Cleveland Clinic

Mellen Center Approaches: Identifying and managing depression in MS

Framework: Depression is a common co-morbidity in the MS population. It affects quality of life and correlates with worsened disease outcome. Our approach is to try to systematically identify and treat this problem early and effectively.

How frequent is depression in the MS population?

The frequency of depression varies depending on the targeted population, the measure used, and the time frame evaluated. In large population studies the prevalence of major depression varies between 26 and 51%. There have been consistent results showing a very high prevalence in the MS population. Best estimates of the 30 day prevalence of major depression in the general population are about 3% (Wilhelm), and in rheumatoid arthritis patients depression appears in about 15%. Depression is therefore common and of significant interest in patients with MS.

RESOURCES:

Sadovnick AD et al. Depression and multiple sclerosis. Neurology 1996;46:628-632

Wilhelm K, Mitchell P, Slade T et al. Prevalence and correlates of DSM-IV major depression in an Australian national survey. J. Affective disorders 2003;75:155-162

Pincus T, Griffith J, Pearce S, Isenberg D. Prevalence of self-reported depression in patients with rheumatoid arthritis. Brit. J. Rheum. 1996;35:879-883

Q. Do interferons used for MS treatment cause or worsen depression?

Initial interest in this issue came about with case reports of an excess suicide risk in the pivotal trial of interferon beta 1b. These initial reports have not been fully substantiated in further research. For example, Patten (2002) analyzed trials data of interferon beta 1a SC TIW and showed no excess of depression in those treated vs. those on placebo. Feinstein (2000) reviewed the existing literature systematically and felt it was premature to conclude that disease modifying agents were associated with depression. Patten (2008) also studied the IMS Canada database and did not find a difference in antidepressant use in interferon beta treated patients and those on copaxone.

Patten (2008) advised vigilant population oversight with screening and ascertainment. When initiating interferons we watch closely for the emergence of depression, but at the present time depression is not an absolute contraindication to the use of these agents.

At the Mellen Center we are cautious about instituting interferon therapy in patients with ongoing depression, and often tend to try glatiramer acetate in this population first. If their depression is under good control we would consider interferons if indicated for their MS.

RESOURCES:

Feinstein A. Multiple sclerosis, disease modifying treatments and depression; a critical methodological review. Multiple sclerosis 2000;6:343-348

Patten SB, Metz, LM. Interferon beta 1a and depression in secondary progressive MS: Data from the SPECTRIMS trial. Neurology 2002;59:744-746

Patten SB. Psychiatric side effects of interferon treatment. Curr Drug Saf. 2006;1:143-150

Patten SB, Williams JV, Metz LM. Anti-depressant use in association with interferon and glatiramer acetate treatment in multiple sclerosis. Mult Scler 2008;14:406-411

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Are there any medicines used in MS patients other than interferons which might affect mood negatively?

Beside the interferons, corticosteroids can have varying effects on mood and sometimes can cause depression. Usually irritability, anxiety and insomnia are the more common behavioral effects. Rarely steroids can cause psychotic behavior. Anticholinergics, sleeping medications, beta blockers, and sometimes anti spasticity medicines such as lioresal can alter mood negatively. All medicines should be evaluated for this potential.

What is the correlation between depression and quality of life?

Depression has a strong correlation with quality of life in the MS population (Mitchell 2004). A study of the NARCOMS registry, which is a self-report registry for patients with MS (Marrie 2009) found that depression was reported by 46% of respondents. Another 16% had scores on CESD (Center for Epidemiologic Studies Depression Scale) ≥21 suggesting undiagnosed depression. In this population the presence of depression correlated with lower socioeconomic status. In a study in a VA population (Williams 2005) depression was independently associated with increased service utilization and increased participation limitations. We note that fatigue is a major co-morbidity in MS and may be an indication of depression, sleep disorder, or related to the MS process itself.

RESOURCES:

Marrie RA et al. The burden of mental co morbidity in multiple sclerosis. Multiple Sclerosis 2009;15:385-92

Williams RM et al Neurology 2005;64:75-80

How should we ascertain depression in an MS patient?

