



ADRAVYABHUTA CHIKITSA (NON-PHARMACOLOGICAL TREATMENT) IN NASH (NONALCOHOLIC STEATOHEPATITIS)- CONCEPTUAL REVIEW

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ABSTRACT

Non alcoholic steatohepatitis (NASH) is the cause behind liver related morbidity and mortality but is also responsible for the increased susceptibility of atherosclerosis, cardiovascular disease and type 2 diabetes mellitus. According to studies Non Alcoholic Fatty Liver Disease (NAFLD)/NASH is having a strong association with obesity, type 2 diabetes mellitus, dyslipidemia etc. A two hit hypothesis has been proposed to describe the pathogenesis of NAFLD the first hit causing steatosis that than progress to steatohepatitis if a second hit occurs. In the view of *Ayurveda* concept the *Medoroga* (metabolic disease), *Prameha*(diabetes) , *Santarpanajanya* (over nourished) *roga nidanas* play a major role in pathogenesis of the disease so the *Chikitsa* mentioned in these disease may help in the management of NAFLD/NASH. Treatment of NAFLD/NASH comprises of pharmacological and non pharmacological method. According to available references no pharmacological agents are currently licensed specifically for NASH therapy. Treatment directed at coexisting metabolic disorders such as dyslipidemia ,Type 2 diabetes mellitus,obesity and hypertension. Current non pharmacological treatment comprises life style modification to promote weight loss and improve insulin sensitivity through dietary changes and physical exercise. *Acharya Charaka* in *Vimanasthana* has classified the *Chikitsa* into *Dravyabhuta* and *Adravyabhuta Chikitsa*. *Adravyabhuta Chikitsa* can be employed in the form of *Vyayama*, *Langhana*, etc. contemporary science also says the non pharmacological treatment is the first line of treatment in NAFLD/NASH. This review article is a meticulous compilation of available *Adravyabhuta Chikitsa* which is are specified in *Medoroga*, *Prameha* and *Santarpanajanya rogas* and trying to understand their scope in treatment of NAFLD/NASH.

Key Words: NASH, NAFLD, *Adravyabhuta Chikitsa*, *Vyayama*, *Langhana*

INTRODUCTION: Non Alcoholic Steato Hepatitis(NASH) is the subtype of Non Alcoholic Fatty Liver Disease (NAFLD)This concept was introduced by Ludwig and his colleagues in 1980 during their study on patients suffering with fatty liver but no prior history of alcohol consumption. Interestingly, prevalence of NAFLD/NASH has doubled during the last 20 years, whereas prevalence of other chronic liver diseases has remained stable or even decreased¹. Non alcoholic steatohepatitis the more serious form of

NAFLD is the cause behind for liver related morbidity and mortality but is also responsible for the increased susceptibility of atherosclerosis, cardiovascular disease and type 2 diabetes mellitus².

The prevalence of NAFLD is increasing at approximately the same rate as obesity. In fact the global prevalence of NAFLD in the general population has been estimated to be 25% where as the global prevalence of NASH has been estimated to range from 3-5%³. Overweight/obesity, diabetes mellitus, metabolic syndrome and patients

with a mysterious increase in hepatic transaminase, cryptogenic cirrhosis and hepatocellular carcinoma (HCC) are high risk groups for NAFLD⁴.

There is no direct reference available in *Samhita* to compare NASH with single disease condition of *Ayurveda*. According to *Acharya Charaka* it is not always possible or it is not always necessary to identify a disease by a name and physician need not to be ashamed himself for not naming disease but physician should construct the *Samprapthi* (pathogenesis) with available *Nidana*(cause), *Dosha*(bodily humor), *Dushya* (body tissues), *Lakshanas*(clinical features) and plan for *Chikitsa*(treatment) on the basis of that. Taking the help of above quotation considering the risk factors of NAFLD it can be anticipated to *Santarpanajanya vyadhi* (the diseases caused due to over nourishment) *nidana* may be a *Nidana* for NAFLD and the disease manifests in *Yakrit* which is basically *Sthana* of *Pitta Dosha*, *Raktavaha Srotas Dusti Nidana* like *Vidaahi* (taking long time for digestion), *Abhishyandi*(which is causing obstruction), *Snigdha* (unctuous), *Ushna*(hot), *Drava*(liquid) etc *Aharas*(food) may also be considered as *Nidana* for NAFLD/NASH. Treatment of NAFLD/NASH comprises of pharmacological and non pharmacological method.

