerebellum, and spinal rope.

On beginning phases oligodendrocytes can mend and re-myelination of the axons happens however over the long haul re-myelination will pause and harm will get perpetual or irreversible with loss of axons[9, 10, 11].

CURRENT TREATMENT

There is as of now no remedy for Different Sclerosis. The target of the medications are to stifle the resistant reaction moderate sickness movement, limit backslides, decline long haul neurologic debilitation, and oversee indications while restricting unfriendly responses. Infection adjusting treatments examined underneath are endorsed for RRMS. Different sorts of MS are commonly treated with similar medications, chemotherapy, anti-inflammatory drugs, monoclonal antibodies, immunosuppressive drugs and corticosteroids are mainly used for the management of multiple sclerosis[12].

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Table 2: The following is the table of FDA approved disease modifying drugs with their mode of action, indications, route of administration and dosing frequency of the drug[13, 14, 15]

Drugs name	**Mode of action**	**Indications**	**Route of administration and dosing frequency**
Ocrelizumab	Anti-CD20 mAb	First line for RMS, PPSM	IV infusion, every 6 months
Ofatumumab	"Anti-CD20 mAb"	First- line for RMS	"SC- injection, every 4 weeks"
Natalizumab	"a4b1 integrin inhibitor"	Second- line for RMS	"IV infusion, every 4 weeks"
Alemtuzumab	"Anti-CD52 mAb"	First line RMS	"IV infusion, once daily"
Mitoxantrone	DNA intercalator	Second line for RMS and SPMS	"IV infusion, every month or 3 months"
Fingolimod	"Sphingosine-1-phosphate inhibitor"	Second- line RMS	"Oral, once daily"
Siponimod	"Sphingosine 1-phosphate receptor modulator"	First line "CIS, RMS, SPMS"	"Oral, once daily"
Ozanimod	"Sphingosine 1-phosphate receptor modulator"	SPMS, 'CIS', 'RMS'	"Oral, once daily"

Dimethyl fumarate and diroximel	“Nuclear factor (erythroidderived 2)−like 2 pathway inhibitor”	Firs-t line for RMS	“Oral, twice daily”
Cladribine	Not fully known	Second line for RMS	“Oral, 4-5 days over 2-week treatment courses”
Teriflunomide	“Dihydroorotate dehydrogenase inhibitor”	First- line for RMS	“Oral, once daily”
Drugs name	**Mode of action**	**Indications**	**Route of administration and dosing frequency**
Glatiramer acetate	Activates T lymphocytes suppressor cells	First line for RMS	“SC- injection, once daily or 3 times weekly”
Interferon β-1a (avonex, rebif)	Suppress expression of inflammatory cytokines	First line RMS, CIS	IM injection, once weekly SC injection, 3 times weekly
Peginterferon β-1 (plegridy)	Suppress expression of inflammatory cytokines	First line RMS, CIS	SC injection every 2 weeks
Interferon β-1b (betaseron)	Suppress expression of inflammatory cytokines	First line RMS, CIS	SC injection every other day after initial dose

Treating Progressive Multiple Sclerosis[16, 17]

Secondary Progressive Multiple Sclerosis:

Siponimod44 is a particular S1P modulator that is endorsed for backsliding types of Various Sclerosis, including dynamic SPMS, which means patients with optional reformist multiple,Ocrelizumab, cladribine, and diroximelfumarate can likewise be utilized for patients with dynamic Auxiliary reformist different sclerosis.

Primary Progressive Multiple Sclerosis:

Ocrelizumab is the only approved DMTs for the management of Primary Progressive Multiple Sclerosis. Dosing is the same as for Relapsing Multiple Sclerosis. Ocrelizumab diminishes movement of clinical inability by roughly one-quarter, and improves other clinical and X-ray markers of fiery and degenerative sickness action in this populace.Some other drugs which are used in multiple sclerosis such as Immunosuppressive agents like azathioprine, methotrexate, cyclophosphamide, other such as Corticosteroids like Methylprednisolone and physical therapy.

Symptomatic treatment [18, 19]

Dalfampridine is a FDA approved drug which used to improve walking in people who have multiple sclerosis, it works by blocking the potassium channels on the surface of nerve fibres.

