Effect of *Unmadagajakesari rasa* on biochemical parameters of patients with *Kaphaja unmada* (Major Depressive Disorder)

Ariyaratna S.R., [1]*, Kulathunga R.D.H.[2], Mendis B.J.[3]

Abstract

Major depressive disorder is one of the most prominent mood disorders affecting both psychic and physical bodies. The World Health Organization emphasized that depression is the fourth most disabling health issue worldwide and affects more than 350 million of global population. The symptoms of major depressive disorder are mostly similar to those of *Kaphaja unmada* mentioned in Ayurveda authentic texts. The present study focused on effects of *Unmadagajakesari rasa* on serum biochemical parameters of the patients who have major depressive disorder and was designed as a one group pre-test, post-test study. In the present study, forty patients were administered the trial drug, *Unmadagajakesari rasa* 250 mg, daily for eight weeks and were assessed by using Hamilton Depression Rating Scale before and after the treatment. Moreover, serum biochemical parameters of the patients were measured before and after the treatment. Accordingly, the mean scores of serum glutamic pyruvic transaminase, serum glutamic oxaloacetic transaminase, blood urea, and serum creatinine of the patients before the intervention were approximately as same as those after the intervention. On the contrary, at the end of the treatment, the mean scores of the serum level of dehydroepiandrosterone sulfate indicated statistically significant decrease in male patients, whereas, it did not indicate statistically significant mean difference in female patients. In view of the above, it can be concluded that *Unmadagajakesari rasa* is a safe medicine; furthermore, serum dehydroepiandrosterone sulphate (DHEAS) can be considered as a probable bio-marker in the diagnosis of *Kaphaja unmada* with special reference to major depressive disorder for male patients.

Keywords: Major depressive disorder, DHEAS, Ayurveda, *Unmadagajakeshari rasa*

Introduction

Depression, a significant contributing factor to the global burden of disease, is the fourth most disabling medical condition worldwide and is expected to be ranked second by 2020[1,2]. The World Health Organization stressed that the burden of depression is 50% higher for females than males[3]. Among global patients who have depression, almost one million of them get committed suicide, which translates to 3000 suicide deaths every day. Of those patients who commit suicides, 20 or more of them attempt to contemplate suicide[4]. The recent epidemiological study explored that the lifetime prevalence of depression in Sri Lanka is 6.6%[5]. In contrast to the above fact, depressive symptoms have been found to be present among 57.7% of school-going adolescents in Sri Lanka[6]. Furthermore, Genetic analysis data of Sri Lanka also stated that female patients with depression have higher heritability than that of male patients.

The main symptoms of major depressive disorder (MDD) are depressed mood, markedly diminished interest or pleasure, significant weight loss when not dieting or significant weight gain, decrease or increase in appetite, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive or inappropriate guilt, diminished ability to think or concentrate, indecisiveness, etc.[7]. Correspondingly, the main symptoms of *Kaphaja unmada* (KU) are mentioned to be *Vakmandata, Chestamandata, Tushnimbahava, Arochaka, Svapnanityata, Agnisada, Sadana*, etc.[8]. In consideration of the above facts, the symptoms of *Kaphaja unmada* which are described in Ayurveda authentic texts are considered to be mostly similar to those of MDD; furthermore, KU has been correlated with MDD in previous studies[9,10,11].

Pharmacological agents are the main treatment modalities for MDD and antidepressants are the drugs

[1]*National Ayurvedic Teaching Hospital, Colombo 08, Sri Lanka.*
2Unit of Kayachikitsa, Institute of Indigenous Medicine, University of Colombo, Rajagiriya, Sri Lanka.
[3]*National Institute of Mental Health, Angoda, Sri Lanka.*

**Correspondence: Ariyaratna S.R., National Ayurvedic Teaching Hospital, Colombo 08, Sri Lanka. Email: saminda.ariyaratne@gmail.com*

of choice that have been recommended by the National Institute for Clinical Excellence as a first-line treatment of depression[12]. *Unmadagajakesari rasa* (UGKR) is considered to be effective in the management of KU and has been mentioned in few Ayurvedic texts such as Bruhathrasarajasundaraya[13], Yogaratnakaraya[14] etc. In addition to the above facts, UGKR, being a herbo-mineral preparation, has acquired the demand of patients owing to its innate qualities such as palatability, effective lesser dose, tastelessness, prolonged shelf life, instant action, etc. Therefore, in the present study, UGKR was used as the trial drug in the management of KU with special reference to MDD.

