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Research Article

COMPARATIVE ASSESSMENT OF THERAPEUTIC POTENTIAL OF *VACHADI* AND HINGWADI GHRITA IN PATIENTS OF MILD TO MODERATE DEPRESSION

PAWAR MADHURI*, WELE ASMITA

Department of Rasashastra and Bhaishajya Kalpana (Ayurvedic Pharmaceutics and Pharmacology), Bharati Vidyapeeth Deemed University, College of Ayurved, Pune, Maharashtra, India. Email: drdalvimadhu08@gmail.com

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ABSTRACT

Objective: This exploratory clinical study dealt with comparative assessment of therapeutic effect of medicated ghee formulations, i.e., *Vachadi Ghrita* (VG) and *Hingwadi* Ghrita (HG) in patients of mild to moderate depression.

Methods: Open label non-randomized standard controlled clinical trial was carried out. Using Hamilton scale test, total 12 patients of mild to moderate depression were diagnosed and then grouped in two Groups (A and B). Patients of Group A and Group B received HG and VG along with standard antidepressants for 60 days, respectively. Pre, mid, and post HAMD scores of both group patients were recorded and compared. Data were analyzed with Friedman and Mann–Whitney statistical test.

Results: Statistical analysis showed a significant gradual change in HAMD values for both study groups after 60 days of treatment ($p<0.05$). However, when the difference between pre- and post-treatment HAMD scores of both groups are statistically analyzed, HG demonstrated significant positive result in a reduction of HAMD scores ($p=0.003$, <0.05) compared to VG. Beneficial effects on patients appetite, bowel movement was seen for both group patients.

Conclusion: Thus, it is concluded that along with antidepressants HG would be the better choice as an adjuvant drug than VG for patients of mild to moderate depression. More studies with the larger number should be done to validate this result.

Keywords: Depression, *Unmad-vishad, Hingwadi* Ghrita*, Vachadi Ghrita*, Medicated ghee formulations, Hamilton scale.

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INTRODUCTION

Depression is estimated to affect 350 million people. The world mental health survey performed in different countries found that on average about one in 20 people reported an episode of depression in the previous year [1]. It is a mood disorder characterized by loss of interest, feelings of guilt, low mood and associated emotional, cognitive, physical, and behavioral symptoms with severe harms for healthy life [2].

In Ayurveda traditional literature two multifactorial mental illness, *viz*., *Unmad* (Insanity) and *Apasmar* (epilepsy) are stated. It is seen that premonitory symptoms of *Unmad* and term *Vishad* can be correlated with symptoms of depression [3-5]. Available antidepressant drugs benefit population suffering from depression still having certain adverse effects [6]. Remarkable acceptance of Ayurveda herbal formulations is seen globally. Thus, as a supportive therapy, it may be helpful to manage depression.

Vachadi Ghrita (VG) [7] and *Hingwadi* Ghrita (HG) [8] are two medicated ghee formulations from Ayurveda stream of medicine broadly claimed to reduce symptoms of psychosis and to improve human cognition, respectively. Along with cow ghee, contents of HG and VG are specified in the formula; thus variations in their actions are narrated in literature. To prove this claim, in earlier research works VG was investigated in animals as well as in humans and proved its positive effect on memory [9,10], while in preclinical studies HG has shown antipsychotic, antiepileptic, and antidepressant activities in animals [11-13]. However, until a date no clinical data are available for these two formulations. Thus, the assessment of their therapeutic potential was done in this clinical study. The purpose of the present study was to compare the effect of HG and VG, which were given as adjuvant drugs, along with standard antidepressant (SAD) drugs in patients of mild to moderate depression.

METHODS

Preparation of HG and VG

Dry form of each ingredient of both formulations was reduced to a fine particle size and then converted into paste form. VG was prepared with a paste of eight herbal drugs which were processed in cow ghee and water. HG was prepared using a paste of four herbal drugs and black salt, which was then processed in animal products**,** *viz.,* cow urine and cow ghee. Both medicated ghee formulations were prepared according to standard protocols given in the Ayurveda classical texts. Analytical evaluation of resultant report is given in Table 1.

