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Original Research Article

A randomized, double blind, standard controlled trial to compare safety and efficacy of two leading brands of Ashwagandha products in patients suffering from mental health related symptoms

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ABSTRACT

Background: Mental health related symptoms are common among the population. Current treatment exhibits serious adverse effects, delayed onset of action and low efficacy. Ashwagandha has a variety of beneficial effects in mental health disorders. We did a comparison of two Ashwagandha brands using a variety of scales for anxiety, depression, stress, and sleep quality.
Methods: The study was conducted in 80 patients suffering from mental health related symptoms. Test product used was: Herbochem +91 Ashwagandha 500 mg capsules and control used was: KSM 66 Ashwagandha 600 mg capsules.
Results: The reduction in the perceived stress scores and Hamilton depression scale scores at day 30/60 from day 0 was higher in the test group as compared with the control group. The reduction in the Beck's anxiety inventory scores at day 30/60/90 from day 0 was higher in the test group as compared with the control group. The increase in the Pittsburgh sleep quality index scores at day 30/60 from day 0 was higher in the test group as compared with the control group. The reduction in the serum cortisol scores at day 30 from day 0 was higher in the test group as compared with the control group. Results showed that, the incidence of adverse events was same in both groups.
Conclusions: It is important to note that test product having 500 mg Ashwagandha, showed better efficacy as compared to control product having 100 mg more (600 mg) of Ashwagandha.

Keywords: Ashwagandha, Mental health, Anxiety, Depression, Stress, Sleep quality

INTRODUCTION

Mental health related symptoms are common among the population. As per World Health Organization (WHO), in 2019, 1 in every 8 people, or 970 million people around the world were living with a mental disorder, with anxiety and depressive disorders the most common. In 2020, the number of people living with anxiety and depressive disorders rose significantly because of the COVID-19 pandemic.[1] In 2017, India had 197.3 million (95% of the total population) persons with mental disorders, accounting for 14.3% of the country's total population.[2,3] Mental health related symptoms, typically include depression that interferes with the patient enjoying a healthy and happy life. In a very large number of cases, it is associated with stress and anxiety, so that most patients suffer from these symptoms concomitantly.[4] A commonly associated problem is that of sleep disorders, that worsen the condition of the patient. In the recent past, prolonged lockdown, social isolation and economic problems have added to the problem of depression leading to major illnesses.[4]

Current treatment of these mixed mental problems leaves much to be desired, and most drugs have serious adverse effects such as sleep disturbances, sexual dysfunction, tolerance and weight gain.[5] The biggest problem with some of these drugs is delayed onset of action in addition to low efficacy.[6]

Ashwagandha (*Withania somnifera*) has demonstrated a variety of beneficial effects in animal and human studies including adaptogenic, anti-stress, anti-anxiety an antidepressant activity.[6] It has also been used for long to treat sleep disturbance.[7]

In this study a formulation Ashwagandha: *Withania somnifera* (WS) was studied in comparison to a marketed brand on a double blind, randomized, basis, using a variety of scales for anxiety, depression, stress and sleep quality. For each of these symptoms a specific scale that has been validated worldwide was used. Primary objective of this study was to compare the reduction in symptoms of anxiety, stress, sleep depression and depression in patients complaining of mental health problems. in either group at day 30, 60 and 90 with the base line scores on day 0. Secondary objective of this study was to compare the reduction in serum cortisol levels at 30, 60 and 90 days in either group, against those at baseline on day 0. To compare the adverse events, if any, produced by either formulation.

METHODS

Study type

This was a prospective, randomized, double blind clinical trial.

Study place

The study was conducted at Vakratunda Hospital, Nashik, Maharashtra.

Study period

The study was done from January 2023 to May 2023.

Selection criteria for the patients (inclusion and exclusion criteria)

Inclusion criteria were: patients of either sex between 18 to 60 years of age; suffering from mental health related symptoms of with stress, anxiety, depression, and sleep disturbance; and patients providing written informed consent. Exclusion criteria were: pregnant and lactating patients; patients with liver, kidney impairment; patients addicted to alcohol or psychotropic drugs; patients with severe other psychiatric illnesses; patients who have participated in any clinical trial in the last six months; and patients taking Ayurvedic medicines containing Ashwagandha.

