



OVERCOMING DEPRESSION WITH HOMOEOPATHY

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ABSTRACT

Depression is a major public health problem that has considerable health as well as socio-economic impact on patient, family and community.^[1,2,5] Nearly 322 million people currently suffer from depression globally of which 18% are Indian,^[3,4,5] Depression affects people from all socioeconomic backgrounds from early childhood to late ages and is more common among females (5.1%) than males (3.6%)^[4] Conventional treatment of depression is not individualized and antidepressant choice is largely dependent on adverse effect and co-morbidities^[16] It also has potentially serious side effects and is not suitable for pregnant women requiring depression treatment or those with multiple physical ailments.^[24,25] Nearly half of the patients stop antidepressants due to fear of dependence or side effects.^[27,28] Among those who continue treatment, nearly 30% remit, 30% show partial response and rest 40% are treatment resistant.^[29,30] Published literature suggests that there is severe shortage of trained mental health professionals in India with only 0.07 psychiatrists per 100,000 populations^[31] Thus, there is an unmet need for depression treatment and patients do search for alternatives. Homoeopathy is safe and cost-effective, and is well tolerated by patients with physical and mental disorders. Homoeopathy can be recommended to patients who develop intolerable side effects to first-line antidepressants, those resistant to standard treatments and augmentation strategies, those who cannot afford the cost of conventional treatment, pregnant women requiring depression treatment and those with multiple co-morbidities. Based on current evidence, Homoeopathy appears promising in treatment of depression^[34 to 41]. There is a need to further strengthen the research based evidence for Homoeopathic treatment of depression through large scale, randomized controlled trials of longer follow up duration.

KEYWORDS: Depression, Homoeopathy, India.

INTRODUCTION

Depression is a common mental disorder and a major public health problem globally.^[1,2] It is characterised by persistent sadness and loss of interest in normally enjoyed activities with inability to carry out routine activities for at least two weeks. People suffering from depression also complain of feelings of worthlessness; guilt; hopelessness; anxiety; restlessness; reduced concentration; indecisiveness; loss of energy; change in appetite; change in sleep and thoughts of self-harm or suicide.

According to the WHO (2017) estimates, 322 million people currently suffer from depression which is equivalent to 4.3% of the total world population and may become the leading cause of disease burden by the year 2030^[3,4]. Depression affects people from all socioeconomic backgrounds from early childhood to late ages and is more common among females (5.1%) than males (3.6%). It is more common in adolescents and young adults, women in reproductive age group (particularly following childbirth), and older adults. The

prevalence rates peak in older adulthood (over 60 years).^[4]

The National Mental Health Survey of India (NMHS), 2015-16 has reported that India is home to an estimated 57 million people suffering from depression which is 18% of the global estimate.^[5] Published literature has reported a higher prevalence of depression among women, among those residing in urban areas and working age adults in India.^[5,6,7] A higher risk and prevalence has been consistently been reported among those living in nuclear families; those who are unmarried, widowed, divorced or separated, or without close inter-personal relationships and those suffering from medical disorders. A depression prevalence rate of 19.5% among higher secondary students has been reported while a prevalence of 3.5% to 8.9% among elderly has been reported from India.^[5,8,9,10] Poverty and socio-economic adversity is positively associated with depression,^[5,11] NMHS has indicated an almost twice the prevalence of current depression in the lowest income quintile group (3.4%) compared to the highest 5 income quintile population (1.9%). Loss of productivity, high

treatment gap and high co-morbidity further increases economic burden in depressed patients.^[5] In India, nearly 67% of the individuals suffering from depression reported disability in area of work, 68% in social life and 70% in family life.^[2] Thus, depression is a major contributor to burden of disease and disability; and has considerable health as well as socio-economic impact on patient, family and community^[2,5].

Aetiology

Depression is caused by a combination of genetic, biological, psychological, social and environmental factors specific to an individual.^[12,13] A family history of depression in a first degree relative increases the risk up to 1.5- 3 times. Patients with a positive family history also have an early onset and increased recurrence.^[12,14] Stressful life events such as loss of a parent in childhood, loss of a spouse, unemployment, suffering from chronic illness and caring for chronically disabled person in family etc often precede the first episode of depression and increase the likelihood of developing subsequent episodes. Depression in turn increases stress and worsen the life situation of patient thus making a vicious circle.^[12,15] Neurotransmitters nor-epinephrine and serotonin have been implicated in aetiological of depression by published studies. Faulty cognitions with a triad of negative view of self, environment and future are known psychological factors that predispose to depression.^[15]

