

EFFICACY OF MADHUTRIPHALA AND GUDARDRAKA YOGA IN THE MANAGEMENT OF MADATYAYA (ALCOHOL WITHDRAWAL)

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ABSTRACT

Background: Alcohol withdrawal is stage of alcoholism characterised by physiological and psychological symptoms. *Madatyaya* (Alcoholism) is a similar condition where there is derangement of both *Shareerika* (Physical) and *Manasika Doshas* (Psychological). Hence a suitable *Shamana Oushadi* (Pacifactory drug) which acts both on body and mind would be an ideal choice. *Madhutriphala & Gudardraka Yoga* indicated in *Madatyaya* is one such formulation. The uniqueness of this *Yoga* (Therapeutic Formulation) is, there is mention of form, route and time of administration of drug with therapeutic indications. Hence an attempt was made to study the efficacy and pharmacological action of the combination drug on alcohol withdrawal symptoms. **Objective:** To study the efficacy of *Madhutriphala* and *Gudardraka Yoga* on alcohol withdrawal symptoms, laboratory parameters like liver function test and ultra sonography of abdomen. **Material and Methods:** 32 diagnosed patients of *Madatyaya* (Alcohol Withdrawal) were selected as single group and orally administered *Ardraka Kalka* (freshly grounded rhizome paste of *Zingiber officinale*) along with *Guda* (Jaggery) 12 grams each in the morning before food and *Triphala Choorna* (dried fruit powders of *Emblia officinalis*, *Terminalia chebula*, *Terminalia bellerica*) and *Madhu* (Honey) 12 grams each at bed time before food for seven days. The patients were assessed by Clinical Institute Withdrawal Assessment for Alcohol- Revised (CIWA-Ar) scale and *Samanya Madatyaya Lakshanas* (Ayurveda Parameters) before, during, after treatment and 1 week after treatment. The results were analysed statistically using SPSS VER.20. **Observation & Results:** Clinical data was collected and analysed using statistical test like Friedman's test, Wilcoxon test for subjective parameters and paired t-test for objective parameters. 30 patients completed the study. Statistical significance was seen in both subjective and objective parameters. **Interpretation & Conclusion:** It is concluded from the study that all the withdrawal symptoms subsided by seven days. The combination drug has got hepatoprotective, nootropic, anxiolytic, antidependence, immunomodulatory and antioxidant property which helped in improving the liver functions and also the cognitive impairment in patients with alcohol withdrawal.

Keywords: *Madatyaya*, Alcohol Withdrawal, *Madhutriphala*, *Gudardraka*

INTRODUCTION

As per WHO report, alcoholism is the third largest risk factor for disease burden. The harmful use of alcohol results in

2.5 million deaths per year. 32,000 young people between the age group of 15 and 29 die out of alcohol related cause, thus re-

sulting in 9% of all death in that age group¹. At least 20 percent of the patients in the mental health settings have alcohol abuse or alcohol related disorders, from all socio-economic backgrounds and both genders.

Those substances, which produces *Mada* (Intoxication) is called *Madya* and the disease caused by the improper use of *Madya* is termed as *Madatyaya*². *Madatyaya* is a *Tridoshaja Vyadhi* where *Kapha Sthana* (seat of *Kapha*) is affected along with the vitiation of *Agni* (Digestive fire). Based on the *Doshas* (Humours) vitiated, *Madatyaya* is classified as *Vataja*, *Pittaja*, *Kaphaja* and *Sannipataja*. *Acharya Sushruta* mentions 4 types of *Madatyaya* as *Panatyaya*, *Paramada*, *Panavibhrama* and *Paanajeerna*³. The treatment principle is to treat the *Kapha Sthana* first. There are many *Shamana Oushadis* in *Ayurveda*, *Madhutriphala & Gudardraka Yoga*⁴ is one among them. It contain *Triphala Choorna* (*Hareetaki*, *Vibhitaki*, *Amalaki*), *Madhu* (honey), *Ardraka Kalka*, *Guda* (Jaggery) each equal parts. It acts as *Deepana* (Appetiser), *Pachana* (Digestive), *Yakruthutejaka* (Hepatoprotective), *Medhya* (Cognitive Enhancer), *Rasayana* (Antioxidant), *Srotoshodaka* (Clearing channels). It helps in subsiding the withdrawal symptoms by reducing the alcohol craving.