HERBAL APPROACHES FOR THE MANAGEMENT OF MULTIPLE SCLEROSIS

Nowadays peoples are eager to use treatment which must be cost effective and with lesser adverse effects. Herbal medicines have lesser side effects or no side effects as compared to conventional drug therapies. Upon several investigations it is reported that There are so many medicinal plants which contain different active constituents like flavonoids, alkaloids, saponins, essential oils, tannins etc; belongs to specific families like araliaceae, zingiberaceae, umbelliferae; have the potential to treat or decrease the progression of multiple sclerosis examples like Ginkgo biloba, Salvia officinalis, Cannabis spp., Crocus sativus, Vitisvinifera. These medicinal plants works by different mode of actions like anti-inflammatory effects, antioxidant effects, reduce oxidative stress, free radical scavenging activity and other mechanisms. [20, 21, 22]

Table 3: The following is the list of medicinal plants those have an potential to treat Multiple Sclerosis's patient or decrease the progression of MS:

Commonname	Biologicalsource Family	Activeconstituents	Pharmacological actions	References
Ginkgo	*Ginkgo biloba* Ginkgoaceae	Flavonoids like quercetin, kaempferol and diterpene lactones like ginkgolides	It improves blood flow, reduce oxidative stress, free radicals scavenging activity, less fatigue, improve cognitive functions	[23]
Ginger	*Zingiberofficinale* Zingiberaceae	Phenolic compounds, volatile oils, sesquiterpenes(bisapolene, zingiberol)	Decrease inflammation, anti-inflammatory effects, antibacterial	[24, 25]

Turmeric	*Curcuma longa* zingiberaceae	Flavonoids, and other polyphenolic compounds like curcuminoid (curcumin)	Antioxidant, antimutagenic, antimicrobial, neuroprotective effects	[26, 27]
Klamathweed	*Hypericumperforatum* Hypericaceae	Flavonoids like quercetin, quercitrin, and tannins, essential oils	Free radical scavenging activity, block lipid peroxidation, antioxidant activity	[28]
Common name	**Biological source family**	**Active constituents**	**Pharmacological actions**	**References**
Valerian	*Valerianaofficinalis* Caprifoliaceae	Alkaloids, terpenes, organic acids, flavones	Gentle sleep aid, antianxiety, show their actions by binding to the GABA-A receptor	[29]
Black cumin	*Nigella sativa* Ranunculaceae	Seed oils (p-cymene, limonene), thymoquinone and flavonoids	Anti-inflammatory, antioxidant, anticholinergic property, enhance remyelation in the CNS	[30, 31]
Ginseng	*Panax ginseng* Araliaceae	Saponins (ginsenosides), phytosterol, carbohydrates	Neuroprotective actions, enhance immunity and CNS activity	[32, 33]
Evening primrose	*Oenotherabiennis* Onagraceae	Fatty acids, phenolic acids, and flavonoids	Anti-inflammatory effects. Anti-asthmatic effects	[34]
Marijuana	*Cannabis spp*. Cannabaceae	Cannabinoids, tetrahydrocannabinol	Reduce neuroinflammatorysignaling, reduce spasticity and pain	[35]

Grapes	*Vitisvinifera* Vitaceae	Tannins (catechin, epicatechin and others), flavonoids and procyanidins	Anti-inflammatory effects, antioxidant activity, improve cognitive functions	[36, 37]
Sudanese frankincense	*Boswelliapapyrifera* Burseraceae	Essential oils like alpha pinene, limonene, and n-hexyl acetate	Improve visuopatial memory of MS patients	[38]
Common names	**Biological source Family**	**Active constituents**	**Pharmacological actions**	**References**
Saffron	*Crocus sativus* Iridaceae	Volatile oils, tannins, terpenes	Decrease inflammation, cytotoxic effects	[39]
Sage	*Salvia officinalis* Lamiaceae	Monoterpenes, flavonoids (apigenin), phenolic acids,	Anti-inflammatory effects, antioxidant, improve cognitive functions	[40]

Conclusion

Multiple sclerosis is an autoimmune disorder that mainly attacks on the central nervous system at different locations. It damage the protective myelin sheath and axons; affects the communication between the neurons. Females are more prone to MS than males. The exact cause of MS is unknown, but according to several reports it may be due to the genetic, environmental factors, viral infections; Epstein-Barr virus. Till now there is no cure for MS and there are various synthetic FDA drugs, monoclonal antibodies which may usedfor the management of Multiple sclerosis. But due to the undesirable side effects of the synthetic medicines peoples are eager to use cost effective medicines with no or less side effects therefore herbal medicines are best choice for them because herbal medicines have no adverse effects or less side effects as compared to that of conventional medicines. They works by different pharmacological actions like anti-inflammatory, antioxidant, reduce oxidative stress and others.

Comment [DS27]: This paragraph is present at the start of the review

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