# INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

**Pharmaceutical Sciences** 

**Review Article.....!!!** 

Received: 28-06-2015; Revised: 19-07-2015; Accepted: 20-07-2015

#### ANTIDEPRESSANTS AND MEDICALLY ILL PATIENTS

D. Ashok Kumar\*, R. Siddarama, K. Siva Kumar Reddy, L. Reddenna

Department of Pharmacy Practice, Rajiv Gandhi Institute of Medical Sciences, Kadapa-516003, A. P., India

### **Keywords:**

Antidepressants,
Depression, Medically ill,
Pharmacotherapy,
Quality of life

# For Correspondence:

#### D. Ashok Kumar

Department of Pharmacy
Practice, Rajiv Gandhi
Institute of Medical
Sciences, Kadapa-516003,
A. P., India

## E-mail:

 $\underline{a shokalex @gmail.com}$ 

#### **ABSTRACT**

Depressions are a commonly met psychiatric condition in medically ill patients. It is recognized to be accompanying with augmented desires for physicians to accelerate death in medically ill patients and it denotes a main risk factor for suicide in this inhabitants. Prevalence rates of depression among medically ill patients range extensively, depending on diagnostic criteria used and patient population studied. Various studies establish that a preceding history of depression, poor social support, physical infirmity, chronic unrelieved pain and existential apprehensions were all accompanying with depression. Patients with end-stage heart disease are stated to certify prevalence rates of 36% for major depression and 22% for minor depression; while, those with end-stage renal disease have rates of depression between 5% and 25%. Evaluating depression in extremely ill patients can be a task for mental health professionals. Momentous attitudinal obstructions from both clinicians and patients can lead to underneath acknowledgment and beneath treatment of depression. Depression is treated with a multiplicity of diverse therapies, such as cognitive behavioral therapy, psychotherapy, and pharmacotherapy. Skilled supervision of depression dismisses suffering and it is a fundamental section of the establishment of widespread end-of-life care. Several of these circumstances can certainly control with advanced psychosocial treatments. Physicians who care for failing patients must be proficient in this perilous area of clinical practice.

#### INTRODUCTION

Depressions are a commonly met psychiatric condition in medically ill patients and significantly affect the quality of life of a failing patient by compelling away faith, intellect of harmony and implication. 1It weakens patients' capability to interrelate with family and loved ones and it disturbs one's ability to establish commercial and applied concerns at the end of life. It is recognized to be accompanying with augmented desires for physicians to accelerate death in medically ill patients and it denotes a main risk factor for suicide in this inhabitants.<sup>3</sup> Patients may be averse to report depressive symptoms to medical staffs, as they may believe that it is a sign of paleness.<sup>4, 5</sup>Prevalence rates of depression among medically ill patients range extensively, depending on diagnostic criteria used and patient population studied. Hinton (1994) established that 11% of patients in the final weeks of life entirely covered their approaches from others while an additional 35% were restrained about selfdisclosure. Devouring a good indulgent of the factors accompanying with depression in patients with innovative diseases is supreme in the acknowledgment of this disorder. Goldberg and Cullen recommended that interruption of key affairs; dependence, ill health, deformity and impending death were psychological issues leading to momentous depressive symptoms. Various studies establish that a preceding history of depression, poor social support, physical infirmity, chronic unrelieved pain and existential apprehensions were all accompanying with depression.

# Risk factors for depression in medically ill patients

- Devouring a terminal diagnosis
- Definite types of cancer: pancreatic cancer, brain tumors
- Comorbidities: hypothyroidism, coronary artery disease, macular degeneration, diabetes mellitus,
- Alzheimer's disease, Parkinson's disease, multiple sclerosis, stroke, Huntington's disease
- Physical disability
- Poor pain and symptom control
- Metabolic deviations: hypercalcemia, tumor generated toxins, uremia, abnormal liver function
- Medications: amphotericin, centrally acting antihypertensive agents, H2-blockers, metoclopramide, cytotoxic drugs, corticosteroids, interferon, interleukin
- Radiation therapy