Aims and Objectives: To study the efficacy of *Madhutriphala* and *Gudardraka Yoga* on subjective parameters of alcohol withdrawal and laboratory parameters like liver function test and ultra sonography of abdomen.

Materials and Methods: 32 diagnosed patients of *Madatyaya* (Alcohol Withdrawal) who fulfilled the inclusion criteria and willing to sign the informed consent form were selected from the outpatient department (OPD) and inpatient department

(IPD) of the SDM College of Ayurveda & Hospital, Hassan and studied as a single group. Institutional Ethical Committee (IEC) clearance was obtained prior to the study Ref. **IEC NO: SDMACAH/IEC/44/13-14 Dated 10th April 2013**. Duration of the study was for 1 week. Assessment was done before and after the study period.

Inclusion Criteria: Diagnosed patients of *Madatyaya* (alcohol withdrawal symptoms)

1. Age between 20-50 years of both gender irrespective of socio-economic status.

Exclusion criteria: The patients suffering from other organic brain diseases, systemic illnesses like Diabetes mellitus, uncontrolled hypertension.

1. Patients suffering from severe withdrawal symptoms like delirium tremens and status epilepticus.
2. Patients suffering from complications of alcohol like cirrhosis, ascites
3. Patients suffering from other psychiatric illnesses.

Assessment criteria:

Subjective parameters:

Samanya Madatyaya Lakshanas⁵:

Aruchi (Reduced Appetite), *Prajagara* (Insomnia), *Bhrama* (Giddiness), *Pralapa* (Delerium), *Roopanamasatam Chaiva Darshanam* (Hallucinations), *Chardi* (Vomiting), *Atisara* (Loose stools), *Hril-lasa* (Nausea), *Shareera Kampa* (Tremors) Grading for *Samanya Madatyaya Lakshanas*: 0-absent 1 - present

CIWA-Ar Scale⁶: Nausea/vomiting, anxiety, paroxysmal sweats, tactile disturbances, visual disturbances, visual disturbances, tremors, agitation, orientation and clouding of sensorium, auditory disturbances, headache.

Each criterion is rated on a scale from 0 to 7, except for orientation and clouding of sensorium which is rated on scale 0 to 4. Scores are added up to all 10 criteria.

Objective parameters: Liver function test- Total bilirubin, Direct bilirubin, Indirect bilirubin, SGOT, SGPT, Total Serum Albumin, Total Protein, Alkaline Phosphate

USG Abdomen

Diagnostic Criteria: Diagnosis was based on the basis of *Samanaya Madatyaya Lakshanas*

1. Diagnostic criteria for Alcohol withdrawal according to ICD-10⁷

The general criteria for withdrawal should be met i.e.

i) There must be a clear evidence of recent cessation or reduction of alcohol after repeated, and usually prolonged or high dose, use of alcohol.

ii) Symptoms and signs are not accounted for by a medical disorder unrelated to alcohol, and not better accounted for by another mental or behavioural disorder

A. Any three of the following signs must be present:

1. Tremor of the tongue, eyelids, or outstretched hands
2. Sweating
3. Nausea, retching or vomiting
4. Tachycardia or hypertension
5. Psychomotor agitation
6. Headache
7. Insomnia
8. Malaise or weakness
9. Transient visual, tactile or auditory hallucinations or illusions
10. Grand mal convulsions.

Plan of study: Patients were screened using CIWA-Ar scale, *Samanya Madatyaya Lakshanas*

Single group exploratory study, patients were selected on the basis of convenience

sampling and treated with *Ardraka Kalka* (freshly prepared) 12 grams⁸ with *Guda* (Jaggery) 12 grams oral administration in the morning before food for 7 days, *Triphala Choorna* 12 grams⁹ with *Madhu* (Honey) 12 grams at bed time before food for 7 days with *Pathya* (Rice gruel diet regimen).

The patients were assessed on day 1 before treatment, day 4, and day 7 after treatment and 1 week after treatments.

