CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1477753

Available online at: http://www.iajps.com *Review Article*

LINES OF TREATMENT IN THE MANAGEMENT OF DEPRESSIVE DISORDERS; A REVIEW OF RECENT LITERATURE

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Abstract:

Introduction: *It is estimated that more than 13% of individuals aged more than 55 years suffer from depressive symptoms, and more than 2% of the same age group show criteria that meets a diagnosis of major depression.*

Aim of work: *In this review we will discuss recent evidence and guidelines of diagnosis, management, and treatment of depressive disorders, with focus on the elderly population.*

Methods: *We did a systematic search for depressive disorder using PubMed and Google Scholar search engines. The terms used in the search were: depressive disorder, depression, management, treatment, diagnosis, antidepressants, psychotherapy.*

Conclusions: *Depression is associated with poor prognosis and quality of life if left untreated. Therefore, it is essential to properly address and treat depression. Elderly individuals can have different presentations of depression, which requires primary health care providers to be extremely suspicious for depression in this age group. Treatment of mild to moderate depression depends mainly on psychotherapy. On the other hand, antidepressants are considered the first line treatment for severe and major depression. Selective serotonin reuptake inhibitors are the first line treatment of major depression in all age groups. This is due to their high efficacy and relative safety.*

Keywords: *depression, therapy, anti depressants, psychotherapy*

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Please cite this article in press Turki Ali Abdullah Al Alyani et al., ***Lines of Treatment in the Management of Depressive Disorders; a Review of Recent Literature.,*** *Indo Am. J. P. Sci, 2018; 05(11).*

INTRODUCTION:

The incidence of depressive disorders has been increasing recently in all age groups, leading to significant health burden, and decreased quality of life. The criteria of major depression is considered met, according to the fifth diagnostic and statistical manual for mental disorders, when the patient demonstrates at least five depressive symptoms daily for at least 14 days[1]. Patients who demonstrate 2-4 depressive symptoms are called to have a depressive episode, or minor depression [1].

It is estimated that more than 13% of individuals aged more than 55 years suffer from depressive symptoms, and more than 2% of the same age group show criteria that meets a diagnosis of major depression[2]. Moreover, the prevalence of major depression is even higher in younger populations, with more than 6% of young adults younger than 55 years suffering from major depression [3]. On the other hand, the prevalence of major depression increases again in individuals older than 85 years, especially those in nursing centers, or who have chronic morbidities [4].

Generally, there are many factors that are associated with increased depression rates in the elderly population. These include female gender, the presence of chronic comorbidities, the presence of altered mental status, the presence of functional dysfunctions, the absence of family members or other close contacts, and having a history of prior depressive episodes during adulthood [5].

Depression management is somewhat similar in both adults and elderly. In both age groups, treatment depends on antidepressants and psychotherapy, which include interpersonal and cognitive therapy. However, the diagnosis of depression itself could be more challenging in the elderly. This is due to the presence of several comorbidities and possible altered mental status. In this review we will discuss recent evidence and guidelines of diagnosis, management, and treatment of depressive disorders, with focus on the elderly population.

METHODOLOGY:

We did a systematic search for depressive disorder using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). Our search also looked for management, and treatment of depressive disorders. All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: depressive disorder, depression, management, treatment, diagnosis, antidepressants, psychotherapy.

Assessment and Diagnosis of depression:

The clinical presentation of depression is generally similar in both adults and elderly. However, there are some key differences that need to be distinguished. For example, an elderly with major depressive disorder could present with somatic symptoms like fatigue, pain, decreased weight, and other symptoms, without realizing they have mood symptoms. Memory dysfunction, withdrawal from the surrounding society, anorexia, incompliance to treatment, decreased self-care, and increased alcohol consumption, could all be alarming signs that should draw the attention of the physician to the presence of an underlying depressive disorder. The patients themselves may not be aware they have a mood disorder and think that these symptoms are a result of a somatic disease. Therefore, clinicians should always suspect depression and do the work-up for depressive disorders [1].

When clinicians suspect the presence of an underlying depressive disorder, assessment of the nine depression symptoms should be done, with main focus on suicidal ideation. This is done by asking the patient if they think of death, hope to die, or plan to commit suicide. Assessment of depressive symptoms should include investigation of their duration and severity, the presence of any associated impairment, and the presence of recent alcohol or other substance abuse. This becomes more challenging as patients become older, because of their tendency to underreport symptoms, which makes it important to also interview the caregiver [6].

As depression in elderly is challenging to detect and treat, several questionnaires have been developed to help physicians manage it. These include the Patient Health Questionnaire, and the Geriatric Depression Scale[7]. These questionnaires are not only used to diagnose depression, but also to follow up patients and assess the efficacy of treatment [7].