- Malnutrition
- Cognitive loss
- Preceding personal history of depression
- Family history of depression
- Age of the patient, more common in younger patients
- Request to withhold or withdraw treatment
- Requests for assisted suicide
- Substance abuse
- Poor social support
- Lack of close confiding relationships
- Financial strains<sup>8</sup>

# Signs of Depression in medically ill Patients

# **Psychological symptoms**

- Dysphoria
- Depressed mood
- Sadness
- Tearfulness
- Lack of pleasure
- Hopelessness
- Helplessness
- Worthlessness
- Social withdrawal
- Guilt
- Suicidal ideation

# **Other indicators**

- Intractable pain or other symptoms
- Excessive somatic preoccupation
- Disproportionate disability
- Poor cooperation or refusal of treatment
- Hopelessness, aversion, lack of interest on the part of the clinician
- Treatment with corticosteroids, interferon, or similar agents

# **History-related indicators**

- Personal or family history of substance abuse, depression, or bipolar illness
- Pancreatic cancer <sup>9-12</sup>

Patients with end-stage heart disease are stated to certify prevalence rates of 36% for major depression and 22% for minor depression; while, those with end-stage renal disease have rates of depression between 5% and 25%. Even though the occurrence of depression seems to rise as medically ill patients decline, differentiating depression that involves treatment from emotional state of grief, fear and sadness is perplexing. <sup>13</sup>Sub-optimally treated depression is accompanying with augmented hospital readmissions; extended hospital stays, and condensed quality of life. Facts specify that palliative care clinicians generally distinguish depression in the patients but incline to misjudge its severity. Conversely, choosing the best clinically applicable and cost-effective antidepressant is perplexing. Evaluating depression in extremely ill patients can be a task for mental health professionals. <sup>14</sup>Even though depressive thoughts and symptoms may exist in 15% to 50% of cancer patients, only 5% to 20% will encounter diagnostic criteria for major depressive disorder (MDD). <sup>15</sup>Momentous attitudinal obstructions from both clinicians and patients can lead to underneathacknowledgmentand beneathtreatment of depression. The amended risk-benefit ratio of selective serotonin reuptake inhibitors (SSRIs) and serotoninnorepinephrinereuptake inhibitors (SNRIs),together with the impendingimportantmorbidity allied with MDD and subsyndromaldepressive symptoms, creates itessential to identify and treat those symptoms even when the reason of the depressivesymptoms is uncertain. The review involved 51 studies equating antidepressants toplacebos. Maximum studies trailed selective serotonin reuptakeinhibitors or tricyclic antidepressants. 16, 17

# **Psychotherapy**

Psychotherapeutic interventions for example dignity therapy, which offers patients to exploit a meaning-centered life appraisal to address existential concerns and help depressed palliative care patients. Personalized psychotherapeutic interventions that deliveranagenda for talking dignity-related matters and existential grief among medically ill patients might help reservationlogic of perseverance all over the failing process. Studies of dignity therapy have been reassuring: 91% of participants statedactuality fulfilled with dignity therapy and more than two-thirds conveyed an enhanced sense of significance. Additional auspicious psychotherapeutic interventions include supportive-expressed group therapy, in which a cluster of progressive cancer patients encounters with a mental health professional and

converses aims, humanizing life's significances, and reclaiming the familiarity of death and dying.<sup>19</sup> Hospital-based inpatient and outpatient palliative care consultation groups are flattering more conjoint. <sup>20</sup>One randomized controlled trial of initial palliative care outpatient consultation for patients with hopeless lung cancer displayed enhanced depression outcomes, better quality of life, and a diffident development in existence.<sup>21</sup>