Clinical Features

The patients suffering from depression often present with feeling sad or depressed most of the day; markedly reduced interest in almost all activities nearly every day; fatigue; reduced capacity to think or concentrate, bodily agitation or slowness; disturbed sleep nearly every day; loss of self-confidence; feelings of guilt; unhappy views of future and recurrent thoughts of death or suicide or suicidal behaviour. Based on the presenting symptoms, depression may be classified as mild, moderate and severe. Children suffering from depression may present with irritability, temper tantrums, crying, separation anxiety, somatic symptoms such as headache or abdominal pain and poor academic performance. In elderly, presenting symptoms may be psychomotor agitation or irritability, poor appetite, somatic complaints and at times psychotic features. The clinical features and classification standards used for depression are the WHO Advisory Committee ICD-10 and the American Psychiatric Association's Diagnostic Statistical Manual (DSM-IV) classification.^[2,16]

Co-Morbidities

Prevalence, co-relates and association studies have reported a strong link of depression with several non communicable diseases (NCDs) including arthritis, hypertension, coronary heart disease, congestive heart failure, chronic obstructive pulmonary disease, diabetes, cancer, substance abuse disorders (alcohol and drugs) and nutritional disorders (under-nutrition, over-nutrition

and obesity) etc.^[17,18,19] Depression is also a known risk factor for acute myocardial infarction.^[20]

Diagnosis

There are no laboratory tests to diagnose depression and psychiatrists rely on clinical symptoms and signs.^[21] Beck Depression Inventory-Primary care (BDI-PC) and Hospital Anxiety and Depression Scale (HADS) are two depression screening tools that exclude somatic symptoms. Brief screening instruments useful in medical settings include Patient Health Questionnaire-depression module (PHQ-9) and Patient Health Questionnaire -2 (PHQ-2).^[3] However, diagnosing depression has its challenges as these screening instruments only count symptoms of depression without any regard to context, stress, personality and coping.^[21] Therefore, often people under severe stress, those who cope poorly and people with depression secondary to medical illness may be diagnosed with major depression.

Medical Management

The conventional treatment of depression is antidepressant medicines, psychotherapy, electroconvulsive therapy and light therapy.^[23] Antidepressant medicines include Tricyclic (TCAs) antidepressants, Monoamine Oxidase Inhibitors (MAOIs), Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin Nor-epinephrine Reuptake Inhibitors (SNRIs) and Nor-adrenergic and Specific Serotonergic Anti-depressants (NASSAs). However, these medicines have many side effects. The side effects of TCAs include confusion, drowsiness, dizziness, blurred vision, increased heart rate, dry mouth, constipation, urinary retention, skin rash, weight gain or loss and sexual dysfunction. MAOIs intake leads to weight gain and it may cause serious side effect including extreme liver inflammation, heart attack, stroke, and seizures. SSRIs side effect includes anxiety, headache, drowsiness, sleeplessness, reduced appetite, dry mouth and decreased libido. Serotonin syndrome may occur after SSRIs intake the symptoms of which include high body temperature, agitation, increased reflexes, tremor, sweating, dilated pupils, and diarrhoea. The side effects of SNRIs are anxiety or agitation, dizziness, insomnia, tiredness, dry mouth, nausea, constipation and increased sweating^[6]. Thus, due to a large number of side effects, these antidepressant medicines adversely affect the health-related quality of life of the suffering patients. Published studies have reported that clinicians are reluctant to prescribe antidepressants where physical illness are associated with it due to possible adverse side effects or drug interactions.^[24] Although depression is more common in females, pregnant women undergoing treatment often stop antidepressant medicines due to concerns about potential harm to foetus; thus leading to high relapse rates in pregnancy.^[25]

Besides potentially serious side effects, the conventional medical management of depression has several challenges. First, individualized treatment is not

available and antidepressant choice is largely dependent on adverse effect and co-morbidities.^[16] Second, the therapeutic effect of antidepressants is evident at least two weeks after starting medicines.^[16] Third, in patients who remain non responsive up to 3-4 weeks, the dose is increased to maximum permissible dosage which increases side effect burden; sometimes one or more additional antidepressants are added from different classes or Lithium/ Aripiprazole/ Thyroid hormones or Psychostimulants are used as an adjunct.^[16,26] Fourth, the treatment of depression is prolonged to months or sometimes years; after discontinuing these medicines the therapeutic effect persists up to only 36 months and the relapse rate is high.^[16] Fifth, studies have reported that compliance is a major issue in depression; nearly half of the patients stop antidepressants due to fear of dependence or side effects without consulting their doctor.^[27,28] Sixth, among those who continue treatment, nearly 30% remit, another 30% show partial response and rest 40% are treatment resistant.^[29,30] Thus, the current treatment of depression is flawed in terms of delayed therapeutic response, prolonged treatment, efficacy, side effects and non-compliance with antidepressants.

