

ASSESSMENT AND MANAGEMENT OF MAJOR DEPRESSIVE DISORDER IN OLDER ADULTS

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SUMMARY

Background: Major depression disorder (MDD) is one of the most common mental disorders world-wide and is prevalent throughout the lifespan, with prevalence estimates of 1-5% in those 65 years of age and older.

Methods: The aim of this mini-review is to briefly summarize clinically relevant topics within the domain of later-life MDD.

Results: The mini-review presents an overview of epidemiology, complications of late life MDD, risk factors and clinical presentation, clinical assessment, general issues relevant to the treatment of the older adult with MDD, drug treatments, discussion of how medical complexity affects drug treatment and other treatment modalities.

Conclusion: The mini-review concludes with a short discussion of clinical and research implications. Treatment of depression in the geriatric population is a complex endeavor and clinicians often are faced with medical, social, and environmental issues which can impede the treatment process. Antidepressant drugs, particularly the SSRI and SNRI antidepressants are helpful, but dosing titration needs to be considered against the backdrop of comorbidity and concomitant medications. Psychotherapy and other approaches are additional avenues to consider in the older individuals with MDD. Future research in particular needs to address older people with more extensive medical complexity as well as the "oldest-old", individuals in their 80's and beyond.

Key words: major depressive disorder – elderly – geriatric - mood disorders - antidepressant medications

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BACKGROUND

According to the World Health Organization (WHO), the global population is ageing so rapidly that between 2015 and 2050, the proportion of the individuals over the age of 60 years will nearly double, from 12% to 22% (WHO <http://www.who.int/mediacentre/factsheets/fs381/en/>).

Additionally, due to advances in preventative and medical care, individuals with chronic or recurrent mental disorders are expected to live longer than has been the case in the past and there will an increase in absolute numbers of older adults with chronic mental health conditions. Major depression disorder (MDD) is one of the most common mental disorders world-wide and is prevalent throughout the lifespan, with prevalence estimates of 1-5% in those 65 years of age and older (Fiske et al. 2009). The aim of this mini-review is to briefly summarize clinically relevant topics within the domain of later-life MDD.

SOURCES OF DATA AND METHODS

The authors (2 geropsychiatrists and a consultation-liason psychiatrist) summarized key topics of relevance to clinical practitioners. The mini-review presents an overview of epidemiology, complications of late life MDD, risk factors and clinical presentation, clinical assessment, general issues relevant to the treatment of the older adult with MDD, drug treatments, discussion of how medical complexity affects drug

treatment and other treatment modalities. The mini-review concludes with a short discussion of clinical and research implications.

RESULTS

Overview of epidemiology

Prevalence is higher for older patients in long-term care facilities, with rates up to 14.4% (Teresi 2001). Late-onset MDD, characterized by disease onset after 60-65 years of age, accounts for at least half of depressive cases in older adults (Aziz & Steffens 2013, Fiske et al. 2009). It is important to keep in mind that MDD represents a minority of depressive syndromes in older adults. Depressive syndromes that do not meet the criteria for MDD, are estimated to be prevalent in 7.2-20% of community dwelling older adults (Morichi et al. 2015). There is only limited data on MDD course in the oldest-old (individuals in their 80s and beyond) (Stek et al. 2006).

Complications of late life MDD

A serious complication of late life depression is suicide, with depression being the predominant risk factor for suicide in this age group (Blazer 2003, Conwell & Brent 1996, Conwell et al. 2002). Rates of completed suicide increase in old age and lethality of attempts increases (Hawton & van Heeringen 2009). Non-suicide mortality rates, particularly in those with cardiovascular

disease, are also increased in these older adults (Aziz & Steffens 2013). Another important consideration is the association between late-life depression and dementia. Studies have identified late life depression as a risk factor for dementia, particularly in those with co-occurring cognitive deficits. Of note is a study that found those with dementia syndrome of depression to be 4.69 times more likely to develop irreversible dementia than those with depression alone at 3 year follow-up (Alexopoulos et al. 1993). Studies have also suggested that late life depression represents a prodromal phase of dementia (Aziz & Steffens, 2013). Furthermore, total health care costs may be 43-52% higher in depressed versus non-depressed older patients (Katon et al. 2003).