Clinical study

In clinical trial, prediagnosed subjects of mild to moderate depression were chosen. Patients, who were willing to participate and met inclusion criteria, were included in the study. Patients are suffering from bipolar depression, depression with dementia, severe depression, and major depressive disorders with another concomitant disease such as hypertension, diabetes mellitus, accidental trauma, and pregnant woman were excluded. Based on this criteria, 12 patients from the age group of 25 to 50 were selected. The patients and their relatives were

Table 1: Physico-chemical analysis of HG and VG

Parameter	HG	VG
Moisture (%)	0.09	0.12
Refractive index	1.4549	1.4542
pH	4.68	5.03
Specific gravity	0.9104 g/ml	0.9223 g/ml
Saponification value	180.81	276.48
Iodine value	39.14	32.57

HG: *Hingwadi* Ghrita, VG: *Vachadi Ghrita*

informed beforehand that study drugs do not have any side effects and were explained about their probable actions. Informed consent was taken from patients before initiating the study. Ethical clearance was taken from Institutional Ethics Committee Bharati Vidyapeeth University, with approval number BVDUCOA/1792/EC/2015-16. 12 patients were nonrandomly grouped in Group A (HG+SAD) and B (VG+SAD). A detailed history of each patient was taken using modern and ayurvedic science case paper. Personal diary was given to patients, where marking of drug consumption, dropped drug doses and any changes they observed in physical and mental attributes was done by patients.

Before starting actual intervention of study drugs, HAMD scores of each patient were recorded as baseline readings. After that, a 10 g dose of HG and VG was administered to patients of Group A and Group B with Lukewarm water. Drugs were administered in the morning and evening for continuous 60 days. Antidepressant drugs recommended by psychiatrist were continued along with study drugs. Follow-up of each patient for general health parameters was taken after every 15th day. HAMD scores of each patient from both groups were recorded on the 30th day and after completion of drug treatment, i.e., on 61st day. Other effects of drugs on patient's appetite, bowel movements were also documented.

Statistical analysis

Premedication, mid and after medication HAMD scores of both groups was statistically analyzed with Friedman test. Data were analyzed and compared for pre- and post-treatment HAMD scores of HG and VG groups. Statistical comparison was done between the two groups using the Mann–Whitney test.

RESULTS

Physicochemical test

Obtained values of HG and VG are compiled with standard values, indicate that both formulations were prepared according to standard methods and attain desired qualities (Table 1).

Hamilton scale test

The result was interpreted for HAMD scores of each group which were obtained using Hamilton scale test. Within each group comparison of HAMD scores was done. On the 61st day, gradual reduction in HAMD scores of group HG+SAD ($p<0.05$) and group VG+SAD ($p<0.05$) was statistically seen (Tables 2 and 3).

Comparative assessment of effect of HG and VG

The result was interpreted for pre- and post-treatment HAMD values of group HG+SAD and group VG+SAD using Mann–Whitney test. The data was expressed as mean difference of ranks. For HG+SAD group it was 3.50, and for VG+SAD group it was 9.50, and the difference was statistically significant ($p<0.05$) (Table 4). Thus, the greater significant effect on reduction in HAMD values of group HG+SAD was seen as compared to group VG+SAD.

Table 2: Pre, mid, and post-treatment HAMD scores of HG+SAD

Group A	Mean rank	Chi-square	Df	p
Pre	3	11.56	2	3.08E-03 (<0.05)
Mid	1.916667			
Post	1.083333			

n=6, $p<0.05$ values are expressed in mean ranks. n: Number of patients, HG: *Hinjewadi* Ghrita, SAD: Standard antidepressants

Table 3: Pre, mid, and post-treatment HAMD scores of Group B

VG+SAD	Mean rank	Chi-square	Df	p
Pre	3	12	2	2.48E-03 (<0.05)
Mid	2			
Post	1			

n=6, $p<0.05$ values are expressed in mean rank by application of the statistical test. n: Number of patients, VG: Vachadi Ghrita, SAD: Standard antidepressants

Effect of drugs on patient's general health

During the treatment period, 90% patients of both groups showed well-formed stools and evacuation was also effortless. 92% patients of both groups persisted regular pattern of appetite, but 8% patients showed a decrease in normal appetite during the treatment period. Two patients from group HG+SAD while one patient from group VG+SAD showed nausea in the initial days of treatment. In a similar way, two patients from each group showed aversion to food. Significant change in BP, pulse, and skin condition and urination was not observed in both groups of patients.