Study procedure

This study was done with the investigational product: Herbochem +91 Ashwagandha 500 mg capsules and comparator: KSM 66 Ashwagandha 600 mg capsules. A total of 80 participants were recruited, and were randomized in two groups in 1:1 ratio. Thus, each treatment group had 40 patients. All concomitant medication and concurrent therapies were documented at baseline/screening and at study days or appropriate visits and at early termination when applicable. Dose, route, unit frequency of administration, and indication for administration and dates of medication were captured. At each visit after the first, the participant returned the unused IP. Depending on the day on which the participant makes the visit, the staff calculated the number of units of the IP that should have been consumed. From the unused units the staff calculated the actual number of units consumed. Compliance was calculated as a percentage, with 100% consumption meaning complete compliance. Efficacy parameters assessed were assed with different scales like, perceived stress score, Beck's anxiety inventory, Hamilton depression rating scale, Pittsburgh Sleep Quality Index, and Serum Cortisol (mcg/dl), safety parameters assessed were: adverse events, clinical examination, laboratory data (haematology), and laboratory data (biochemistry).

Study ethical approval

Ethics committee approval was taken from Navsanjeevani Hospital Ethics Committee, Nashik.

Statistical analysis

After data was entered into the study database, a system of computerized data validation checks was implemented and applied to the database on a regular basis. The study database was updated in accordance with the resolved queries. All changes to the study database were documented. Descriptive analysis including tables and figures were done for this study. Scores related to objectives of the study were determined along with their percentages. Change in scores at day 30/60/90 from day 0 scores were calculated to determine statistical significance.

RESULTS

Perceived stress score graphs

As seen in Figure 1, change in scores at day 30/60/90 from day 0 scores were statistically significant for both test and control groups ($p<0.0001$). The reduction in scores at day 30/60 from day 0 was higher in the test group as compared with the control group. It is further important to note that this better efficacy in stress scores was seen with test product having 500 mg Ashwagandha, as compared to control product having 100 mg more (600 mg) of Ashwagandha.

Beck's anxiety inventory

As shown in the Figure 2, change in scores at day 30/60 (only test)/90 from day 0 scores were statistically significant for both test and control groups (p=0.01 or below). The reduction in scores at day 30/60/90 from day 0 was higher in the test group as compared with the control group. It is further important to note that this better improvement in anxiety scores was seen with test product having 500 mg Ashwagandha, as compared to control product having 100 mg more (600 mg) of Ashwagandha.

Hamilton depression rating scale

As shown in the Figure 3, change in scores at day 30/60/90 from day 0 scores were statistically significant for both test and control groups (p<0.0001). The reduction in scores at day 30/90 from day 0 was higher in the test group as compared with the control group. It is further important to note that this better improvement in depression scores was seen with test product having 500 mg Ashwagandha, as compared to control product having 100 mg more (600 mg) of Ashwagandha.

Pittsburgh sleep quality index

As seen in the Figure 4, change in scores at day 30/60/90 from day 0 scores were statistically significant for both test and control groups (p<0.0001). The increase in scores at day 30/60 from day 0 was higher in the test group as compared with the control group. It is further important to note that this better sleep quality scores were seen with test product having 500 mg Ashwagandha, as compared to control product having 100 mg more (600 mg) of Ashwagandha.

Serum cortisol

As shown in the Figure 5, change in scores at day 30/60/90 from day 0 scores were statistically significant for both test and control groups (p<0.01). The reduction in scores at day 30 from day 0 was higher in the test group as compared with the control group. It is further important to note that this reduction in serum cortisol was seen with test product having 500 mg Ashwagandha, as compared to control product having 100 mg more (600 mg) of Ashwagandha.

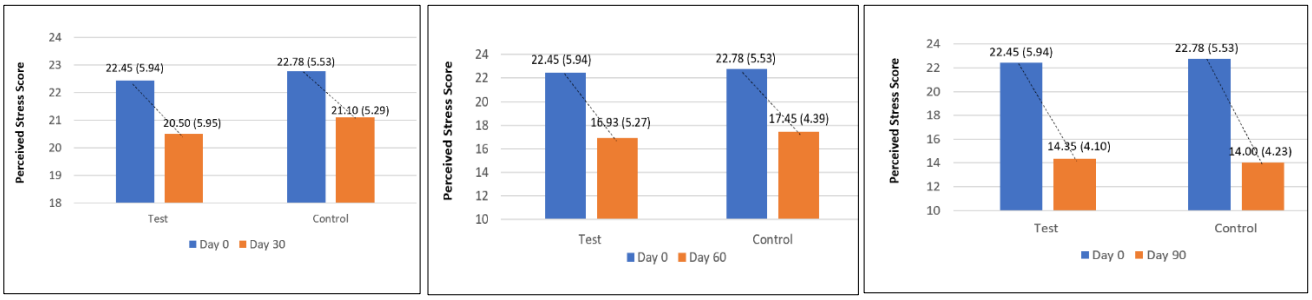

Figure 1: Perceived stress score.