Dehydroepiandrosterone sulphate (DHEAS) is the most abundant steroid hormone in humans with serum concentration 250-500 times higher than dehydroepiandrosterone (DHEA)[15]. It is considered to be the precursor molecule that circulates throughout the peripheral tissues of the body and becomes into its desulphated form, DHEA. Higher level of DHEA is associated with increased memory and attention scores[16]; furthermore, it is considered to improve human performances in stressful situations[17]. The objective of the present study was to find out the effect of UGKR on biochemical parameters of the patients who have MDD. Furthermore, it comprises two specific objectives and one of them was to find out whether there was any association between serum level of DHEAS and the pathophysiology of depression. The other specific objective was to find out the effect of UGKR on biochemical parameters such as serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), serum creatinine (SC), and blood urea (BU) of the patients with MDD.

Material and Method

The present study was carried out at the outpatient clinic of *Kayachikitsa* of National Ayurveda Teaching Hospital-Borella and was designed as a one group pre-test, post-test study, which comes under the quasi-experimental clinical trial[18]. The total duration of the study was eight weeks and the procedure of follow up assessment was carried out at every two weeks interval for the entire period. Moreover, this study accrued forty patients with KU with special reference to MDD. The consecutive sampling technique was used to gather patients. The ethical approval for the study has been granted from the ethical review committee for research in Institute of Indigenous Medicine met on 25.09.2014 under the registration no. ERC 14/23.

As the first task of the study, UGKR 250mg pills were produced under the formula mentioned in Bruhat rasarajasundaraya; accordingly, the main ingredients of UGKR were purified forms of *Parada, Gandaka*, *Manahshila*, seeds of *Dhattura* as well as decoctions of *Vacha* and *Brahmi*[19].

After completion of the psychiatric, psychological, and physiological assessments, 250mg of *Unmadagajakesari rasa* was given to each patient daily for eight weeks. Prior to the commencement of the treatment, and at the end of the treatment period, blood samples of the patients were collected early in the morning and analyzed them to measure serum levels of DHEAS, SGPT, SGOT, SC, and BU. Moreover, the quantitative data were analyzed using univariate and bivariate statistical methods and the paired sample t-tests were used to find out the differences between before and after the treatment; furthermore, 95% confidence level ($t < 0.05$) was used to make decisions.

The study was conducted in accordance with the ethical principles that have their origin in the declaration of Helsinki 2008, and local regulations were also considered. The approval of the ethical review board was taken from the Institute of Indigenous Medicine prior to the patient enrollment at the clinical site.

Moreover, patients (18yrs-60yrs) who fulfilled DSM IV-TR diagnostic criteria for MDD with moderate and severe in severity level according to HAM-D were enrolled in the study irrespective of sex, race, caste, occupation and religion. In addition to the above, they were required to have the ability to read, understand, fill and sign a written informed consent form to participate in this study.

In contrast to the above, those who have *Aganthuja unmada*, other types of *Nija unmada*, *Apasmara*, depression with the history of suicidal behaviors, other types of mood disorders, organic mental disorders, severe personality disorders, schizophrenia, generalized anxiety disorders, and patients who have a history of any of above disorders were excluded from the study. Further, Alzheimer's disease, dementia, parkinsonism, hypothyroidism, hyperthyroidism, uncontrolled diabetic mellitus, mental retardation, hepatic impairments, and renal impairments were excluded from the study.

Pregnant or breastfeeding women, patients who were under treatment for abuse of alcohol or drugs and

patients who have very severe MDD according to HAM-D, were also excluded.

Results

Data related to the effects of UGKR on biochemical parameters of the patients with MDD are presented in this section.

Table 1 shows that the mean scores of symptoms of Major depressive disorder before and after the treatments were 19.98 and 6.20 respectively, giving the mean difference of 13.78; thus, 68.97% of improvement was found.

In addition to that, Table 2 provides data related to the biochemical parameters such as DHEAS, SGPT, SGOT, BU, and SC. Accordingly, the mean scores of DHEAS tests of the female patients before and after the treatment were found to be 1.78µmol/L and 1.85µmol/L, respectively, giving the mean difference of (-) 0.073µmol/L. On the contrary, the mean scores of DHEAS tests of the male patients before and after the treatment were 3.93µmol/L and 2.92µmol/L, respectively, giving the mean difference of 1.015µmol/L. The mean scores of SGPT tests of patients before and after the treatment were 32.33U/L and 27.98U/L respectively, giving a mean difference of 4.35U/L. Moreover, the mean scores of SGOT tests of patients before and after the treatment were 28.025U/L and 26.30U/L respectively, giving a mean difference of 1.725U/L. The mean scores of SC tests of male patients before and after the treatment were found to be 86.11µmol/ L and 87.59µmol/ L, respectively, giving a mean difference of 1.482µmol/ L. The mean scores of SC tests of female before and after the treatment were 68.36µmol / L and 69.50µmol/ L, respectively, giving a mean difference of 1.138µmol/ L. The mean scores of the BU tests of the patients before and after the treatment were 3.44mmol /L and 3.66mmol /L, respectively giving the mean difference of 0.2mmol /L.