Published literature suggests that there is severe shortage of mental health professionals in India; the available mental health manpower being 0.07 psychiatrists per 100,000 population. These psychiatrists often work with insufficient training, supervision and support to identify, follow-up and refer patients suffering from depression.^[31] This lack of trained mental health professionals results in unmet need of depression treatment and contributes to patient's search for alternatives.

Homoeopathic Treatment of Depression

Homeopathy treats patients on basis of the natural law of healing – “Similia Similibus Curantur” which means “likes are cured by likes”. Homoeopathy has a holistic approach towards ‘man’ in health and disease. It believes that body and mind are integrated. According to homoeopathic concept mental/emotional states, especially if prolonged may lead to physical illness and physical disease is accompanied by a change in the mental/emotional state. In homoeopathy, a detailed case history is taken to ascertain the totality of signs and symptoms of each patient along with patient's background, environment and daily routine. It takes attempts to go to the root level of disease in each individual patient by taking into account the psychological, social and environmental factors specific to an individual. Homoeopathic literature gives detailed description of mental disorders, case taking of mentally diseased and describes large number of medicines suitable for depression.^[32,33]

The benefits of using Homoeopathy for the treatment of depression are many. First, is that Homoeopathy offers “individualized” treatment based on “totality of

symptoms” in “individual patient” comprises of all changes observable in on physical as well as mental/emotional sphere. Homoeopathic “similimum” is the medicine that matches the totality of the patient's physical and mental/emotional symptoms, irrespective of “which came first”.^[33] Second, Homoeopathy has no known side effects. It is therefore also suitable for pregnant women and patient suffering from multiple physical ailments that require depression treatment but are hesitant to take conventional medicines due to fear of side effects. Third, Homoeopathy has proven cost-effectiveness and therefore suitable for treating depression, the condition being strongly associated with poverty and unemployment.^[5,11]

Published studies have reported efficacy of Homoeopathic treatment for depression. Davidson RT et al (1997) conducted an observational study among twelve patients who had major depression, social phobia, or panic disorder in a clinical set-up. The duration of treatment was 7 to 80 weeks. This study reported an overall 58% response rates to individualized homeopathic treatment in the clinical global improvement scale (n = 12) and 50% according to the self-rated SCL-90 scale (n = 8), and the Brief Social Phobia Scale (n = 4).^[34] Katz et al (2005) conducted a randomised, double-dummy, double-blind parallel group clinical general practice trial for treatment of depressive episodes. Patients were randomised to receive verum Fluoxetine and placebo homeopathy, or verum homeopathy and placebo Fluoxetine, or placebo homeopathy and placebo Fluoxetine. The recruitment target was thirty patients and recruitment duration was nine months. Suicidal and psychotic patients were excluded. The primary outcome measures were HAM-D (Hamilton Depression Rating Scale) and CGI (Clinical Global Impression). This study could not enrol sufficient number of patients and concluded that a trial of this design in general practice is not feasible, because of recruitment difficulties, many of them linked to patient preference.^[35]

Adler UC et al (2006) published a case series of fifteen patients treated with individualized homeopathy for depression in Brazil. After an average of seven weeks of treatment, fourteen patients (93%) reported a response rate of more than 50% decrease in Montgomery & Asberg depression scale (MADRS). One patient had clinical worsening and was referred to conventional antidepressant therapy. The MADRS mean scores (\pm dp) decreased from 24.9 (\pm 5.8) to 9.7 (\pm 8.2, $p < .0001$) in the second evaluation proving the efficacy of Homoeopathy in treatment of depression.^[35] Adler UC et al (2011) conducted a prospective double-blind double-dummy placebo controlled randomised 8-week, single-centre trial with the aim to investigate the non-inferiority and tolerability of individualized homeopathic prescription of Q-potencies (LM potencies) in acute depression, using fluoxetine as active control. The mean Montgomery & Asberg Depression Rating Scale