Major depression is a disorder characterized by the presence of 5 of the following symptoms for at least two weeks:

- A depressed mood for most of the day /most days
- A loss of pleasure or interest in ones usual activities (anhedonia)
- Sleeping problems
- Fatigue
- Psychomotor retardation or agitations
- Reduced appetite with weight loss or the opposite
- A negative self-image
- Feelings of guilt or self –blame
- Reduced concentration
- Thoughts of death, suicidal thinking

In the MS population definitions of depression may be difficult as some of these cardinal symptoms can be caused by the MS itself and not depression (e.g. sleeping problems, fatigue, reduced concentration) There are problems related to studies ascertaining depression in this population related to lack of blinding, selection, diagnostic criteria, and selection of appropriate control groups (Schiffer 1990). In addition, Minden and Schiffer (1991) have identified that DSM-IV criteria may not be the only appropriate criteria for diagnosing depression in MS, they demonstrated that depression in MS patients includes symptoms such as anger, irritability, worry, and discouragement, which are not symptoms associated with MDD in the DSM-IV.

At the Mellen Center we have adapted the PHQ-9 survey for our patients. This is a validated scale using 9 criteria for depression rating each on a 0-3 scale. We administer it via computer consoles in our center, but it can be administered as a simple paper check off sheet. It has been validated in primary care and obstetrical clinics but not for the MS population. Construct validity was shown compared to self reported sick days, clinic visits, symptom related difficulty and the Short-form General Health Survey. Levels of depression correlate well with PHQ-9 scores in this population:

- 0-4 minimal
- 5-9 mild
- 10-14 moderate
- 15-19 moderately severe
- 20-27 severe

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We studied the correlation between PHQ-9 and ICD-9 codes in our MS population and found a strong correlation between higher PHQ-9 scores and the presence of psychiatric ICD-9 codes.

While other screening tests are available, we have found this useful in our population.

We note that other neurological issues can look like depression in this population. These include pseudobulbar affect, patients with chronic pain, patient with frontal lobe irritability, dementia, and abulia, and patients with severe MS related fatigue. These other possibilities need to be considered in the MS population. When the differential is unclear we consider neuropsychological assessment to assist us.

We also note the high prevalence of anxiety disorders in the MS population as well as the presence of adjustment disorder in this group of patients, both of which may need to be addressed.

RESOURCES:

Kroenke K, et al. The PHQ-9. J Gen Int Med 2001;16:606-613

Minden SL & Schiffer B (1991). Depression and mood disorders in multiple sclerosis. Neuropsychiatry, Neuropsychology, & Behavioral Neurology, 4(1), 62-77

Q: Would we consider any testing in patients with MS and depression?

Other than standard MS diagnostic testing and monitoring, we would consider testing for hypothyroidism or hyperthyroidism, altered electrolytes and calcium, anemia, and low vitamin D levels.

What is the risk of suicide in the MS population?

The rate of suicide varies between studies, but all are consistent in showing an excess rate of suicide compared with age matched controls in the population studied. Sadovnick et al (1991) surveyed deaths from 2 MS clinics in Canada, and found that of these 28% were due to suicide. They concluded that there was a 7.5 x greater rate of suicide than in age matched controls. This study is subject to bias since it is based on MS center populations. Brønnum-Hansen (2005) performed a full population study of Danish mortality figures on all patients diagnosed with MS between 1953 and 1966. They showed 115 suicides vs. an expected 54 suicides representing an excess rate of 2.1 with a slightly higher rate in the first year and a steady rate after that over up to 40 years. This second study probably provides a better estimate of population risk of suicide.

RESOURCES:

Brønnum-Hansen H, et al. Suicide among Danes with multiple sclerosis. JNNP 2005;76:1457-1459

Sadovnick AD et al. Cause of death in patients attending multiple sclerosis clinics. Neurology 1991;41:1193-6

How do we ascertain and manage patients at immediate risk of suicide?

At the Mellen Center we specifically inquire about depression and suicidal risk each visit. If we identify a patient at risk, we assess what the risk may be. Some questions that can be used for this include “Have you felt that life is not worth living?”, “How close to acting on thoughts of suicide are you?”, and “What would you do if you had thoughts of suicide?” If the patient appears at high risk we will contact one of our affiliated health care providers who deals with these issues. If not available we either see if the patient can be seen immediately in the psychiatry department or failing this be assessed in the emergency room.

If antidepressants are used, what antidepressants should be used in MS patients?

There are few randomized blinded trials of antidepressant therapy in the MS population. Schiffer (1990) studied desipramine in 24 patients with MS in a double blinded trial with psychotherapy. There was a trend to ‘modest benefit’, but this study was likely underpowered to show an effect. Ehde (2008) did a parallel, placebo controlled, double blinded study of paroxetine in 42 patients and showed a reduction of depression as measured by the Hamilton depression rating scale vs. controls but with a non significant P value. There is therefore little evidence guiding treatment decisions in this population. Mohr et al (2001) compared sertraline, cognitive behavioral therapy and supportive-expressive therapy in 63 MS patients and found superior efficacy on various measures using sertraline or CBT.