Even though, SSRIs and SNRIs turn out to be a strength in treating depression, placebo controlled trials have generated diverse results in depressed cancer patients. <sup>22</sup>Mirtazapine has comparatively few drug interactions; the side effects of sedation and weight gain may be wanted among patients with insomnia and impaired appetite. <sup>23-25</sup>A total of 3603 patients were involved (i.e., suffering from physical illnesses comprising stroke, Parkinson's disease, HIV/AIDS, cancer and researchers establish that antidepressants were more effective than placebos, even though patients in receipt of antidepressants were additional probable to experience adverse effects, comprising sexual dysfunction and dry mouth. For every six people in receipt of treatment, one more could be predictable to help at between six and eight weeks if they were taking antidepressants. <sup>26</sup>

# **Psychostimulants**

Psychostimulants can progress cancer-related fatigue and quality of life while enhancing the action of antidepressants. <sup>27, 28</sup>

# $\textbf{Pharmacotherapy}^{29\text{-}31}$

Depression is treated with a multiplicity of diverse therapies, such as cognitive behavioral therapy, psychotherapy, and pharmacotherapy. Pharmacotherapy comprises first-generation antidepressants (tricyclic antidepressants and monoamine oxidase inhibitors) and second-generation antidepressants (selective serotonin reuptake inhibitors [SSRIs], serotonin and norepinephrine reuptake inhibitors, and selective serotonin and norepinephrine reuptake inhibitors) displayed in table 1. In general, the efficiency and efficacy of first- and second-generation antidepressants is analogous. At present, there is no proof of considerable alterations amongst the SSRIs in efficacy, effectiveness, or broad acceptability for the treatment of depression. Generally, there is respectable proof that the SSRIs are usually well accepted and have analogous side effect profiles, most particularly gastrointestinal problems, sexual dysfunction, and sleep disturbances. Based on cost only, citalopram and sertraline should reflect the SSRIs of first-choice when starting treatment of depression. As with all drugs, antidepressants should practice after cautious contemplation of benefits and risks. Clinicians should select an antidepressant on the basis of the evidence and cost.

# **Novel agents**

A mounting body of preclinical research proposes that glutamate may intricate in the pathophysiology of MDD. Ketamine controls glutamate neurotransmission as an N-methyl-daspartate receptor antagonist. Recent appraisal of a single dose IV of ketamine in a placebo-controlled, double-blind trial found that depressed patients receiving ketamine proficientmajorenhancement their depressive symptoms.<sup>32, 33</sup> Transdermal selegiline help patients who have trouble taking oral medications, comprising antidepressants. The dose-related nutritivenecessities like tyramine restraintand cautious monitoring for drug interactions may frontier the use of selegiline in medically ill patients. Use the approach of start low, when beginning and regulating antidepressants because patients with cancer and other progressive illnesses frequently have associated organ failure and are at danger of drug interactions. Cautiouslyappraisal patient's medication lists for agents that are no extendedhelpful or probablycausal to depressive symptoms to benefit reduce the risk of adverse pharmacokinetic and pharmacodynamics interactions. Patients with extreme guilt, anhedonia, hopelessness, or contemplative thinking along with anassociateddeficiency in quality of life may help from pharmacotherapy.<sup>34</sup>

Table 1-Differences in Specific Side Effects, Specific Drug Interactions and Acquisition Cost between the SSRIs<sup>34</sup>

SSRIs*	Specific Side Effects†	Specific Drug Interactions	Usual Adult Maintenance Dose	% Difference in Acquisition Cost
Sertraline	Diarrhea		100mg PO QD	
Citalopram			40mg PO QD	+ 5.2%
Fluoxetine IR		CYP450	20mg PO QD	+ 419.7%
		interactions	-	
Paroxetine	Anticholinergic (e.g., blurred vision,	CYP450	20mg PO QD	+ 471.7%
HC1	constipation, dry mouth),	interactions		
	discontinuation syndrome (e.g., flu-like			
	symptoms, insomnia, sensory			
	disturbances), Sedation, sexual			
	dysfunction, weight gain			
Paroxetine	Same as paroxetine HCl but incidence	CYP450	25mg PO QD	+ 4802.8%
HC1	rate may be lower	interactions		
Escitalopram			10mg PO QD	+ 5621.1%
Fluoxetine		CYP450	90mg QW	+ 6378.8%
		interactions		
Paroxetine	Same as paroxetine HCl but incidence	CYP450	20mg PO QD	+ 9643.0%
mesylate	rate may be lower	interactions		

CYP450 = cytochrome P450 system; ER = extended-release; HCl = hydrochloride; IR = immediate-release; PO

<sup>=</sup> by mouth (orally); QD = once daily; QW = once weekly; SSRIs = selective serotonin reuptake inhibitors.