Risk factors and Clinical presentation

It is important to identify those at risk for late life depression so that targeted assessment can be initiated. A large meta-analysis of 20 studies (23,000 subjects), found female gender, sleep disturbance, disability, prior depression, and bereavement to be significant across all categories of risk factors (Cole & Dendukuri 2003). If risk factors for or symptoms of depression are identified, screening tests for depression such as the GDS, PHQ-9, HAM-D and BDI are useful in confirming the presence of depression. These have been validated for use in geriatric patients (Glover & Srinivasan 2013).

The clinical identification of late-life MDD is often sub-optimal due to different phenomenology than younger counterparts, reluctance to report symptoms, attributing symptoms to medical illness, cognitive decline and assumption that observed changes are “normal” with aging (Morichi et al. 2015). Compared to younger counterparts, older patients are more likely to present with cognitive changes, specifically in the areas of executive dysfunction, cognitive processing speed and memory (Morimoto et al. 2015). Somatic features such as weight loss, constipation, early morning awakening, fatigue and pain can be more commonly seen in the elderly, while younger patients may be more likely to voice dysphoria, guilt and anhedonia (Hegeman 2012, Gillin et al. 1981).

Clinical assessment

The psychiatric diagnostic interview is similar to that used for younger adults, however there are important differences. Often older adults present with family members or caregivers, thus it is important to spend time alone with the patient to discuss sensitive topics and to allow the patient to speak freely. Collateral information is particularly important for those with cognitive impairment or poor insight into illness (Silver et al. 2004). Functional assessment should include activities of daily living (ADLs) such as dressing, bathing, etc. in order to recommend the appropriate level of care. Office-based cognitive examination should be performed at the initial visit, even if solely to establish a cognitive baseline. If cognitive deficits are found, sorting out if those deficits indicate an underlying cognitive disorder versus dementia

syndrome of depression can be challenging. Other common diagnostic considerations include mood disorders secondary to general medical condition, substance induced mood disorder, bipolar disorder, other forms of depression such as minor depression or persistent depressive disorder, bereavement and adjustment disorders (Glover & Srinivasan 2013). Screening for anxiety is prudent as prevalence of anxiety disorders in older adults with depression approaches 50% (Fiske et al. 2009).

Treatment of the older adult with MDD

Treatment of depression in the geriatric population is a complex endeavor and clinicians often are faced with medical, social, and environmental issues which can impede the treatment process. Multiple modes of treatment may be necessary in order to effect adequate response.

Psychopharmacologic treatment of depression in the elderly can be challenging. Older patients often have more medical conditions than younger patients. As such, they are more likely to have multiple providers, incoordination of care, and polypharmacy (potentially leading to drug-drug interactions) as compared to younger peers. Various medical conditions, including diabetes mellitus, cardiovascular disease, and cerebrovascular disease, all have been associated with increased rates of depression (Aziz & Steffens 2013, Park & Reynolds 2015). Socially, older patients may be more reticent to see mental health providers as compared to younger patients, having experienced decades of social stigma preventing them from seeking care. Other issues, such as losses of friends, family, homes, dignity, independence, also can contribute to low mood states (Aziz & Steffens 2013). Finally, elderly patients may have environmental challenges such as inadequate access to transportation for medical appointments and pharmacies (to say nothing of grocery stores, houses of worship, and other destinations) so their access to care and therapeutic interventions may be limited (Aziz & Steffens 2013).

Drug treatments

Research evidence for depression treatment in the elderly is relatively limited (Mulsant et al. 2014). However, studies such as IMPACT, PROSPECT, and MANAS focused on elderly patients, in order to determine best practices (Hall & Reynolds 2014). It is commonly advised to avoid TCA and MAOI medications in elderly patients, for reasons of tolerability, serious side effects, and potential for drug-drug interactions. Antidepressants in the SSRI (escitalopram, sertraline, etc) and SNRI categories (venlafaxine, desvenlafaxine, duloxetine, etc) are considered to be safer choices, with other antidepressants such as bupropion and mirtazapine also deemed reasonable. One group recommends utilizing a depression treatment algorithm *regardless* of specific psychiatric symptoms, medical comorbidities, and the desire to avoid specific side effects (Mulsant et al. 2014). The SSRI and SNRI antidepressant drugs are widely used first line agents in geriatric depression