(MADRS) depression scores differences were not significant at the 4th ($P = .654$) and 8th weeks ($P = .965$) of treatment. Non-inferiority of homeopathy was indicated because the upper limit of the confidence interval (CI) for mean difference in MADRS change was less than the non-inferiority margin at 4th and 8th week. There were no significant differences between the percentages of response or remission rates or tolerability in both groups. The Q-potencies of Arsenicum album, Calcarea carbonica, Lycopodium clavatum, Natrum muriaticum, Phosphorus, Sulphur and Sepia were found useful for the treatment of depression.^[37]

Oberai et al (2013) reported a prospective, non-comparative, open-label observational study to evaluate the role of individualised homeopathic medicines in the management of depressive episodes with follow up of twelve months including six months of observation period. Homeopathic medicines were prescribed in 30, 200 and 1M potencies and repetition of medicines was done when necessary. Eighty-three patients (35 males and 48 females), who fulfilled the inclusion and exclusion criteria were enrolled in the study and 67 patients completed the follow-up. The study was analysed as per intention to treat, however, 16 (19.27%) patients could not be followed-up due to non-compliance. A statistically significant ($P = 0.0001$, $P < 0.05$) difference was observed in mean scores of Hamilton Depression Rating Scale (HDRS) using the paired t-test, from baseline to six and twelve months. Statistically significant differences were also observed in the Beck Depression Inventory (BDI) and Clinical Global Impression (CGI) scales. During six-month observation period, continued improvement was noticed in all the assessment parameters. No patient reported any adverse event during the study period. The most frequently used medicines were Natrum muriaticum ($n = 18$), Arsenicum album ($n = 12$), Pulsatilla nigricans ($n = 11$), Lycopodium clavatum ($n = 7$) and Phosphorus ($n = 6$).^[38]

Alder et al (2013) conducted a randomized, partially double-blind, placebo-controlled, four-armed trial to investigate the specific effect of individualized homeopathic Q-potencies (LM potencies) compared to placebo and the effect of an extensive homeopathic case taking (case history I) compared to a shorter, rather conventional one (case history II) in the treatment of acute major depression (moderate episode) using a 2×2 factorial design with a six-week study duration per patient was performed. Only 44 patients instead of pre planned 228 could be randomised (2:1:2:1 randomization: 16 homeopathic Q-potencies/case history I, 7 placebo/case history I, 14 homeopathic Q-potencies/case history II, 7 placebo/case history II). This study had to be terminated prior to full recruitment, was underpowered for hypothesis testing and remained inconclusive.^[39]

Macias-Cortes E et al (2015) conducted a randomized, placebo-controlled, double-blind, double-dummy, superiority, three-arm trial with a 6 week follow-up study in a public research hospital OPD in Mexico City with aim to assess the efficacy and safety of the homeopathic individualized treatment versus placebo or fluoxetine in peri-menopausal and post-menopausal women ($n=133$) with major depression (moderate to severe intensity) according to DSM-IV. The outcomes measures were change in the mean total score among study groups on the 17-item Hamilton Rating Scale for Depression, Beck Depression Inventory and Greene Climacteric Scale, after 6 weeks of treatment, response and remission rates, and safety. Efficacy data were analyzed in the intention-to-treat population (ANOVA with Bonferroni post-hoc test). After a 6-week treatment while individualised Homeopathy and fluoxetine both showed significantly better results than placebo in response definition; individualised Homeopathy also improved menopausal symptoms scored by Greene Climacteric Scale.^[40]

Viksveen P et al (2017) conducted a pragmatic trial using the "cohort multiple randomised controlled trial" design to test the effectiveness of adjunctive Homeopathic treatment compared to usual care alone, over a period of 12 months in patients ($n=485$) with self-reported depression. The primary outcome measure was the Patient Health Questionnaire (PHQ-9) at 6 months. Secondary outcomes included depression scores at 12 months; and the Generalised Anxiety Disorder (GAD-7) outcome at 6 and 12 months. The trial over-recruited by 17% ($n=566$) and 47% of the patients received adjunctive Homeopathic treatment. An intention-to-treat analysis of the offer group at 6 months reported a 1.4-point lower mean depression score than the no offer group (95% CI 0.2, 2.5, $p=0.019$). Results were maintained at 12 months. Secondary analyses showed similar results for anxiety (GAD-7). No adverse effects in offer group were reported during the study period. This trial provided preliminary support for acceptability and effectiveness of adjunct Homeopathic treatment for patients with self-reported depression. The limitations of this trial included short follow up duration of 6 months and lack of blinding of the researcher who collected questionnaire responses and carried out statistical analyses.^[41]