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At the Mellen Center we evaluate other comorbid factors when deciding on antidepressant therapy *(See table)*. This helps guide the selection of antidepressants.

Medication	Population to consider in	Use caution:
SSRIs	Any MS	If on other serotonergic medications
SNRIs	Any MS	
Patients with migraine or neuropathy	If on other serotonergic medications	
TCAs (eg amitryptiline, nortryptiline)	Sleep disruption, neuropathic pain, nocturia	Cognitively impaired, diabetic, avoid in cardiac disease, patients with urine retention
duloxetine	Neuropathic pain	
bupropion	Smokers wishing to quit	Patients at risk for seizures
Not first line, not useful for anxiety component		

We tend to start these medicines at low doses, slowly titrating them to efficacy or intolerance. We carefully monitor for side effects.

RESOURCES:

Goldmann Consensus group. Goldmann Consensus statement on depression in MS.Mult Scler 2005;11:3328-337

Mohr DC, Boudewyn AC, Goodkin DE, et al. Comparative outcomes for individual Cognitive-Behavior Therapy, Supportive-Expressive Group Psychotherapy, and Sertraline for Treatment of Depression in Multiple Sclerosis. J. Consulting and Clinical Psychology 2001;69:942-949

Schiffer RB, Wineman NM Antidepressant pharmacotherapy of depression associated with multiple sclerosis. Am J Psychiatry. 1990;147:11

Do we use other medicines for depression?

In some patients with depression anxiety is a major cofactor. Most of the antidepressants have an anxiolytic component. The addition of a low dose benzodiazepine may be beneficial but side effects of sedation and habituation have to be considered.

If patients have a significant bipolar history we refer them to psychiatry for further management.

What is the role of health psychology in this population?

Health Psychology is an outpatient behavioral medicine clinic intended to help MS patients with MS related psychological conditions. Health psychology services at the Mellen Center are most actively used in the following situations: 1) Adjustment and coping with the diagnosis and associated fears, 2) Family and couples adjustment issues, including caregiver burnout and communication issues, 3) Non-compliance to treatment regiment, 4) Needle anxiety or phobia, 5) Pain management related to MS, 6) Wellness principles, 7) Fatigue and energy conservation, 8) MS related mood disorders, 9) and Relaxation skills Training.

Several treatment modalities are employed in the treatment of the above conditions. The effectiveness of Cognitive Behavioral Therapy has been well examined in the literature and thus several of the CBT principles are utilized in our treatment. In addition, behavioral strategies, such as relaxation training, assertiveness training and fear hierarchies are appropriately utilized for pain management, couples therapy, needle phobia and assertiveness. Lazarus and Folkman's coping literature is utilized, Motivational Interviewing, as well as methods from interpersonal theories. The goals of health psychology are appropriate coping and

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adjustment to MS and the disease process, improved functioning in several domains, and emotionally and physically healthy lifestyles.

Referrals to health psychology should optimally be for patients with adjustment disorders, recent depression, both of which are more amenable to the presently available therapies. Patients with issues of abuse, long standing depression, or concurrent drug and alcohol abuse issues are better served by appropriate referrals to psychiatry and addiction medicine.

Key Numbers:

National Suicide Hotline: 1-800-273-TALK (8255)

National MS Society: 1-800-667-7131

REFERENCES:

Larcombe, NA & Wilson, PH (1984). An evaluation of cognitive-behavioral therapy for depression in patients with multiple sclerosis. British Journal of Psychiatry, 145, 366-371.

Howard I, Turner R, Olkin R & Mohr DC (2006). Therapeutic alliance mediates the relationship between interpersonal problems and depression outcome in a cohort of multiple sclerosis patients. Journal of Clinical Psychology, 62(9), 1197-1204.

Mohr D & Cox D (2001) Multiple Sclerosis: Empirical literature for the clinical health psychologist. Journal of Clinical Psychology, 57(4), 479-499.

Lazarus RS & Folkman S (1984). Stress, appraisal and coping. New York: Springer Publishing Inc.

Rollnick S, Miller WR & Butler CC (2008). Motivational interviewing in a health care setting: Helping patients change behavior. New York: Guilford

Klerman GL, Weissman MM, Rounsaville BJ, Chevron ES (1984). Interpersonal psychotherapy of depression. New York: Basic Books