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Comparative Study to evaluate the Effect of a Herbal Preparation & Shirodhara in the Management of Major Depressive Disorder

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Abstract: Depression is one of the most global public-health issues. In *Ayurvedic* Psychiatry, it is a complex disorder under the general category of *Manas Roga.* Patients usually show compliance with pharmacological antidepressant treatment which has many unpleasant side effects & it is quite expensive. With this issue, we have undertaken this study to assess comparative effect of *Herbal* preparation & *Shirodhara* in management of major depressive disorder (MDD).Total 30 patients with mild and moderate type of major depressive disorder were included in a non-blind randomized controlled, open clinical study.The study population was collected from the OPD and IPD of *Kayachikitsa* at National Institute of Ayurveda and Hospital, Jaipur. Patients were divided into two groups named as Group A was given 5 gm herbal preparation t.d.s. p.o. for 42 consecutive days & Group B was given 5 gm herbal preparation t.d.s. p.o. for 42 consecutive days with *Shirodhara* therapy (oil dripping therapy) by medicated plain *Ashwagandha* oil for 14 consecutive days. For the measurements of efficacy, the subjective parameters like clinical symptoms and objective parameters included HDRS-item 17, CGI-S were administered at baseline and the day of 42 and Clinical Global Improvement scales (CGI-I) was evaluated only the day of 42. End of treatment, the clinical symptoms and the HDRS 17, CGI-S and CGI-I score was found highly significant ($p<0.001$) improvement in both groups. So this study claimed that selected herbal preparation & *Shirodhara* both are effective and safe in mild and moderate condition of major depressive disorder.

Key Words: Major Depressive Disorder, *Herbal* Preparation, *Shirodhara* and *Nardostachys jatamansi.*

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INTRODUCTION

Depression is one of the most global public-health issues and common disease on human race. Major depression is associated with significant personal, social and economic burden also. According to World Health Organization (WHO), depression is the leading cause of disability as measured by years lost due to disability (YLDs) and the 4th leading contributor to the global burden of disease in 2000. By the year 2020, depression is projected to reach 2nd place for all ages, and among both sexes.[1] Depressive symptoms are also found in up to 36% of all medically ill patients and co-morbidity of MDD with medical illness has been found to significantly increase in morbidity, mortality and cost of medical illnesses.[2] So it is a worldwide problem. 50% of Patients treated with antidepressant medications in modern science discontinue antidepressant treatment due to the side effects or insufficient response. Such patients are often reluctant to take synthetic antidepressant in their appropriate doses due to their anticipated side effects including dry mouth, constipation and sexual dysfunction. So there is a need for more effective and less toxic and cost-effective antidepressant treatment. *Ayurvedic* herbs may offer advantages in term of safety and tolerability, possibly promising results for the treatment of depression. Besides, the recent scientific study also showed that some *Ayurvedic* plants such as *Nardostachys jatamansi*,[3] *Lavandula stoechas*[4], and *Withania somnifera*,[5] etc. individually reported for the treatment of depressive disorder but synergistic effects is not known exactly. So keeping in view all the above facts the present study was undertaken on account of following objectives.

AIMS & OBJECTIVES

The study was undertaken with the following specific objectives-

1) To assess the effectiveness of a herbal preparation for major depressive disorder.
2) To Assess & compare the effectiveness of herbal preparation & *Shirodhara* in the management of major depressive disorder.

MATERIALS & METHODS

Selection criteria

The study population was collected from the OPD and IPD of Kayachikitsa at National Institute of Ayurveda and Hospital, Jaipur, Rajasthan.30 number of patients who were diagnosed according to *Diagnostic and Statistical Manual of Mental Disorders, Fourth edition*, (DSM-IV) in initial screening for major depression. Particular inclusion and exclusion criteria was followed to take final subject-

Inclusion criteria: The following inclusion criteria was followed for selecting the patients-

1) Males or females between the age of 20 and 65 years old.
2) Subjects who were fulfilled the DSM-IV criteria for the diagnosis of major depressive disorder without psychotic features and with single or recurrent episode for minimum two weeks.
3) Subjects who had mild or moderate major depressive disorder and must had minimum total score at least 10 and maximum 18 on the 17 item of Hamilton Depression Rating Scale ─ item 17 (HDRS 17) at baseline visit.
4) Each subject was a level of understanding sufficient to agree to all required tests and examinations and sign an informed consent document.

Exclusion criteria: The following was followed as exclusion criteria for selecting the patients-

1) Age less than 20 and more than 65 years.

2) Present use of prescription drug for major depressive disorder.
3) At significant risk of suicide on the basis of the clinical judgment.
4) Pregnant, breast –feeding or planning to become pregnant during the study.
5) Current history of illness with hepatic, renal, gastroenterologic, respiratory, cardiovascular (including IHD), endocrinologic, neurologic, immunologic or hematological diseases and infectious diseases etc.
6) Significantly abnormal laboratory test and finding of electrocardiograph.
7) Current use of drug abuse or alcohol dependence.
8) Diagnosis of panic disorder, generalized anxiety, dementia, bipolar disorder, schizophrenia, or any other psychiatric disorders.