It is also essential to carefully check drugs that the patient already takes, as these can be the source of depressive symptoms or suicidal ideation. It is also important to check thyroid levels, glucose levels, blood counts, vitamin B12 levels, and folate levels, as these may detect an underlying cause of the depression. The Mini-Mental State Examination is also routinely used in elderly to detect the presence of any altered mental status which could be associated with depression [8].

Pharmacological Treatment:

Treatment rate of depression and depressive disorders is usually low, especially in the elderly patients. In fact, most patients do not receive any kind of depression treatment. Even those who receive treatment, many of them do not receive it adequately[9]. On the other hand, when left untreated, depression in all age groups can have poor prognosis with significant effects on quality of life. Moreover, the prognosis of most comorbidity has been found to be worse in individuals who have an associated depression. It has been also found that depression can cause exacerbation of symptoms of associated diseases like hypertension and diabetes [1].

To achieve ideal treatment of depression in the presence of associated comorbidities,, management should be planned by a multidisciplinary team that can plan the ideal interventions to address both depressive and somatic symptoms[10]. The presence of altered mental status or severe depressive symptoms may lead to drug incompliance. Therefore, it is important to involve family members of caregivers in the treatment plan to improve compliance [10].

Antidepressants:

Generally, most clinical trials on antidepressants have shown efficacy in improving depressive symptoms when compared to placebo [11]. Efficacy rates, remission rates in young adults are similar to those in the elderly. However, some studies have found that benefits of using antidepressants in the elderly may be mild. In fact, a meta-analysis concluded that as the patients age, the efficacy of antidepressants declines significantly [12]. The possible reasons for this decreased activity in older patients could be the presence of other comorbidities like cardiovascular diseases, which make clinicians prescribe lower doses of the antidepressant [9].

Indications and guidelines for the treatment of depression with antidepressants in the elderly are somewhat the same as those in the adults. Generally, the routine use of antidepressants in the presence of any depressive symptoms should be stopped, and depression criteria must be completely met before the initiation of an antidepressant therapy. Generally, antidepressants are the first line management in major depression, whereas in mild depression it is preferred to start with psychotherapy [13].

Side effects of antidepressants and their interaction with other drugs are of major concern when treating an elderly patient. For example, antidepressants are contraindicated in patients who recently had a myocardial infarction, hepatic or renal disease. This can many times lead to insufficient treatment of depression, or poor compliance to treatment [14]. Moreover, these patients have a higher risk of developing severe adverse events due to interaction between their drugs and the newly-prescribed antidepressants [14].

Among all antidepressants, selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors, tricyclic antidepressants, and monoamine oxidase inhibitors are considered the most important and efficient antidepressants. The first line treatment in managing major depression in all age groups is selective serotonin reuptake inhibitors [8]. This is because these drugs have a relatively safe profile along with improved efficacy when compared to other antidepressants like tricyclic antidepressants, which carry a risk of developing cardiovascular events. In addition, selective serotonin reuptake inhibitors do not lead to the development of anticholinergic side effects, and high doses of them cannot be fatal. However, they can still interact with other drug, which poses a treatment in patients with several comorbidities. Moreover, they have been associated with an increased risk of osteoporosis and falls. The dose of selective serotonin reuptake inhibitors is generally the same in both adults and elderly, except for extremely old patients who may require lowering the dose [15].

Rates of sexual side effects following the use of selective serotonin reuptake inhibitors and other antidepressants are the same in both adults and elderly, along with rates of incompliance to treatment due to these side effects [13].

It is still unknown, however, how these drugs actually work and establish their effects. Generally, depression is thought to be result neurotransmitters imbalances that involve serotonin, dopamine, and norepinephrine, along with other neurotransmitters[15]. Most antidepressants are hypothesized to correct this imbalance between neurotransmitters, and thus improve the symptoms. Other hypotheses that explain depression and the mechanism of antidepressants include the involvement of other neurotransmitters like glutamate [16]. One other hypothesis states that cytokines can affect the brain leading to depression, and antidepressants can decrease the effects of cytokines [17].

Treatment-Resistant Depression:

Only 30% of elderly patients with depression will achieve persistent remission following initial antidepressants treatment, while the remaining 70% will need additional therapy [13]. In these cases, the

first step is to increase the antidepressant dose until it reaches the highest dose. The initiation of another antidepressant could also be considered[10]. It is also important to consider the use of psychotherapy as an adjuvant to antidepressants.

No solid evidence is currently present on the most efficient antidepressants combination in resistant cases. However, some studies have suggested the use of a combination therapy that includes lithium when treating adults with resistant depression. These lithium-containing combinations have been found to achieve remission in 42% of cases [18].

In a recently published clinical trial, 181 elderly patients with depression were randomized to receive different combinations of antidepressants. Authors concluded that the combination of venlafaxine added to aripiprazole was associated with the best efficacy, with a remission rate that reached 44% [19]. The use of electroconvulsive therapy has also been associated with high efficacy in resistant depression [10].