DISCUSSION

In this era, increase in stress levels in human's life leads to develop CNS or mood disorders. Depression in the varied age group is now becoming a challenge in front of health providers. SAD offer compelling effects but have limitations due to their side effects. Although several alternative medicine remedies are encouraged for the treatment of mood disorders, only a few of them are documented.

In this non-randomized clinical exploratory study, we have investigated the therapeutic potential of two medicated ghee formulations, i.e., VG and HG. In Ayurveda literature, it is revealed that medicated ghee formulations are prepared using different lipid drugs. It is well documented that cow ghee is a superior source as a lipid base. It possesses Snigdha (unctuous), Agnidipan (increase cellular metabolism), and Majja dhatu pariposhan (nourishment of brain tissue) properties [14]. It helps to facilitate the positive effects of herbal drugs which are added in the preparation of medicated ghee formulations [15]. *Goghrita* promotes longevity and protects the normal functioning of bio components of the body as well as intellect and memory [16].

It is well narrated that to enhance the pharmacological action of compound formulation, raw drugs having similar properties and actions are processed together and hence, due to synergistic action, such Ayurveda formulations produce certain targeted action [17]. Thus, potent raw drugs having targeted action toward the brain, when boiled with cow ghee and with liquid media produces variant therapeutic actions, *viz.,* antipsychotic, antiepileptic, and antidepressant and improvement of learning and memory. Study drug HG, contains four herbal drugs, i.e., Hiṅgu (*Ferula narthex boiss*) [18], Śuṇṭhi (*Zingiber officinale*) [19], Marich (*Piper nigrum*) [20], and Pippali (*Piper longum*) [21], along with animal source drugs, *viz., Goghrita* (Cow ghee) [22], *Gomutra* (Cow urine) [23], and mineral drug *Sauvarcala lavaṇa* (Black salt) [24] show a variety of pharmacological actions toward different systems including CNS. While other study drug VG consists of Goghrita (Cow ghee), Vacha (*Acorus calamus*), Guduchi (*Tinospora cordifolia*), Shankhapushpi (*Convolvulus pluricaulis*), Haritaki (*Terminalia chebula*), Shati (*Hedychium spicatum*), Vidang (*Embelia ribes*), Shunthi (*Z. officinale*), and Apamarg (Achyranthes aspera). Eight herbal drugs of VG have been reported for their antipsychotic, antistress, antidepressant, and nootropic activities [25-30].

In accordance to Ayurveda, *Vishad* and premonitory symptoms of *Unmad* may develop due to vitiation of functional entities (*Vata, Pitta* and *Kapha*) along with an increase in *Tama* and *Raja* attributes of *Mana* (mind). Increase of greed, anger, fear, and jealousy leads to retard the normal thought processing of human being. Hence suppression in their consideration, decision, expression, and determination power leads into depressive conditions [31].

Study drugs HG and VG are having *Kaṭu Rasa* (pungent taste) and *Uṣṇa Vīrya* (hot potency) which mostly help to pacify *vāta* and *kapha doṣha* and reduce obstructions in *srotas* (micro channels), thus producing positive effects in the management of CNS disorders. The combinations of herbal drugs of VG and herbal and animal drugs of HG treated with

Table 4: Comparative analysis of before and after treatment HAMD scores of study groups HG+SAD and VG+SAD

Group	n	Mean of ranks	Sum of ranks	Mann–Whitney U test	Z value	p value
Group HG+SAD	6	3.50	21	0	–2.929	0.003
Group VG+SAD	6	9.50	57			