STUDY DESIGN & GROUPING

This was a non-blind, randomized, controlled clinical trial.

Total 30 numbers of patients was randomly divided into two groups named as Group A and Group B. Each group with 15 numbers of patients.

Study Drug Selection and Manipulation

Herbal preparation was made by the combination two indigenous medicinal plants of *Nardostachys jatamansi* and *Lavandula stoechas*. Group A was given 5 gm herbal preparation t.d.s. p.o. for 42 consecutive days & Group B Was given 5 gm herbal preparation t.d.s. p.o. for 42 consecutive days with *Shirodhara* therapy (oil dripping therapy) by medicated plain *Ashwagandha* oil for 14 consecutive days.

Efficacy and Safety Assessment of Selected Drugs

For the measure of efficacy the particular clinical symptoms was evaluated, and the HDRS 17, CGI-S was administered at the day of baseline and day of 42. The CGI-I was assessed at final day of study. The laboratory examinations such as haematolological (total leucocytes count, differential leucocytes count, erythrocyte sedimentation rate and hemoglobin concentration), biochemical (serum bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, fasting blood sugar, serum creatinine, serum urea, high density lipoprotein, low density lipoprotein, total cholesterol, total triglyceride and Electrocardiogram was performed at baseline day and the day of 42.

Statistical analysis

The quantitative data was assessed by using paired '*student t*' test when compared before and after study in a single group and unpaired '*student t*' test was followed for intergroup comparison. For the assessment of qualitative data *Wilcoxon t-test* was done in a single group. The value was expressed as mean ± SD (standard error of mean).

RESULTS & DISCUSSION

End of treatment, all the clinical symptoms were showed significant improvement in group B ($p<.05$, $p<.01$) except in the symptom i.e. feeling of worthlessness or excessive or inappropriate guilt but in group A the symptoms such as diminished interest or pleasure, insomnia or hypersomnia and fatigue or loss of energy was found significant improvement ($p<.05$, $p<.01$) when compared to baseline.

Table: 1: Clinical Symptoms of All Randomized Patients of "Major Depressive Disorder" from baseline to end of treatment.

Symptoms	**Therapy Group**	**Baseline Day n (%)**	**Day 42 n (%)**	**Changes from Baseline n (%)**	**p value**
Depressed mood	Group A	13 (86.66%)	11 (73.33%)	02 (13.33%)	>0.05 ns
	Group B	12 (80%)	07 (46.66%)	5 (33.33%)	<0.05*
Diminished interest or pleasure	Group A	13 (86.66%)	08 (53.33%)	05 (33.33%)	<0.05*
	Group B	15 (100%)	05 (33.33%)	10 (66.66%)	<0.01**
Significant weight loss or weight gain	Group A	05 (33.33%)	02 (13.33%)	03 (20.00%)	>0.05 ns
	Group B	07 (46.66%)	03(20.00%)	04 (26.66%)	<0.05*
Insomnia or hypersomnia	Group A	12 (80.00%)	05 (33.33%)	07 (46.66%)	<0.01**
	Group B	14 (93.33%)	05 (33.33%)	09(60.00%)	<0.01**
Psychomotor agitation or retardation	Group A	07 (46.66%)	04 (26.66%)	03 (20.00%)	>0.05ns
	Group B	08 (53.33%)	03 (20.00%)	05 (33.33%)	<0.05*
Fatigue or loss of energy every day	Group A	11 (73.33%)	04 (26.66%)	07 (46.66%)	<0.01**
	Group B	13 (86.66%)	05 (33.33%)	08 (53.33%)	<0.01**
Feeling of worthlessness or excessive or inappropriate guilt	Group A	10 (66.66%)	07 (46.66%)	03 (20.00%)	>0.05 ns
	Group B	12 (80.00%)	09(60.00%)	03 (20.00%)	>0.05 ns
Diminished ability to think or concentrate, or indecisiveness	Group A	10 (66.66%)	07 (46.66%)	03 (20.00%)	>0.05 ns
	Group B	11 (73.33%)	07 (46.66%)	04 (26.66%)	<0.05*

Table 2 and 3 showed that the score of HDRS 17, CGI-S was significantly (p<.001) decreased in both groups when compared to baseline and CGI-I also showed significant effects when compared to day 14. In intergroup comparison more improvement showed in Group B where study population was administered Shaman therapy with Shirodhara.