Statistical Analysis: Statistical analysis was done using SPSS VER.20.

Friedman's test was applied to analyse the significance of the change in subjective parameters. Wilcoxon's signed rank test was applied for post hoc which showed significance in Friedman's test, to interpret the time of significant change.

Paired t-test was applied for analysing the significance of objective parameters.

Observation and results: 45 patients who came to the OPD with the complaints of alcohol related problems were screened with CIWA-Ar scale and 32 patients who fulfilled the inclusion criteria were selected and registered for the study. Out of 32 patients, 2 patients withdrew from the study. The drop outs were due to poor family support and economic constraints.

The observation was done on 32 patients in which maximum patients (50%) were between the age group of 41-50 years and there were 2 female patients who developed withdrawal symptoms in their 4th decade of life. In about 40.6 % patients were from moderate work category. It was seen from the present study that 93.8 % patients were Hindus and married people among which 28.1 % were uneducated and 16 patients (50%) were from lower socio economic status. It was observed that maximum patients (78.1%) started alcohol intake during second decade of their life.

About 59.4 % were consuming alcohol as an eye opener drink. 43.8 % of the patients in the study were consuming 180-360 ml of alcohol per day on daily basis. Maximum patients 50 % preferred whisky as their choice over other types of alcohol. 62.5% patients had nicotine addiction along with alcohol. 23.5 % patients had positive family history of alcohol use. 53.1 % patients were of *Vata-Pitta Prakruthi* (Physical Constitution) individuals, 78.1% patients were of *Rajasika Prakruthi* (Mental Constitution), 23 patients (71.9%) were *Avara Satva* individuals. It was seen in the study group that about 81.2% patients were using mixed diet and 50 % of the patients were having *Vishamagni* (Erratic Appetite).

Among 32 patients, 11 patients (34.4%) had mild withdrawal symptoms, 18 patients (56.3%) had moderate withdrawal and about 3 patients (9.4%) had severe withdrawal. (Table 2)

Among 30 patients who completed the study, maximum patients 30 (100%) had *Shareera Kampa* as a predominant symptom, 29 patients (96.7%) had *Prajagara* as a second major symptom, 20 patients (66.7%) had *Hrillasa*, 14 patients (46.7%) had *Aruchi*, 10 patients (33.3%) had *Chardi*, 7 patients (23.3%) had *Pralapa*, 5 patients (16.7%) had *Roopanam Asatam Darshanam* while 3 patients (10%) each had *Atisara* and *Bhrama* as their symptoms. (Table 1)

Among 30 patients the symptoms like anxiety, agitation, *Prajagara* (Insomnia), *Pralapa* (Delirium), *Hrillasa* (Nausea), *Chardi* (Vomiting), *Aruchi* (Reduced Appetite), Paroxysmal Sweating, headache each reduced by 50 % with $p < 0.001$. *Shareera Kampa* (Tremors) reduced by 42.1 % with $p < 0.001$. (Table 3)

In the present study it was observed that the combination drug had hepatoprotective action which was evident through various liver function test. Significant changes were seen in few parameters and no changes were seen in other parameters like SGPT, Total proteins, USG Abdomen. (Table 4)

DISCUSSION

Although alcohol withdrawal syndrome may be complex, therefore careful evaluation and available treatments should ensure safe detoxification for most patients. Alcohol has an effect on multiple neurotransmitter system in the brain. When alcohol is stopped abruptly, the person's nervous system suffers from uncontrolled synapse firing. For the person suffering from *Madatyaya* due to heavy and prolonged consumption of alcohol, the first aim of the treatment should be safer resolution of withdrawal state. The alcohol withdrawal symptoms are *Vata* predominant *Vata-Pitta* condition. Tremors, anxiety, auditory, tactile, visual hallucinations and headache are due to *Vata* predominance. Sweating, agitation are *Vata-Pitta* predominant. Nausea and vomiting are *Vata-Kapha* predominant. Complete abstinence from alcohol relieves the withdrawal symptoms by 7 days. The other factors like nutritional deficiency poor physical health, other systemic pathologies, lack of emotional and family support etc. increase the severity of the withdrawal state.