Data are expressed as mean and sum of ranks using Mann–Whitney test. n=6, p<0.05. HG: *Hinjewadi* Ghrita, VG: *Vachadi Ghrita*, SAD: Standard antidepressants

cow ghee transmit the aqueous and lipid soluble active principles and serve different therapeutic effects toward CNS. In earlier research works, a small number of research studies have been undertaken on HG and VG. The potential of HG as an antipsychotic, antiepileptic, and antidepressant formulation has been proven in the previous works [11-13]. In recent studies, VG showed nootropic activity in animals [9]. Magdum and Pawar. interpreted in their research work that VG has a significant effect on healthy human's memory, which is evaluated using PGI memory scale test [10].

Reduction in HAMD scores indicates a positive effect of treatment drugs. In this study, along with SAD, both formulations showed significant effects on gradual reduction of HAMD scores when analyzed through Hamilton scale test (widely used for investigating different medicament by modern fraternity). Thus, the result of the study confirms their therapeutic potential in the treatment of mild to moderate depression as $p < 0.05$. The study also enlightens that minimum 30 days' treatment is required to get desired effects of medicated ghee formulations as a decrease in HAMD scores were statistically evaluated from the 30th day to the 60th day. These two drugs have shown beneficial effects on patient's appetite and maintaining of a healthy pattern of bowel movements. As a result, HG and VG may remain supportive to reduce certain adverse effects of conventional antidepressant drugs. This positive effect of both drugs might be perceived due to unctuous property of cow ghee, which is processed with pungent, hot potency herbal drugs, thus responsible to present carminative and lubrication actions to the alimentary canal. In initial days of treatment, for 3-4 days, two patients from each group were complaining about nausea and aversion to food. They were asked to consume warm water for whole day, thereafter, those symptoms were not appeared again.

In comparison to VG, the contents of HG are predominantly of pungent taste and having hot potency due to the addition of cow urine and two drugs of Piperine family. In earlier studies, it is supported that phytoconstituents of *P. nigrum and P. longum* contribute pungent quality and used as a bio-availability enhancer. Equally, both possess anti-inflammatory, antidepressant, anticonvulsion, and antioxidant effects [32]. One of the contents of HG, i.e., cow urine is searched as bio-enhancer, and this is concluded that cow urine based medicines would definitely prove to be potential medicines [33]. Natural antioxidants scavenge the free radicals and avoid the excess ROS formation in the body. As a natural drug, an aqueous solution of black salt was proven for its free radical scavenging activity and hence might be acting as an antioxidant [34].

Thus as a compound formulation of all those drugs, HG had produced a greater therapeutic effect as compared to VG, when HAMD scores were statistically analyzed ($p<0.05$, Table 3). This unique synergism of distinctive ingredients of HG might be exhibiting antidepressant action. Thus, it would be used as an adjuvant drug in the management of mild to moderate depression in comparison to VG.

Moreover, according to modern science, an adequate amount of serotonin helps to regulate sleep, appetite, and mood and inhibits pain. Research supports that some of the depressed people have reduced serotonin transmission [35]. Depletion of neurotransmitters, *viz*., Noradrenaline and 5 Hydroxytryptamine (Serotonin) leads to the development of depression-like state. Antidepressants which are used in treatment block the mechanism of enzymes and amines which permit free release of neurotransmitters [36]. Thus, with this theory, we can interpret that HG might be helping either to increase serotonin transmission or reduce depletion of the neurotransmitter whereas VG might be having different action on different neurotransmitters.

The study is limited to the very small sample size and focused on a single parameter. Therefore, systematic clinical study with a higher number of patients should be planned using other parameters. Integrative thought process should be raised in the planning of further study for the administration of HG and VG formulations in patients of depression to minimize drug dose and adverse effects of SAD.

CONCLUSION

HG and VG showed a significant effect on reduction in HAMD scores after 60 days of treatment. In this study, it is confirmed that HG has *a* remarkable effect on reduction of HAMD scores compared to VG. Thereby, it is concluded that HG might be the better choice while treating patients of mild to moderate depression as an adjuvant drug.

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