There are no current FDA (Food and Drug Administrative Agency) approved pharmacologic treatment options for NASH⁵. Current non pharmacological treatment comprises life style modification to promote weight loss and improve insulin sensitivity through dietary changes and physical exercise. Fortunately NAFLD it is reversible⁶. Thus, this is a need of hour to explore the effective non pharmacological effective treatment available in *Ayurveda*

which may help in NAFLD/NASH. So complex pathophysiologic process of NASH may be halted and protect the liver from further consequences.

MATERIALS AND METHODS

All the relevant information is collected from Ayurvedic classical texts like Bruhatraye's and Laghutraye's, Contemporary text books, peer review journals, research articles with digital source

Pathogenesis

The basic defect in the occurrence of hepatic steatosis is the imbalance between import and export of fat to and from liver. Imbalance of cytokines (tumor necrosis factor and adiponectin) leads to insulin resistance (IR) which causes increased lipolysis from adipose tissue with rapid delivery of fatty acids to liver. An excess of de novo fat synthesis in the liver, excess of dietary intake of fat, reduced β oxidation of fatty acids and reduced dissemination of very low density lipoprotein (VLDL) also contribute to the occurrence of hepatic steatosis. Insulin resistance as explained by homeostasis model assessment for insulin resistance (HOMA-IR) or insulin tolerance test (ITT) in India patients with NAFLD have shown IR in 83% to 98% of patients with IR also common in so called lean patients with NAFLD⁷.

A two hit hypothesis has been proposed to describe the pathogenesis of NAFLD the first hit causing steatosis that than progress to steatohepatitis if a second hit occurs⁸. Second Hit Such As Oxidative Stress And Cytokines Producing Inflammation /Fibrosis And Progression to NASH. The new concept in the pathogenesis include the concept of lipotoxicity, inadequate hepatocyte regeneration and apoptosis with multiple events acting in parallel. In reality

progression probably follows hepatocellular injury caused by a combination of several different hit including⁹.

NAFLD/NASH is considered to be a hepatic manifestation of metabolic syndrome. The incidence of NAFLD/NASH has been rapidly increasing globally in line with the increased prevalence of obesity, and is currently the most common chronic liver disease¹⁰. Recently, the incidence of NAFLD and NASH was reported to be 46% and 12%, respectively, in a largely middle-aged population¹¹.

CLINICAL FEATURES:

NAFLD is usually asymptomatic although it may be associated with fatigue and mild right upper quadrant discomfort. It is commonly identified as an incidental detection of fatty liver on ultrasound or during work up for raised liver enzymes¹². Jaundice and other symptoms and signs of liver failure only occur when patients may have advanced to cirrhosis or HCC¹³. Some of the patients are detected to have above findings during evaluation for other illness or while being evaluated for symptoms such as dyspepsia and generalized weakness. The only clinical sign that is elicited in patients with NASH may be hepatomegaly¹⁴.

MANAGEMENT OF NAFLD/NASH

As a marker of the metabolic syndrome identification of NAFLD should prompt screening for and treatment of cardiovascular risk factors in all patients. However in recognition of the greater morbidity associated with NASH as opposed to simple steatosis, liver targeted treatment should be focused particularly on those patients with NASH¹⁵.

NON PHARMACOLOGICAL TREATMENT

Current treatment comprises life style modification to promote weight loss and improve insulin sensitivity through dietary changes and physical exercise. Weight reduction of 7 to 10% will show significant improvement in histological and biochemical NASH severity¹⁶. For dietary intervention, a hypocaloric diet (500–1000 kcal) is a recommended strategy in NAFLD¹⁷.

PHARMACOLOGICAL TREATMENT OF NASH

No pharmacological agents are currently licensed specifically for NASH therapy. Treatment directed at coexisting metabolic disorders such as dyslipidemia, type 2 diabetes mellitus, obesity and hypertension¹⁸.