CONCLUSION

Based on current evidence, Homeopathy appears promising in treatment of depression. It can be recommended to patients who develop intolerable side effects to first-line antidepressants, those resistant to standard treatments and augmentation strategies, those who cannot afford the cost of conventional treatment, pregnant women requiring depression treatment and those with multiple co-morbidities. There is a need to further strengthen the research based evidence for Homeopathic treatment of depression through large

scale, randomized controlled trials of longer follow up duration.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

REFERENCES

1. Depression Fact Sheet. Available at <http://www.who.int/mediacentre/factsheets/fs369/en/> Assessed on 15.08.17.
2. Depression in India, Let's talk. World health organisation, 2017. Available at http://www.searo.who.int/india/depression_in_india.pdf. Assessed on 15.08.17.
3. Depression and other common mental disorders. Global Health estimates. Geneva: World Health Organisation, 2017.
4. Pattanayak RD, Sagar R. Depressive Disorders in Indian Context: A Review and Clinical Update for Physicians. *Journal of the association of Physicians of India*, September 2014; 62.
5. Gururaj G, Varghese M, Benegal V et al and NMHS collaborators group. National Mental Health Survey of India, 2015-16: Summary. Bengaluru, National Institute of Mental Health and Neuro Sciences, NIMHANS Publication, 2016; 128.
6. Charlson FJ, Baxter AJ, Cheng HG, Shidhaye R, Whiteford HA. The burden of mental, neurological, and substance use disorders in China and India: a systematic analysis of community representative epidemiological studies. *Lancet*, 2016; 388: 376–89.
7. Shidhaye R, Gangale S, Patel V. Prevalence and treatment coverage for depression: a population-based survey in Vidarbha, India. *Soc Psychiatry Psychiatr Epidemiol*, 2016; 51: 993–1003.
8. Kumar KS, Akoijam BS. Depression, Anxiety and Stress among Higher Secondary School Students of Imphal, Manipur. *Indian J Community Med*, Apr-Jun 2017; 42(2): 94-96.
9. Sengupta P, Benjamin AI. Prevalence of depression and associated risk factors among the elderly in urban and rural practice areas of a tertiary care institution in Ludhiana. *Indian J Public Health*, 2015; 59: 3-8.
10. Dey AB, Soneja S, Nagarkar KM, Jhingan HP. Evaluation of the health and functional status of older Indians as a prelude to the development of a health programme. *Natl Med J India*, 2001; 14: 135-8.
11. Nandi DN, Banerjee G, Boral GC, Ganguli H, Ajmany S, Ghosh A, Sarkar S. Socio economic status and prevalence of mental disorders in certain rural communities in India. *Acta Psych Scand*, 1979; 59: 276–93.
12. Raman Deep Pattanayak, Rajesh Sagar. Depressive Disorders in Indian context: A review and clinical update for physicians. *Journal of the association of physicians of India*, 2014; 62.
13. Sullivan P F, Neale MC, Kendler KS. Genetic Epidemiology of Major Depression: Review and Meta-Analysis. *American journal of psychiatry*, October 2000; 157(10): 1552-1562.
14. Levinson DF. The genetics of depression: a review. *Biol Psychiatry*, 2006; 60: 84-92.
15. Radu T. Cognitive behavioral therapy and Aaron Beck. *The Journal of Nervous and Mental Disease*, 2012; 200: 840-42.
16. Gelder M, Harrison P, Philip C. Shorter oxford Textbook of Psychiatry. Oxford University Press, 2009; 218-261.
17. Wilhelm K, Mitchell P, Slade T et al. Prevalence and correlates of DSM-IV major depression in an Australian national survey. *J Affect Disord*, 2003; 75: 155–62.
18. Patten SB, Beck CA, Kassam A et al. Long-term medical conditions and major depression: strength of association for specific conditions in the general population. *Can J Psychiatry*, 2005; 50: 195–202.
19. Egede LE. Major depression in individuals with chronic medical disorders: prevalence, correlates and association with health resource utilization, lost productivity and functional disability. *Gen Hosp Psychiatry*, 2007; 29: 409–16.
20. Moussavi S, Chatterji S, Verdes E et al. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. *Lancet*, 8 Sep 2007; 370(9590): 851-8.
21. Jacob KS. Depression: a major public health problem in need of a multi-sectoral response. *Indian J Med Res*, October 2012; 136: 537-539.
22. Jacob KS. Major depression: a review of the concept and the diagnosis. *Adv Psychiatric Treat*, 2009; 15: 279-85.
23. Rush AJ, Nierenberg AA. Mood disorders: Treatment of depression. In: Sadock BJ, Sadock VA, Ruiz P, editors. *The Comprehensive Textbook of Psychiatry*. Vol. 1, 9th ed. Philadelphia: Lippincott Williams and Wilkins, 2009; 1734.
24. Taylor D, Meader N, Bird NV et al. Pharmacological interventions for people with depression and chronic physical health problems: systematic review and meta-analyses of safety and efficacy. *The British Journal of Psychiatry*, 2011; 198: 179–188.
25. Cohen LS, Altshuler LL, Harlow BL, et al. relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. *JAMA*, Feb 2006; 295(5): 499-507.
26. Kirsch I, Deacon BJ, Huedo-Medina TB, Scoboria a et al. Initial severity and antidepressant benefits: A meta-analysis of data submitted to the Food and