The present work was carried out to know the efficacy of the compound formulation (*Madhutriphala* and *Gudardraka*), and how fast it relieves the symptoms of alcohol withdrawal.

Pharmacological action of *Madhutriphala* & *Gudardraka* Yoga: As *Madatyaya* is a *Kapha Pradhana Tridoshaja Vyadhi* associated with *Agni Dushti*, hence a drug

which is beneficial both for treating Agni and Kapha Dosha would be a better choice in the management of Madatyaya. Madhutriphala and Gudardraka Yoga is one such compound formulation which mainly acts as Deepana, Pachana, Tridosahara, Rasayana (Antioxidant), Vatanulomana, does Dhathu Poshana, Hradya (cardioprotective), and hepatoprotective, along with Medhya (nootropic) properties. The Madhutriphala which is administered at the night time is useful in doing the Vatanulomana, Rasayana property of Triphala helps in treating Prajagara (Insomnia).

Triphala Prayoga has been mentioned in most of the liver pathologies in our classics. Presence of fats, carbohydrates and proteins in Triphala Choorna will inhibit the absorption of alcohol. Honey acts as Hradya (Cardioprotective), does Srotoshodhana and by virtue of its Yogavahi property it helps in increasing the bio-availability and better absorption of the drug. Madhu and Guda helps in nourishing the Dhathus i.e., it supplements the micro nutrients. Supplementation of fructose has a proven action on alcohol metabolism, helps in thiamine, magnesium and calcium deficiencies. It helps in the conversion of aldehyde to acetaldehyde.

The Gudardraka mentioned in the morning time acts as a Srotoshodaka, Kaphahara, Deepana, Pachana and also supplements certain vital nutrients which are required for a person who is afflicted with alcohol. The hepatoprotective actions of Amla appear to be mediated by its free radical scavenging, antioxidant, anti-inflammatory and modulation of the xenobiotic detoxification process and lipid metabolism. Various studies have shown that Amalaki Choorna when given in combination with other compound formulations is

said to improve their liver functions. A study shows that honey exerts potent antioxidant activity and significant protection in hepatic disorders associated with chronic alcoholism. The protective effect is attributed to its antioxidant mechanisms and inhibition of oxidative degeneration of lipids. The hepatoprotective activity of Guda is proved on animal models. Ardraka apart from doing Amapachana also acts anti-dependent/antitolerant agent against psychoactive substances which is proven from many studies. (Table 5)

In Yogaratnakara and Ashtanga Hrudaya, the duration of the disease Madatyaya is 7 or 8 days. The combination drug is also indicated for 7 days with Pathya (Diet Regimen) in Mada, Moorcha, Unmada and Kamala. The most appreciable part of the drug is that there is mention of Amayika Prayoga (Therapeutic Indications), Oushada Kalpana (Form of administration) and Oushada Sevana Kala (Time of administration), although dosage form has not been mentioned standard dosage of Choorna and Kalka was adopted which is a unique concept mentioned in Vanga Sena Samhita.

CONCLUSION:

Overall it can be concluded from the statistical analysis and clinical evaluation, all the withdrawal symptoms subsided by 7 days and not much significant changes seen in USG abdomen as the study period was only for 7 days. There was not much statistical significance seen in other symptoms like auditory, visual and tactile disturbances as these symptoms got subsided by 4th day of treatments which was clinically significant. The combination drug Madhutriphala & Gudardraka Yoga which has a combined effect on nervous system, gastrointestinal system, and hepatobiliary system was

found to useful in reducing the alcohol withdrawal symptoms.