(Frank 2014, Franck 2013, Kok et al. 2012). A review of online databases including MEDLINE, EMBASE, International Pharmaceutical Abstracts, and CINAHL which focused on the SNRI drugs compared 15 studies involving venlafaxine (n=10) and duloxetine (n=5) in geriatric depression (Franck 2013). Overall, the review found venlafaxine and duloxetine appear to be similar in efficacy and tolerability in treating late life MDD, however, venlafaxine may have fewer drug interactions and has been well-studied in the elderly (Franck 2013). Recent work has also noted stimulant drugs and adjunct atypical antipsychotics (Lavretsky et al. 2015, Lenze et al. 2015) as important additions to the treatment armamentarium for late-life MDD.

How medical complexity impacts drug treatment

Patient sensitivity to side effects may be elevated in the elderly, both from medication interactions and because somatizing of emotions and experiences (perceiving physical sensations strongly and negatively) is not uncommon in patients of advanced age (Hegeman et al. 2015). Thus, starting antidepressant dosing at half the recommended starting dose is reasonable, to maximize tolerability (Frank 2014).

Remaining cognizant of properties of medications (such as anticholinergic qualities), following up on serum electrolytes (for medication-induced hyponatremia), and monitoring EKGs (for medication-induced QTc prolongation) now are considered routine elements of care. In addition, monitoring for serotonin toxicity ("serotonin syndrome," either fully-developed or partially evident) is of utmost importance, as individual drugs and drug-drug interactions may yield these effects. Providers should be aware of the serotonergic activities of psychiatric and non-psychiatric medications (eg, tramadol), as combining medications can lead to this serious, yet preventable, syndrome. Utilization of computer programs to check medication interactions can help clinicians make safe medication choices. Clinicians are directed to the American Geriatrics Society (AGS) "Beers Criteria," which list medications to be avoided in treating older adults (Campanelli 2012, Hanlon et al. 2015). Classes of psychiatric medications including SSRI/SNRI antidepressants, antipsychotics, benzodiazepines, and other sedative/hypnotics are reviewed, with levels of evidence and strength of recommendations listed. Readers are directed to www.geriatricscareonline.org for updated Beers resources thru the AGS, including suggested alternative medications and fact sheets for clinicians/patients.

Other treatment modalities

The use of psychotherapeutic and supportive interventions (particularly cognitive behavioral therapy (CBT) and problem solving therapy) can be helpful, providing patients are able/willing to engage (Cuijpers et al. 2014).

For patients with severe depression including decreased oral intake, decreased physical activity, psychosis, and/or suicidal ideation, referral to a geriatric psychiatry specialist may be warranted (Frank 2014). Medication augmentation, partial hospitalization participation, inpatient psychiatric hospitalization, and/or interventions such as electroconvulsive therapy (ECT) may need to be considered. Some authors note that the frequency of ECT, low baseline cognitive function, advanced age, and female gender increase the risk of post-ECT cognitive impairment (Kerner & Prudic 2014), issues which are important to address with older patients.

DISCUSSION

Treatment of later life depression must be considered thoughtfully. Careful selection of antidepressant medication; augmentation with other strategies such as psychotherapy, supportive interventions, or electroconvulsive therapy; and monitoring for medication effects and side effects are key elements of care provision. SSRI and SNRI medications are first-line choices for elderly depressed patients. Monitoring for hyponatremia, QTc prolongation, medication interactions, and adverse effects are crucial elements of patient care. For all patients, whether being managed with medications or having additional interventions, providers are encouraged to continue close monitoring of patient symptomatology during the course of treatment - including assessing for paradoxically worsening depression, worsening anxiety states, worsening cognitive processing, and suicidal thinking. Any of these issues may merit a higher level of care such as geriatric psychiatry referral, partial hospitalization participation, or inpatient psychiatric hospitalization. On the research front, more data is needed on both drug and psychotherapeutic treatments, particularly as it relates to individuals with more extensive medical complexity.

CONCLUSIONS

Older-old patients with MDD, those individuals in their 80s and beyond represent a rapidly growing subgroup of the elderly population and there is a limited evidence-base for how these individuals should best be managed (Stek et al. 2006). Given changing demographics, such information is needed to help advance care for a rapidly expanding population of older patients with MDD.

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