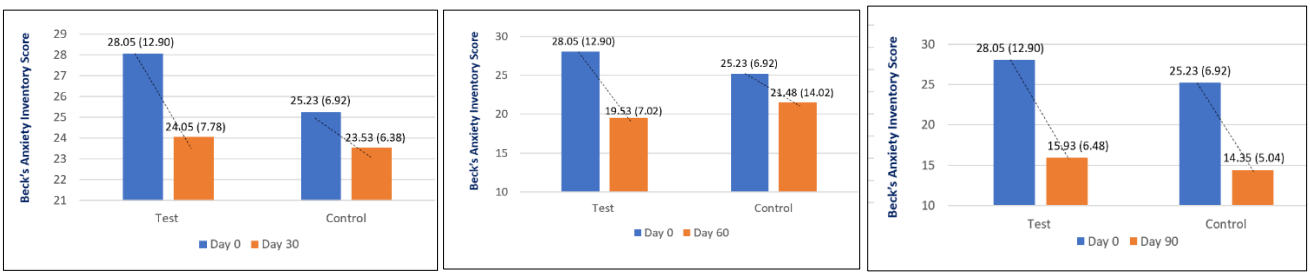

Figure 2: Beck's anxiety inventory.

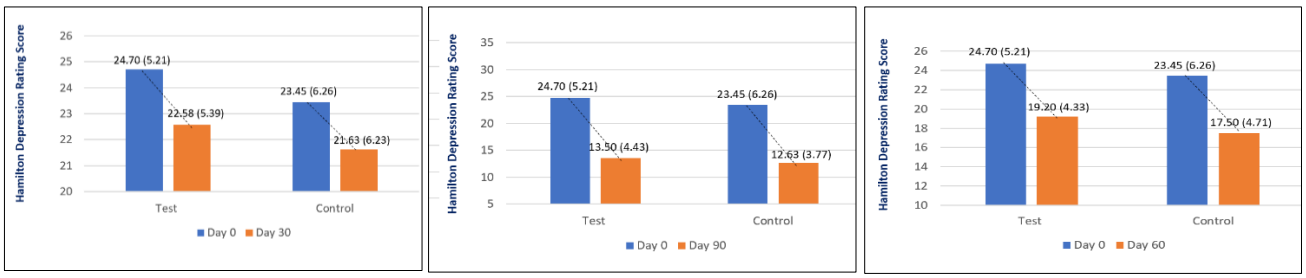

Figure 3: Hamilton depression rating scale.

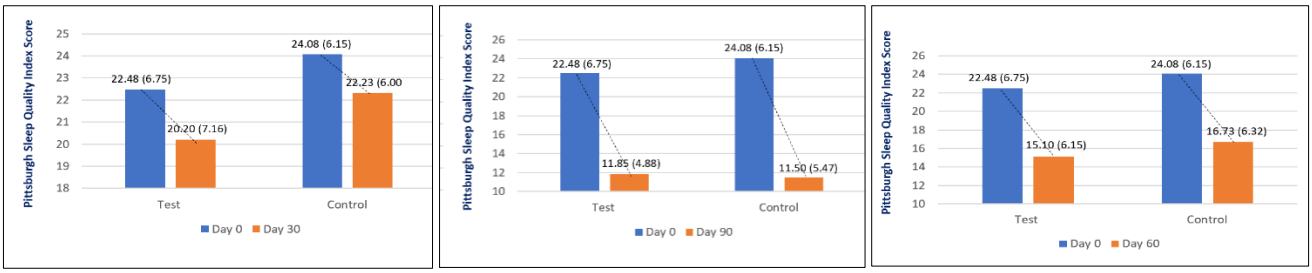

Figure 4: Pittsburgh sleep quality index.

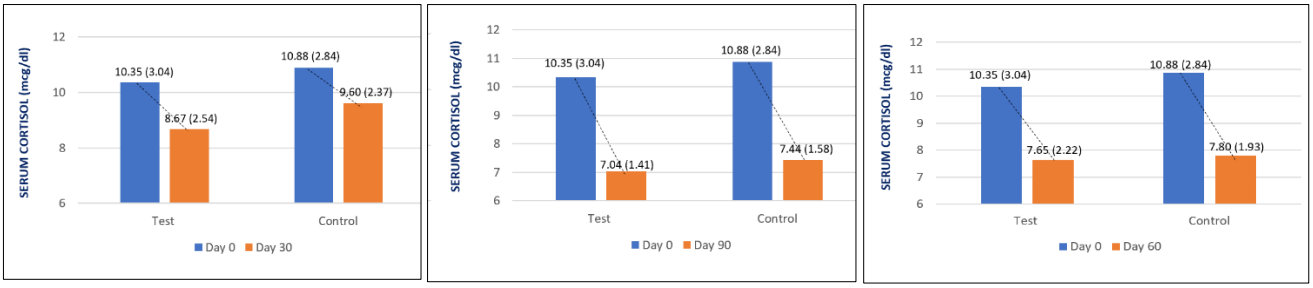

Figure 5: Serum cortisol.