- Drug Administration. *PLoS Med*, 2008; 5(2): 45. doi: 10.1371/journal.pmed.0050045.
27. Di Matteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med*, 2000; 160: 2101–7.
 28. Melartin TK, Rytala HJ, Leskela US et al. Continuity is the main challenge in treating major depressive disorder in psychiatric care. *J Clin Psychiatry*, Feb 2005; 66(2): 220-7.
 29. Al-Harbi KS. Treatment-resistant depression: therapeutic trends, challenges, and future directions. *Patient Prefer Adherence*, 2012; 6: 369–388.
 30. Al-Harbi KS, Qureshi NA. Neuromodulation therapies and treatment-resistant depression. *Med Devices (Auckl)*, 2012; 5: 53–65.
 31. Mugisha J, Abdulmalik J, Hanlon C et al. Health systems context(s) for integrating mental health into primary health care in six Emerald countries: a situation analysis. *Int J Ment Health Syst*, 2017; 11: 7.
 32. Thakur T. Homoeopathic perspective of mental disorders. *WJPPS*, 2017; 6(4): 790-797.
 33. Hahnemann S. *Organon of Medicine*, 5th & 6th edition, New Delhi: B Jain Publishers (P.) Ltd, Reprint edition, 2000.
 34. Davidson JRT, Morrison RM, Shore J et al. Homeopathic Treatment of Depression and Anxiety. *Alternative Therapies*, January 1997; 46-49.
 35. Katz T, Fisher P, Katz A et al. The feasibility of a randomised, placebo-controlled clinical trial of homeopathic treatment of depression in general practice. *Homeopathy*, Jul 2005; 94(3): 145-52.
 36. Adler UC, de Paiva NM, Cesar ADT et al. Homeopathic treatment of depression: series of case report. [Tratamento homeopático da depressão: relato de série de casos]. *Revista de Psiquiatria Clinica*, 2008; 35(2): 74–78.
 37. Adler UC, Paiva NM, Cesar AT et al. Homeopathic individualized Q-potencies versus Fluoxetine for moderate to severe depression: Double-blind, randomized non-inferiority trial. *Evid Based Complement Alternat Med*, 2011: 520182.
 38. Oberoi P, Balachandran I, Janardhanan Nair K R et al. Homoeopathic management in depressive episodes: A prospective, unicentric, non-comparative, open-label observational study. *Indian J Res Homoeopathy*, 2013; 7: 116-25.
 39. Adler UC, Kruger S, Teut M et al. Homeopathy for Depression: A Randomized, Partially Double-Blind, Placebo-Controlled, Four-Armed Study (DEPHOM). *PLoS One*, 2013; 8(9): 74537.
 40. Macias-Cortes E, Llanes-Gonzalez L, Aguilar-Faisal L et al. Individualized Homeopathic Treatment and Fluoxetine for Moderate to Severe Depression in Peri- and Postmenopausal Women (HOMDEP-MENOP Study): A Randomized, Double-Dummy, Double-Blind, Placebo-Controlled Trial. *PLoS One*, 13 Mar 2015; 10(3): 0118440.
 41. Viksveen P, Relton C, Nicholl J. Depressed patients treated by homeopaths: a randomised controlled trial using the "cohort multiple randomised controlled trial" (cmRCT) design. *Trials*, Jun 2017; 18(1): 299.