<sup>\*</sup>The SSRIs are expressed as generic name and are listed in ascending order based on acquisition cost, with sertraline, the least costly SSRI, used as the comparator. Although sometimes used, fluvoxamine is not approved by the U.S. Food and Drug Administration for treating depression and, therefore, is omitted from the table. †Specific side effects are listed if the incidence rate is significantly higher compared with other SSRIs.

#### **CONCLUSION**

Diagnosing and treating depression in medically ill patients comprised instinctive tasks. Clinicians should have a low inception for treating depression in terminally ill patients. Psychostimulants, because of their quick onset of action, are beneficial agents and are usually well tolerated. Selective serotonin reuptake inhibitors and tricyclic antidepressants may also be used. Psychological interventions comprising prompting concerns and assigning the potential for connection, meaning, reconciliation, and closure in the dying process can also simplify surviving. Skilled supervision of depression dismisses suffering and it is a fundamental section of the establishment of widespread end-of-life care. Even though treatment of pain and other symptoms at the end of life has enhanced, depression and other psychological symptoms and disorders stay upsetting for medically ill patients. Several of these circumstances can certainly control with advanced psychosocial treatments. Physicians who care for failing patients must be proficient in this perilous area of clinical practice.

#### CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

#### REFERENCES

- 1. Block SD: Assessing and managing depression in the terminally ill patient. Ann Intern Med 2000; 132:209–218.
- 2. Periyakoil VJ, Hallenback J: Identifying and managing prepartory grief and depression in end of life. Am Fam Physician 2002; 65:883–890.
- 3. King DA, Heisel MJ, Lyness JM: Assessment and psychological treatment of depression in older adults with terminal or life threatening illness. Clin Psychol Sci Pract 2005;12:339–353.
- 4. Chochinov HM, Wilson KG, Enns M, Mowchun N, Lander S, Levitt M, Clinch J: Desire for death in the terminally ill. Am J Psychiatry 1995; 152:1185–1191.
- 5. Breitbart W, Rosenfeld B, Pessin H, Kaim M, Funesti- Esch J, Galietta M, Nelson C, Bresicia R: Depression, hopelessness, and desire for hastened death in terminally ill patients with cancer. JAMA 2000; 284:2907–2911.
- 6. Maguire P: Improving the detection of psychiatric problems in cancer patients. Soc Sci Med 1985; 20:819–823.
- 7. Hinton J: Can home care maintain and acceptable quality of life for patients with terminal cancer and their relatives. Palliat Med 1994;8:183–196.
- 8. Wilson KG, Cochinov HM, de Faye BJ, Breitbart W: Diagnosis and Management of Depression in Palliative Care. In: Chochinov HM, Breitbart W (eds): Handbook of Psychiatry in Palliative Medicine. Oxford University Press, 2000, pp. 25–49.
- 9. Goldberg RJ. Systematic understanding of cancer patients who refuse treatment. Psychother Psychosom. 1983;39:180-9.
- 10. Maltsberger JT, Buie DH. Countertransferance hate in the treatment of suicidal patients. Arch Gen Psychiatry. 1974;30:625-33.
- 11. Burt R. Taking Care of Strangers. New York: Free Pr; 1979.
- 12. Holland JC, Korzun AH, Tross S, Silberfarb P, Perry M, Comis R, et al.Comparative psychological disturbance in patients with pancreatic and gastric cancer. Am J Psychiatry. 1986;143:982-6.