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Table1: Shows observation on Samanya Madatyaya Lakshanas:

Sl.No.	Complaints	Frequency	%
1.	Aruchi (Reduced Appetite)	14	46.7
2.	Chardi (Vomitting)	10	33.3
3.	Prajagara (Insomnia)	29	96.7
4.	Atisara (Loose stools)	3	10
5.	Bhrama (Giddiness)	3	10
6.	Hrillasa (Nausea)	20	66.7
7.	Pralapa (Delerium)	7	23.3
8.	Shareerakampa (Tremors)	30	100
9.	Roopanam Astamchaiva Darshanam (Hallucinations)	5	16.7

Table2: Shows CIWA-Ar Scores of 32 patients of Madatyaya:

CIWA-Ar Score	%	Total
0-9 (Mild Withdrawal)	34.4	11
10-19 (Moderate Withdrawal)	56.3	18
>20 (Severe Withdrawal)	9.4	3
Total	100	32

Table3: Shows the effect of Madhutriphala and Gudardraka Yoga on 30 patients of Madatyaya:

Signs & symptoms	Mean Score		% of reduction in mean score	p- value
	BT	AT		
Aruchi (n=14)	2.00	1.00	50	0.001
Chardi (n=10)	2.00	1.00	50	0.002
Prajagara (n=29)	2.00	1.00	50	0.001
Bhrama (n=3)	2.00	1.00	50	0.083
Hrillasa (n=20)	2.00	1.00	50	0.001
Pralapa (n=7)	2.00	1.00	50	0.008
Shareera Kampa (n=30)	1.90	1.10	42.10	0.001
Roopanam Asatam Darshanam (n=5)	2.00	1.00	50	0.025
Anxiety (n=23)	2.00	1.00	50	0.001
Agitation (n=20)	2.00	1.00	50	<0.001
Paroxysmal Sweating (n=21)	2.00	1.00	50	0.001
Headache (n=21)	2.00	1.00	50	0.001

Table 4: Shows effect of Madhutriphala and Gudardraka Yoga on laboratory parameters:

Parameter	Mean		Diff. Mean	% of reduction	SD	SE Mean	T-Value	P-Value	Remarks
	BT	AT							
T.Bilirubin	1.41	1.03	0.38	26.95	0.45	0.08	4.63	<0.001	S
D.Bilirubin	0.85	0.65	0.20	23.52	0.30	0.05	3.67	0.001	S

n									
I.Bilirubin	0.58	0.48	0.10	17.24	0.23	0.04	2.35	0.025	S
SGOT	122.79	64.03	58.75	47.85	100.06	18.26	3.21	0.003	S
SGPT	71.20	56.16	15.03	21.12	53.92	9.84	1.52	0.138	NS
Total Proteins	7	6.86	0.1	2	0.64	0.11	1.22	0.231	NS
Albumin	4.24	4.44	-0.20	-4.71	0.45	0.08	-2.38	0.024	S
ALP	70.78	63.65	7.13	10.07	18.95	3.46	2.06	0.048	S

Table 5: Shows the pharmacological profile of Madhutripkala and Gudardraka Yoga

Effect of drug	Madhu	Haritaki	Vibhitaki	Amalaki	Ardraka	Guda
Antibacterial ^{10,11}	+	-	-	-	-	-
Anti-Diarrhoeal ^{10,11,12}	+	-	-	+	-	-
Anti-Ulcerogenic ^{10,11,13,14}	+	-	+	+	-	-
Antioxidant ^{15,16,17,18,19}	+	+	-	+	+	+
Anxiolytic ^{20,21}	+	-	-	-	+	-
Cognitive enhancer ^{20,22}	+	-	-	-	+	-
Immunomodulator ^{23,24,25,26}	-	+	+	+	+	-
Hepatoprotective ^{27,28,29,30}	-	+	+	+	-	+
Neuroprotective ^{31,32}	-	+	-	-	+	-
Antidepressant ¹⁷	-	-	-	+	-	-
Anticonvulsant ³³	-	-	-	+	-	-
Antidependence/Antitolerant ³⁴	-	-	-	-	+	-
Anti-inflammatory/Analgesic ^{35,36}	-	-	-	+	+	-
Nootropic ³⁷	-	-	-	-	+	-
Gastroprotective ³⁸	-	-	-	-	+	-
Antiemetic ²¹	-	-	-	-	+	-
Cardioprotective ³⁹	-	-	-	-	+	-
Pancreatoprotective ⁴⁰	-	-	-	+	-	-
Antimicrobial ⁴¹	-	-	-	+	-	-
Tranquiliser ⁴²	+	-	-	-	-	-

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Source of support: Nil
Conflict of interest: None Declared