Depression Treatment in Patients with Comorbid Conditions:

Elderly patients who have associated comorbid conditions are generally considered more vulnerable to dependency and even mortality with minimal stresses. This is generally called frailty state[20]. It is usually challenging for primary care physicians to distinguish between a frailty state and a major depression. This can sometimes lead to the unnecessary prescription of antidepressants to old individuals. However, the nature of frailty is still unclear, with significant overlap between it and depression. A previous study has concluded that the presence of frailty is considered to be an independent risk factor that predicted depression [21]. In cases of frailty with the absence of major depression, it is preferred to put the patient under vitamin D treatment and regular exercising program [20].

One significant limitation of most trials on major depression treatment is their exclusion of patients who have associated comorbidities. This has led to the absence of solid evidence on depression treatment in these subgroups. However, it is generally accepted that in these subgroups of patients, classic antidepressants therapy is often efficient[22]. Antidepressants are also accepted for the use in elderly patients who are completely dependent or who live in nursing homes [22].

In many cases, major depression can be associated with significant alteration in mental status or dysfunctional cognition. In these cases, antidepressants therapy can also improve mental status and recover cognition. Generally, the depression and dementia are significantly associated and can predispose the development of one another and addressing depression can many times improve or even reverse dementia. Moreover, these patients can also show higher efficacy from other nonpharmacological interventions like cognitive behavioral therapy, caregiver education, and music therapy [23].

Psychotherapy for Depression Treatment:

Generally, the first line treatment when treating mild to moderate depressive disorder is psychotherapy[1]. Psychotherapies in depression patients include behavioral therapy, problem solving psychotherapy, and interpersonal psychotherapy. The effects of psychotherapy are generally similar to those of antidepressants, with cognitive behavioral psychotherapy leading the best outcomes. However, the effects of psychotherapy in general and cognitive behavioral therapy specifically, are still not clear in extremely old patients, or those with frailty status. In general, psychotherapy can still be considered in elderly patients with frailty or severe comorbidities which prevent them from receiving proper antidepressants therapy.

In elderly patients with major depression, the most efficient modality of treatment so far is electroconvulsive therapy, with efficacy that can be as high as 80% [8]. In fact, electroconvulsive therapy is also beneficial for the management of severe resistant depression, psychotic depression, incompliance to treatment, or refusal to intake food and drinks [8].

Some studies have suggested regular exercise for the treatment of depression. However, no solid evidence is present to support the efficacy of exercise on severe depression [24].

Maintenance of Treatment:

Despite advances in depression treatment, it is still not well known when is the best time to stop treatment against depression once remission is reached. Few studies have assessed these issues, and a systematic review and meta-analysis of these studies have concluded that following adequate antidepressants and psychotherapy treatment, the relapse risk within 3 years. Was 28% less than patients with insufficient or no treatment. Moreover, the administration of proper antidepressants therapy was associated with a significant decrease in relapses when they were continued following remission. Long-term effects of selective serotonin reuptake

inhibitors were found to be similar to those of tricyclic antidepressants. These results and outcomes are similar in all age groups including adults and elderly [25].

On the other hand, discontinuation of antidepressants when remission was achieved, led to 36.2% relapses[25]. However, another study on antidepressants maintenance therapy concluded that risk of recurrence at 2, and 3 years was not significantly different between placebo groups, and antidepressants maintenance groups, but they found higher risk of recurrence only at 1 year in the placebo group.

Due to this contradiction between different studies, no clear recommendations on how long to continue maintenance therapy have been established. Generally, it is accepted to continue antidepressants for a year following remission in any elderly patient who had a single major depressive episode. On the other hand, patients who had two episodes of major depression are recommended to continue antidepressants treatment for at least two years following remission. Finally, patients who had three or more episodes of major depression are recommended to continue antidepressants treatment for at least three years following remission, and are preferred to remain on treatment for life [26].

Other important factors to consider when deciding the duration of maintenance therapy are patients' preferences, the degree of severity of depression episode (especially the last one), number of treatment protocols attempted before remission, latency period between depression episodes, side effects of antidepressants drugs, and the presence of predisposing factors for depression [26].

CONCLUSIONS:

Depressive disorders and major depression are considered significant psychological problems with increasing incidence and large burden on the society. Depression is associated with poor prognosis and quality of life if left untreated. Therefore, it is essential to properly address and treat depression. Elderly individuals can have different presentations of depression, which requires primary health care providers to be extremely suspicious for depression in this age group. Otherwise, diagnostic approaches are usually similar in different age groups. Treatment of mild to moderate depression depends mainly on psychotherapy. On the other hand, antidepressants are considered the first line treatment for severe and major depression. Antidepressants include selective serotonin reuptake inhibitors, tricyclic antidepressants, and other types which are considered less important than these two. Selective serotonin reuptake inhibitors are considered to be the first line treatment of major depression in all age groups. This is due to their high efficacy and relative safety. In cases of resistant depression, combinations of antidepressants should be attempted until the patient reaches remission.

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