Based on the observed results of perceived stress score, Beck's anxiety inventory, Hamilton depression rating scale, Pittsburgh sleep quality index and serum cortisol (mcg/dl) levels it can be concluded that "test product" has shown better efficacy than "control product".

Safety results seen in this study were as follows.

Adverse events

The incidence of adverse events was same in both groups. Three subjects in each arm reported adverse events. All events resolved without any sequelae. No serious adverse events were reported in the study.

Clinical examination

The test and control groups were similar with baseline clinical examination findings. The changes observed in oral temperature, blood pressure (systolic and diastolic), pulse rate and respiratory rate on day 90 as compared with day 0 (baseline) were not significant.

Laboratory data (hematology)

The test and control groups were similar with baseline haematology findings. The changes observed in hematology parameters on day 90 as compared with day 0 (baseline) were not significant.

Laboratory data (biochemistry)

The test and control groups were similar with baseline biochemistry findings. The changes observed in biochemistry parameters on day 90 as compared with day 0 (baseline) were not significant. Based on these results it is observed that the "test product" is as safe as the "control product".

DISCUSSION

Our study showed the better efficacy of test product (product: Herbochem +91 Ashwagandha 500 mg capsules had good efficacy in terms of perceived stress score, Beck's anxiety inventory, Hamilton depression rating scale, Pittsburgh sleep quality index and serum cortisol (mcg/dl) levels and it was better than the comparator: KSM 66 Ashwagandha 600 mg capsules.

Paul mentioned that Ashwagandha has been used as a traditional Rasayana herb for a long time. Traditional uses of this plant indicate its ameliorative properties against a plethora of human medical conditions. He mentioned that Ashwagandha was found to be especially active against many neurological and psychological conditions like Parkinson's disease, Alzheimer's disease, Huntington's disease, ischemic stroke, sleep deprivation, amyotrophic lateral sclerosis, attention deficit hyperactivity disorder, bipolar disorder, anxiety, depression, schizophrenia and obsessive-compulsive disorder. Results shown in this study are in line with the Paul, wherein he provided activites of *Withania somnifera* (Ashwagandha).[10]

Koboyama mentioned that the neurodegenerative diseases commonly induce irreversible destruction of central nervous system (CNS) neuronal networks, resulting in permanent functional impairments. Effective medications against neurodegenerative diseases are currently lacking. Ashwagandha (roots of *Withania somnifera* Dunal) is used in traditional Indian medicine (Ayurveda) for general debility, consumption, nervous exhaustion, insomnia, and loss of memory. In this review, we summarize various

effects and mechanisms of Ashwagandha extracts and related compounds on in vitro and in vivo models of neurodegenerative diseases such as Alzheimer's disease and spinal cord injury. As mentioned by Kuboyama, our study has shown efficacy in mental disorders like depression, anxiety, stress, sleep quality.[11]

A study done by Speers showed that Ashwagandha exhibited noteworthy anti-stress and anti-anxiety activity in animal and human studies. It also improved symptoms of depression and insomnia. He also mentioned that Ashwagnadha may alleviate these conditions predominantly through modulation of the hypothalamic-pituitary-adrenal and sympathetic-adrenal-medullary axes, as well as through GABAergic and serotonergic pathways. Our study results are in line with the study done by Speers.[7]

A study done by Chandrashekhar showed that, the treatment group that was given the high-concentration full-spectrum Ashwagandha exhibited a significant reduction in scores on all the stress-assessment scales, relative to the placebo group. The serum cortisol levels were substantially reduced in the Ashwagandha group, relative to the placebo group. The adverse effects were mild in nature and were comparable in both the groups. No serious adverse events were reported. Our results are in line with the study done by Chandrashekhar.[12]

A study done by Lopresti showed that, no participant in the trial had any adverse events reported. Ashwagandha intake was also associated with greater reductions in morning cortisol as compared with the placebo. Our study results are in line with the study done by Lopresti.[13]

Limitations

Present study was done only in 160 patients. Future studies in larger sample size can be done to further explore detailed activity. This study was done only in single centre, future studies can be done on all India basis as well at the international level.

CONCLUSION

Based on the observed results of perceived stress score, Beck's anxiety inventory, Hamilton depression rating scale, Pittsburgh sleep quality index and serum cortisol (mcg/dl) levels it can be concluded that "test product" has shown better efficacy than "control product". Based on the observed results it can be concluded that the "test product" is as safe as the "control product". This study showed that in terms of efficacy the test product showed better results and in terms of safety it had similar profile to the control product.

This study has clearly shown that Ashwagandha test product (500 mg Ashwagandha) with lesser as better than the control product (600 mg Ashwagandha). Our study has clearly helped to understand the efficacy of test product with 500 mg Ashwagandha i.e. better efficacy than control product containing 600 mg of Ashwagandha.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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