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## **Research Article**

# EFFICACY OF MRUDVEEKADI KASHAYA IN THE MANAGEMENT OF MADATYAYA (ALCOHOL WITHDRAWAL SYMPTOMS)

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#### ABSTRACT

Alcohol withdrawal is characterized by a cluster of symptomswhich develop on total or partial withdrawal of alcohol intake after long use. Withdrawal state is one of the indicators of dependence syndrome. Alcohol withdrawal constitutes physical and psychological symptoms. Madatyaya (Alcoholism) is a similar condition where there is derangement of both Shareerika Dosha (Physical) and Manasika Dosha (Psychological). Hence a suitable Shamana Oushadi (Pacificatory drug) which acts upon both the body and mind would be an ideal choice. In Ayurvedic literature, Mrudveekadikashaya– a combination drug in decoction form, is specifically indicated in Trishna (thirst), Mrucha (syncope) Mada (intoxication), and Mativibhrama (Disorientation). These indications have striking similarities to that of symptoms seen in alcohol withdrawal. Therefore, an attempt was made to study the efficacy and pharmacological action of the combination drug on alcohol withdrawal symptoms. 37 diagnosed patients of Madatyaya (Alcohol Withdrawal symptoms) were registered as single group, for oral administration of Mrudveekadikashaya15ml thrice daily with lukewarm water before food for the period of one month. 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. The results were analyzed statistically using SPSS VER.20. There was Statistical significant result in subjective symptoms of Madatyaya and Objective Parameters. Mrudveekadikashaya showed better results in the Management of Alcohol withdrawal symptoms and significant changes was observed in impaired liver functions.

Keywords: Ayurveda, Alcohol withdrawal symptoms, Madatyaya, Mrudveekadikashaya, Herbal management of Alcoholism, Alcoholism

## INTRODUCTION

Since antiquity man has been using Madya (alcohol)as a part of social and cultural life. Madya has nectar like properties when used judicially following all norms, otherwise it acts as a poison.<sup>1</sup>As per WHO report, alcoholism is the third largest risk factor for disease burden. The abuse of alcohol results in 2.5 million deaths per year. 32,000 young people between the age of 15 and 29 die out of alcohol related cause, thus resulting in 9% of all death in that age group.<sup>2</sup> At least 20% of the patients in the mental health settings have alcohol dependent or alcohol related disorders, from both the genders and all the socioeconomic backgrounds.<sup>3</sup>

"That which produces Mada (Intoxication) is called Madya," the disease produced due to improper use of Madya is called Madatyaya.<sup>4</sup> One should consume Madya along with food judiciously. Madatyaya is produced when person takes the Madya without considering Prakriti, Satmya, Agni, etc.

Madatyaya is a Tridoshaja Vyadhi.<sup>5</sup> where Kapha Sthana (seat of Kapha) is affected along with the vitiation of Agni (Digestive fire).<sup>6-8</sup> There are many Shamana Oushadis in Ayurveda, among which Mrudveekadi Kashayais one. It contains Mrudveeka (*Vitis vinifera*), Yastimadhu (*Glycyrrhiza glabra*), Madhooka (*Madhuka longifolia*), Pippali (*Piper longum*), Kharjura

(*Phoenix dactylifera*), Chandana (*Santalum album*), Sariva (*Hemidesmus indicus*), Musta (*Cyperus rotundus*), Laja (*Oryza sativa*), Usheera (*Vetiveria zizanioides*). It is specifically indicated in the complaints of Trishna (thirst), Mrucha (syncope) Mada (intoxication), and Mativibhrama (Disorientation).<sup>9</sup> It has the property of Tridoshahara, (pacifies three doshas), Predominantly Vata-pittahara, Deepana (Appetizer) pachana (Digestive) Rasayana (adoptogens), Seetaveerya pradhana, (cold potency), Balya (Nourshing), Medhya (Cognitive-Enhancers), Yakritduttejaka (Stimulates and protects the liver), Chardi nigrahana (Controls vomiting) and trishna nigrahana (quenches thirst).

Aims and objectives: To study the efficacy of Mrudveekadi kashaya on subjective parameters of alcohol withdrawal and objective parameters like liver function test.

## MATERIALS AND METHODS

37 diagnosed patients of Madatyaya (Alcohol Withdrawal) who fulfilled the inclusion criteria and consenting, were selected from the outpatient (OP) as well as inpatient (IP) department of Manasaroga, SDM College of Ayurveda & Hospital, Hassan who were studied as a single group. Institutional Ethical Committee (IEC) clearance was obtained prior to the study [IEC NO: SDMACAH/IEC/119/13-14 Dated 5<sup>th</sup>April 2014] Duration of the study was for 1 month. Assessment was done before and after the study period.