Table 2: Hamilton Depression Rating and Clinical Global Impression –Severity score of All Randomized Patients of "Major Depressive Disorder" from baseline to end of treatment

Parameters	**Therapy Group**	**Baseline (Mean ±SD)**	**Day 42 (Mean ±SD)**	**t value**	**p value**
HDRS 17	Group A	15.33±2.09	11.53±2.07	12.192	< 0.001***
	Group B	15.40±1.72	9.13±2.48	12.982	< 0.001***
CGI-S	Group A	4.40 ±0.63	3.33±0.49	5.870	< 0.001***
	Group B	4.20 ±0.77	2.27±0.70	12.614	< 0.001***

Note: Each value represents the mean ± SD; Statistical analysis was done by Student's paired t-test when *p<0.05, **p<0.01, ***p<0.001as compared to baseline. ns= Not Significant

Table 3: Clinical Global Impression –Improvement score of All Randomized Patients of "Major Depressive Disorder" from baseline to end of treatment

Parameter	**Therapy Group**	**Day 14 (Mean ±SD)**	**Day 42 (Mean ±SD)**	**t value**	**p value**
CGI-I	Group A	3.60±0.63	3.00±0.65	3.674	< 0.001***
	Group B	3.33±0.49	2.33±0.62	5.916	< 0.001***

Note: Each value represents the mean ± SD; Statistical analysis was done by Student's paired t-test when *p<0.05, **p<0.01, ***p<0.001as compared to baseline. ns= Not Significant

In intergroup comparison it showed significant difference between two groups it means both groups has not similar function and it is also find out that group B more effective than group A.

Table 4: Intergroup Efficacy Measure of Major Depressive Disease Score

Efficacy measure	Treatment Group	N	End of treatment (Mean)	SD	t value	p value comparison between groups
HDRS 17	Group A	15	11.53	2.07	2.747	<0.05
	Group B	15	9.13	2.48		
CGI-S	Group A	15	3.33	0.49	4.943	<0.01
	Group B	15	2.20	0.68		
CGI-I	Group A	15	3.00	0.66	2.439	<0.05
	Group B	15	2.33	0.62		

Note: Each value represents the mean, n = 15; Statistical analysis was done by Unpaired t test when *p<0.05, **p<0.01, ***p<0.001as compared to Group 1. ns= Not Significant

The vital signs including blood pressure, pulse rate, body weight was assessed at final day of study. The laboratory examinations such as haematolological (total leucocytes count, differential leucocytes count, erythrocyte sedimentation rate and hemoglobin concentration), biochemical (serum bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, fasting blood sugar, serum creatinine, serum urea, high density lipoprotein, low density lipoprotein, total cholesterol, total triglyceride and Electrocardiogram had showed no significant changes in any groups at the end of treatment.

Nardostachys jatamansi, *Lavandula stoechas* were the ingredients of tested herbal preparation. The above plants having *katu* (pungent) *tikta* (bitter) and *kasaya* (astringent) *rasa*; *laghu* (light), *tiksna* (sharp), and *ruksa* (un-unctuous) *gunas* (attributes); *usna* (hot) *virya* (potency); and *katu viapka*. According to basic *Ayurvedic* theory, these properties help to decrease the *kapha dosha*.[6] As the depression is *kapha* predominant diseases so the above plants possibly reduce the symptoms of severity in this study. Not only that, these plants have specific action on *medhya* (memory), *anidra* (insomnia) and *manasa dosha*. Due to their *usna* and *tiksna guna* it assists to breakdown the *avarana* of *tama guna* and increase the *satva guna* and at the same time it nourishes the *sadhaka pitta* that helps to purify the *manovaha srotasa*, the microcirculation of psychiatric system

Shirodhara helps to change the **psychoneuroimmunologic function** of brain but how it works or what level in the brain it works is not clear till date. However, few hypothesis can be drawn out of its mode of action. When lukewarm oil poured on forehead it starts the action from the **tactile stimulation** of the skin innervated by the first branch of the **trigeminal nerve**. Then possibly impulses transmitted to the **thalamus** through the **principal nucleus** and forward to the **cerebral cortex**. The impulses from the forehead cause a **somato-autonomic reflex**, and changes in levels of various neurotransmitters including, **serotonin, thyroid releasing hormone** (TRH), and **catecholamine.** And resulting in sympathetic suppression and physioimmunologic changes of peripheral circulation.When a constant stream of any liquid is poured over the forehead from a fixed height it results in pressure on the skin over the forehead. This pressure stimulates the **pacinian receptors** or the **mechano-receptors** that present on the skin, which in turn lead to mechanical deformation of the receptors, which result in the change in the membrane potential. Then it leads to generation of action potential, which is passed to the cerebral cortex via brain stem or the RAS & may helps to change the chemical level in the brain. Other way **Shirodhara** may help to make **interpersonal relationship** between patients and prescribers during the therapy that focuses on the **interpersonal behavior** by fostering adaptation to current interpersonal task and situations.

CONCLUSION

Finally this study suggests that the selected herbal preparation along with Shirodhara can be used in mild and moderate condition of major depression.

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