- 13. Block SD. Assessing and managing depression in the terminally ill patient. ACP-ASIM End-of-Life Care Consensus Panel. American College of Physicians -American Society of Internal Medicine. Ann Intern Med.2000;132(3):209-218.
- 14. Chochinov HM, Wilson KG, Enns M, et al. Prevalence of depression in the terminally ill: effects of diagnostic criteria and symptom threshold judgments. Am J Psychiatry.1994;151(4):537-540.
- 15. Massie MJ. Prevalence of depression in patients with cancer Natl Cancer Inst Monogr. 2004;(32):57-71.
- 16. Robinson JA, Crawford GB. Identifying palliative care patients with symptoms of depression: an algorithm. PalliatMed. 2005;19(4):278-287.
- 17. Endicott J. Measurement of depression in patients with cancer. Cancer. 1984;53(10 suppl):2243-2249.
- 18. Chochinov HM. Dignity-conserving care-a new model for palliative care: helping the patient feel valued. JAMA. 2002;287(17):2253-2260.
- 19. Kissane DW, Grabsch B, Clarke DM, et al. Supportive expressive group therapy: the transformation of existential ambivalence into creative living while enhancing adherence to anti-cancer therapies. Psychooncology. 2004;13(11): 755-768.
- 20. Strong V, Waters R, Hibberd C, et al. Management of depression for people with cancer (SMaRT oncology 1): a randomised trial. Lancet. 2008;372(9632):40-48. 21.
- 21. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med. 2010;363(8):733-742.
- 22. Gartlehner G, Hansen RA, Morgan LC, et al. Comparative benefits and harms of second-generation antidepressants for treating major depressive disorder: an updated metaanalysis. Ann Intern Med. 2011;155(11):772-785.
- 23. Kast RE, Foley KF. Cancer chemotherapy and cachexia: mirtazapine and olanzapine are 5-HT3 antagonists with good antinausea effects. Eur J Cancer Care (Engl). 2007; 16(4):351-354.
- 24. Anttila SA, Leinonen EV. A review of the pharmacological and clinical profile of mirtazapine. CNS Drug Rev. 2001; 7(3):249-264.
- 25. Pae CU. Low-dose mirtazapine may be successful treatment option for severe nausea and vomiting. Prog Neuropsychopharmacol Biol Psychiatry. 2006;30(6): 1143-1145.
- 26. Saarto T, Wiffen PJ. Antidepressants for neuropathic pain. Cochrane Database Syst Rev. 2007;(4):CD005454.
- 27. Pereira J, Bruera E. Depression with psychomotor retardation: diagnostic challenges and the use of psychostimulants. J Palliat Med. 2001;4(1):15-21.
- 28. Jackson V, Block S. # 061 Use of Psycho-Stimulants in Palliative Care, 2nd ed. End of Life/Palliative Education Resource Center. Medical College of Wisconsin. http://www.eperc.mcw.edu/EPERC/FastFactsIndex/ff\_061.htm. Accessed December 28, 2012.
- 29. Gartlehner G, Hansen RA, Thieda P, et al. Comparative Effectiveness of Second-Generation Antidepressants in the Pharmacologic Treatment of Adult Depression. Comparative Effectiveness Review No. 7. (Prepared by RTI International-University of North Carolina Evidence-based Practice Center under Contract No. 290-02-0016).
- 30. White C, Wigle PR, Eichel E, Albert LG, Udorn L. Answers to your questions about SSRIs. J Fam Pract. 2010;59(1):19-25.
- 31. Clinical Pharmacology. Gold Standard Multimedia, Inc. 2010.
- 32. Berman RM, Cappiello A, Anand A, et al. Antidepressant effects of ketamine in depressed patients. Biol Psychiatry. 2000;47(4):351-354.
- 33. Irwin SA, Iglewicz A. Oral ketamine for the rapid treatment of depression and anxiety in patients receiving hospice care. J Palliat Med. 2010;13(7):903-908.
- 34. Attard A, Ranjith G, Taylor D. Alternative routes to oral antidepressant therapy: case vignette and literature review. J Psychopharmacol. 2010;24(4):449-454.