#### **Inclusion criteria**

Diagnosed patients of Madatyaya (alcohol withdrawal symptoms) Age between 18-50 years of both genders irrespective of socio-economic status.

## **Exclusion criteria**

- Subjects suffering from systemic diseases like diabetes mellitus and uncontrolled hypertension, alcoholic liver cirrhosis, ascites.
- Subjects suffering from organic brain diseases and other psychiatric illnesses.
- Subjects suffering from severe withdrawal symptoms like delirium tremens and status epilepticus.

## Subjective Parameters Samanya madatyaya lakshanas

Complaints of:- Aruchi (Reduced Appetite), Prajagara (Insomnia), Bhrama (Giddiness), Pralapa (Delirium), Roopanamasatam Chaiva Darshanam (Hallucinations), Chardi (Vomiting), Atisara (Loose stools), Hrillasa (Nausea), Shareera Kampa (Tremors) Grading for Samanya Madatyaya Lakshanas: 0 to 3 except for Hrillasa which is rated on scale 0 to 2

**CIWA-AR SCALE**<sup>10</sup>: Nausea/vomiting, anxiety, paroxysmal sweats, tactile disturbances, visual 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.

## **Diagnostic criteria**

Diagnosis was based on the basis of Samanaya Madatyaya Lakshanas and ICD-10 Criteria for alcohol withdrawal.

1. Diagnostic criteria for Alcohol withdrawal according to ICD-10

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 behavioral 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 and Samanya Madatyaya Lakshanas. Single group study, patients were selected on the basis of convenience sampling and treated with Mrudveekadikashaya, Oral administration 15ml thrice daily  $\frac{1}{2}$  an hour before food with Luke warm water for one month. The patients were assessed on day 1 before treatment,  $3^{rd}$  day,  $7^{th}$  day, and on  $30^{th}$  day after treatment.

## Statistical analysis

Statistical analysis was done using SPSS VER.20. Friedman's test was applied to analyze 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 analyzing the significance of objective parameters.

## **OBSERVATIONS**

55 patients who presented themselves at the OPD with the complaints of alcohol related problems were screened with CIWA-Ar scale and 37 patients who fulfilled the inclusion criteria were selected and registered for the study. Out of 37 patients, 2 patients withdrew from the study, due to economic constraints and Health complications.

The maximum number patients were in the age group of 41-50 years (56.8%; 21patient), started consuming alcohol due to peer pressure (64.9%; 24 patients), had a history of alcohol consumption during the second decade of life (83.8%; 31 patient), had early morning use of alcohol l(70.3%; 26 patients), had history of daily consumption of alcohol (91.9%; 34 patients),) preferred Rum than other brands of alcohol (40.5%; 15 patients) and consumed about 180-360 ml of alcohol (45.9%; 17 patients).

Nausea/ vomiting (94.28%; 33 patients), Tremors (100%; 35 patients), Paroxysmal sweats (42.85%; 15 patients), Anxiety (100%; 35 patients), Agitatio n(74.2%; 26 patients), Orientation disturbances (20%; 7 patients), Tactile Disturbances (14.2%; 5 patients), Auditory disturbances (25.71%; 9 patients), Visual disturbances (14.2%; 5 patients), Headache (77.14%; 27 patients), Aruchi (86.5%; 32 patients), Atisara (24.3%; 9 patients), Bhrama (67.6%; 25 patients), Prajagara (100%; 35 patients) was noted in this study.

## RESULTS

There was Statistical significant result in subjective symptoms of Madatyaya like, Nausea/ vomiting (50%; p < 0.001), Tremors (50%; p < 0.001), Paroxysmal sweats (47.71%; p < 0.001), Anxiety (50%; p < 0.001), Agitation (50%; p < 0.001), Orientation (44.5%; p 0.014), Tactile Disturbances (42.10%; p 0.046), Auditory disturbances (45.36%; p 0.005), Visual disturbances (42.10%; p 0.046), Headache (48.48%; p < 0.001), Aruchi (50%; p < 0.001), Atisara (45.36%; p 0.005), Bhrama (48.48%; p < 0.001), Prajagara (50%; p < 0.001).