Table 1: Overall effect of *Unmadagajakesari rasa* on Major Depressive Disorder, according to the HAM-D (n-=40)

Assessment tools	MEAN			% of relief	SD	SE	t value	df	p value
	BT	AT	difference						
HAM-D	19.98	6.2	13.78	68.97	2.43	0.39	35.799	39	0.000

Table 2: Effects of *Unmadagajakesari rasa* on biochemical parameters of the patients with Major Depressive Disorder.

Biochemical Parameters	MEAN			SD	SE	t Value	df	p Value
	BT	AT	Difference					
DHEAS (Male)	3.93	2.92	1.015	1.104	0.221	4.596	24	0.000
DHEAS (Female)	1.78	1.85	-0.073	1.224	0.316	-0.231	14	0.821
SGPT	32.33	27.98	4.350	11.270	1.782	2.441	39	0.019
SGOT	28.03	26.30	1.725	6.296	0.995	1.733	39	0.091
SC (Female)	86.11	87.59	-1.482	8.084	1.617	-0.917	24	0.038
SC (Male)	68.36	69.50	-1.138	9.551	2.466	-0.461	14	0.652
BU	3.44	3.64	-0.200	0.703	0.111	-1.780	39	0.083

Discussion

The table-01 revealed that there was 68.97% of the improvement and the data were statistically significant (p<0.000). Therefore, it is obvious that *Unmadagajakesari rasa* reduced the severity of major depressive disorder.

According to the table-02, the mean scores of DHEAS tests of the male patients before and after the treatment were found to be 3.93 μmol and 2.92 μmol respectively, giving the mean difference of (+)1.015 μmol and the change was statistically highly significant(p<0.000). This difference is a relatively high figure. Therefore, the above data provide clues that elevated levels of serum DHEAS are associated with the pathophysiology of depression in males. Furthermore, the mean scores of DHEAS tests of the female patients before and after the treatment were 1.78μmol and 1.85μmol respectively, giving the mean difference of (-) 0.073μmol and the change was statistically insignificant (p<0.821). Therefore, the data emphasize that there is not any remarkable positive or negative association between serum DHEAS and pathophysiology of depression in female patients.

SGPT and SGOT are enzymes mainly found in hepatic and cardiac cells. They are also found in kidneys, muscles, and pancreas in smaller quantities. Both SGPT and SGOT are released into blood when the liver or the heart gets damaged; thereby increasing the levels of those two enzymes in blood. Moreover, certain medication can also raise the levels of both enzymes in blood. The normal range of SGPT in blood for males and females is similar to that of SGOT and it ranges from 0 U/L to 40 U/L. Referring to this study, the mean scores of both enzymes of patients before and after the treatment were within the expected range.

Creatinine is a chemical waste product of creatine and is entirely removed from the body by kidneys; therefore, SC level increases in blood when kidney function is abnormal. The normal ranges of SC in males and females are considered to be 80-115 μmol/L and 53-97 μmol/L, respectively. In the present study, the mean scores of SC level in male and female before and after the treatment were within the expected range.

Moreover, the normal level of BU exceeds in patients who have heart attack, congestive heart failure, gastrointestinal bleeding, dehydration, pyelonephritis, kidney failure, acute tubular necrosis, and urinary tract obstruction; conversely, lower level of BU is associated with liver failure, low protein diet, malnutrition, and overhydration. The normal range of BU for males and females is 2.8-7.2 mg/dl. This study revealed that the mean scores of BU of these patients before and after the treatment were also within the normal range.

Based on the above facts, it is obvious that UGKR has not caused any remarkable change in biochemical parameters such as SGPT, SGOT, SC, and BU of those patients.

Conclusion

The study revealed that elevated levels of serum DHEAS were associated with pathophysiology of depression in male patients. Considering the above fact, serum DHEAS can be considered as a probable bio-marker for MDD in males. Furthermore, it is obvious that UGKR did not cause statistically significant change in biochemical parameters viz. SGPT, SGOT, SC, and BU of the patients; therefore, it can be concluded that UGKR is a clinically safe medicine for the treatment of MDD.

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