There was Statistical significant result in Objective Parameters like, Total bilirubin (23.28%; p<0.001), Direct bilirubin (23.17%; p<0.001), Indirect bilirubin (20.63%; p 0.008), SGOT (42.54%; p<0.001), SGPT (31.60%; p<0.001), Total proteins (7.43%; p<0.001), Albumin (1.58%; p 0.033), Alkaline phosphate (6.12%; p 0.008)

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## Table 1: Samanya Madatyaya Lakshanas

Sl.No.	Complaints	No. of Patients	Percentage		
1.	Nausea/Vomiting	33	94.28%		
2.	Tremors	35	100%		
3.	Paroxysmal sweats	15	42.85%		
4.	Anxiety	35	100%		
5.	Agitation	26	74.2%		
6.	Orientation disturbances	07	20%		
7.	Tactile disturbances	05	14.2%		
8.	Visual disturbances	05	14.2%		
9.	Auditory disturbances	09	25.71%		
10.	Headache	27	77.14%		
11.	Aruchi	32	86.5%		
12.	Prajagara	35	100%		
13.	Atisara	09	24.3%		
14.	Bhrama	25	67.6%		

## Table 2: CIWA-Ar Scores of 35 patients of Madatyaya

CIWA-Ar Score	No. of Patients	Percentage
10-19 (Mild to Moderate Withdrawal)	17	48.6%
>20 (Severe Withdrawal)	18	51.4%
Total	35	100%

## Table 3: Effect of Mrudveekadikashaya on 35 patients of Madatyaya

Signs & symptoms	Mean rank		% of reduction	p- value	
	BT	AT	in mean score	_	
Nausea/Vomiting (n=33)	2.00	1.00	50%	< 0.001	
Tremors (n=35)	2.00	1.00	50%	< 0.001	
Paroxysmal sweats (n=15)	1.97	1.03	47.71%	< 0.001	
Anxiety (n=35)	2.00	1.00	50%	< 0.001	
Agitation (n=26)	2.00	1.00	50%	< 0.001	
Orientation disturbances (n=7)	1.93	1.07	44.5%	0.014	
Tactile disturbances (n=5)	1.90	1.10	42.10%	0.046	
Visual disturbances (n=5)	1.90	1.10	42.10%	0.046	
Auditory disturbances (n=9)	1.94	1.06	45.36%	0.005	
Headache (n=27)	1.98	1.02	48.48%	< 0.001	
Aruchi (n=32)	2.00	1.00	50%	< 0.001	
Prajagara (n=35)	2.00	1.00	50%	< 0.001	
Atisara (n=9)	1.94	1.06	45.36%	0.005	
Bhrama (n=25)	1.98	1.02	48.48%	<0.001	

## Table 4: Effect of Mrudveekadi Kashaya on objective parameters

Parameter	Me	ean	Diff.	% of	SD	SE Mean	T-Value	P-Value	Remarks
	BT	AT	Mean	reduction					
Total bilirubin	1.46	1.12	0.34	23.28	0.57	0.097	3.53	0.001	S
Direct bilirubin	0.82	0.63	0.19	23.17	0.28	0.047	4.04	0.001	S
Indirect bilirubin	0.63	0.50	0.13	20.63	0.27	0.047	2.81	0.008	S
SGOT	86.80	49.87	36.9	42.54	30.61	5.17	7.13	0.001	S
SGPT	49.89	34.12	15.7	31.60	17.00	2.87	5.48	0.001	S
Total proteins	7.13	6.60	0.44	7.433	0.52	0.088	4.95	0.001	S
Albumin	4.42	4.35	0.07	1.583	0.20	0.033	2.22	0.033	S
Alkaline	81.49	76.50	4.99	6.123	10.44	1.766	2.83	0.008	S
phosphate									

## Table 5: Pharmacological profile of Mrudveekadi kashaya

ſ	Hepato protective	Draksha, Yastimadhu, Pippali, Kharjura, Musta, Usheera
Γ	Anxiolytic	Draksha, Yastimadhu, Usheera
	Antioxidant	Draksha, Pippali, Kharjura, Laja
	Nootropic	Draksha, Yastimadhu, Pippali, Kharjura, Sariva, Usheera
Γ	Antidepressant	Draksha, Pippali, Chandana, Usheera
ſ	Antipsychotic	Sariva, Chandana
Γ	Anticonvulsant	Yastimadhu, Madhooka, Musta
Γ	Sedative& Tranquilizer	Chandana, Musta

## DISCUSSION

Alcohol has an effect on multiple neurotransmitter systems in the brain. Whenalcohol intake is stopped abruptly; acute alcohol ingestion has an inhibitory effect at N-methyl-D-aspartate (NMDA) receptors, reducing excitatory glutamatergic transmission and has an agonistic effect at gamma-aminobutyric acid type-A (GABA<sub>A</sub>) receptors. During prolonged exposure to alcohol, NMDA receptors are up-regulated and GABA<sub>A</sub>receptors are downregulated, leading to tolerance. The roles are reversed during abstinence, with enhanced NMDA receptor function; reduced GABAergic transmission and dysregulation of the dopaminergic system, leading to many of the symptoms and signs of AWS.<sup>11</sup>the most severe manifestations of withdrawal include delirium tremens, hallucinations, and seizures.

In Ayurvedic context, Alcohol withdrawal may present with following symptoms like, vitiation of Vata causes headache, insomnia, vivid dreams, hallucinations, anxiety, restlessness, constipation & tremor and vitiation Pitta causes gastric disturbances, excessive sweating, giddiness, aggression & violence and vitiation of Kapha cause excessive sleep, depression, lethargy, heaviness in the body, nausea & vomiting while vitiation of Tridosha causes combination of the above clinical feature. In general *Vata-pitta* predominant Tridoshaja (bodily humor) and Rajas (psychic principle)is the main Manodosha (psychic humors)involved in the pathology of Alcohol dependence & withdrawal.<sup>12</sup>

#### Pharmacological action of mrudveekadi kashaya

As Madatyaya (Alcohol withdrawal symptoms) is Vata-pittapra dhanatridoshaja Vyadhi, Administration of Mrudveekadi Kashaya helps in mitigating aggravated Vata Pitta Dosha with correction Kapha Dosha.

- Mrudveekadi Kashaya as Medhya (cognitive enhancers) and Rasayana (Adoptogens) Drugs like Mrudveeka (Draksha), Yastimadhu, Pippali, Chandana<sup>13</sup>,- it controls the cognitive and perceptional disturbances like Hallucinations, Vivid dreams, Anxiety and Autonomic over activity like Tremors, Sweating, Insomnia, Tachycardia etc.
- Deepana- Pachana<sup>13</sup> (Stimulant and digestive): Drugs like Pippali, Musta, Sariva, Laja, Usheera- Corrects the Agni, Corrects the GI problems in alcoholism.
- Trishna and Chardi Nigrahana<sup>13</sup> (Controls vomiting and quenches thirst): Drugs like Mrudveeka, Yastimadhu, Chandana, Kharjura, Sariva, Usheera, Laja along with that it controls Anorexia.
- Yakritduttejaka<sup>13</sup> (Stimulates and protects the liver): Drugs like Mrudveeka, Yastimadhu, Pippali, Sariva, in this yoga as proven Hepato-protective and stimulant action on Alcohol induced Hepatotoxicity.(Table 5)

The ingredients in this Kashaya have pharmacological properties like anti-anxiety, antipsychotic, antidepressant, anticonvulsant, antioxidant, sedative and tranquilizingby various pharmacological and animal study of individual drug. All this properties might have helped in reducing Alcohol withdrawal symptoms. (Table 5)

Mrudveekadi Kashaya supplements macro and micro nutrients and helps in vitamin B-complex deficiencies. It is rich in Fructose, Supplementation of fructose has a proven action on alcohol metabolism; it helps in the conversion of aldehyde to acetaldehyde helps in reducing withdrawal symptoms quickly.

## CONCLUSION

Overall it can be concluded from the statistical analysis and clinical evaluation, all the withdrawal symptoms subsided by 7 days. Study continued further statistically there were significant changes seen in impaired liver function test also; The Mrudveekadi kashaya is having combined effect on Nervous system, gastrointestinal system, and Hepato-biliary system. It is also found in useful in reducing the alcohol withdrawal symptoms. Gastrointestinal Symptoms: Anorexia, Nausea/ vomiting, Diarrhea- reduced 3rd day of treatment, Neurological Symptoms: Tremors, Anxiety, Insomnia- Reduced significantly at the end of 4<sup>th</sup> day (30 patients), But 5 patients persisted with fine hand tremors and Insomnia, even after the treatment because of chronic dependence of alcohol i.e., protracted withdrawal it may require up to 6 months to get recovered. Cognitive Disturbances: Auditory, Visual and Tactile Hallucinations significant changes seen by 4<sup>th</sup> day. In this study patients were well motivated about the ill effects of alcohol by motivation along with medicine Anti-craving property of kashaya is observed and helps in relapse prevention.

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