AYURVEDIC LINE OF MANAGEMENT OF NASH

When we observe the prevalence of NAFLD/NASH and its pathogenesis it has been observed that compared to general population it is more prevalent in overweight/ obese, type 2 diabetes mellitus, metabolic syndrome patients and in pathogenesis of NAFLD/NASH two hit hypothesis has been explained first hit is the stasis and in second hit it may proceed to NASH. In the view of *Ayurveda*, concept of *Medoroga*, *Prameha*, *Santarpanajanya roga* (over nourished diseases) *nidanans* play a major role in pathogenesis of the disease so the *chikitsa* mentioned in these disease may help in the management of NAFLD/NASH.

CHIKITSA

According to famous quotation of *Sushruta Samhita* “*Sankshepat kriya yogo nidana privarjana*” i.e. avoiding the cause of the disease is the first line of the treatment. *Acharya Charaka* in *Vimanasthana* has classified the *Chikitsa* into *Dravyabhuta* and *Adravyabhuta*

*Chikitsa*¹⁹. *Dravyabhuta Chikitsa* : The elimination of the morbid factors of disease is stated to be achieved by variety of measures like *Vamana* , *Virechana*, *Basthi*, *Raktamoshana*, *Nasya* etc will fall into *Dravyabhuta Chikitsa* where some medicine is administered to the patient to treat the disease²⁰.

Adravyabhuta Chikitsa : The drugs are generally not employed in this case ,where the *Chikitsa* is done without the administration of any medications to the patient. In conventional parlance such type of therapeutics can be described as psycho and physic therapies. The measures like *Bhaya Darshana*(causing fright), *Vismaapana* (causing surprise), *Vismaarana* (obliteration of memory), *kshobhana* (shocking), *Harshana* (exciting), *Bhtsrana* (chiding), *vadha* (threatening for murder), *Baadhana* (binding), *Swapna* (inducing sleep), *Samvahana* (massage)²¹ etc done in *Unmade* , *Apasmaradi Manasika Rogas*.

In many circumstances such *Adravya Chikitsa* have been explained here are few references. *Acharya Sushruta* while explaining about *Pravrudda Prameha Chikitsa* has stated that with oral medication one must follow *Vyayama*(exercise) ,*Yudha Krida* (wrestling), *Gaja, Turaga Rata Yana*(riding the elephant and horse), *Padati Charya* (walking) *Parikramana*, *Astra*(according to *shastra* using *dhanush*),*Upastra*(not following the *shaastra* while using *dhanush*)²². *Acharya Charaka* while concluding the *Chikitsa* of *Prameha* said *Vidi Vat Vyayama*, *Snana*, *Udvaratana* etc will help in *Prameha Shanti*²³, in *Sthoulya Chikitsa*, *Acharya Susrutha* said *Vyayama* as the *Adravyabhuta Chikitsa*²⁴. *Charaka* is of opinion that *Kapha Medhohara Annapana*, *Prajagara*, *Vyavaya* ,*Vyayama*,

Chinta,*Ruksha Udvaratana* etc²⁵. In *Santarpana Janya Vyadhi Chikitsa* also the *Vyayama*,*Upavasa*,*Swedana* is mentioned as the *Adravyabhuta Chikitsa*²⁶. So avoiding *Diwaswapana*, doing exercise, coming out of comfort zone exposing the body for physical exertion will act as the *Chikitsa* as rightly said in *Upashaya* concept “*Oushada Aharavihara Upayogah Sukanubandha* ²⁷” here *Oushada*,*Ahara* and *Vihara* will helps in giving relief from disease.

VYAYAMA

“*Shareera Ayasa Janka Vyayama Uchyate*” that which make the body to get tired is called as *Vyayama*. *Vyayama* produces the lightness in the body it gives the ability to do work, stability, resistant to discomfort and alleviation of doses²⁸. it stimulates the power of the digestion and due to this *Karma* of *Vyayama* it has been included as one type of *Langhana*.

This has been quoted as one the *Adravya Chikitsa* where *Acharya Susruta* says *Prameha Rogi* must walk about 100 *yojana* or more than that²⁹ in how many days not mentioned, 1 *yojana* is equal to 7.2km³⁰, by doing so for an year the patient becomes free from disease³¹.

PHYSICAL ACTIVITY

The exercise program should be tailored to a patient's preference and capacity, depending on physical fitness level, stage of the liver disease, and other co morbidities. According to references minimal activity was noticed in majority of NAFLD patients³². All NAFLD patients should perform aerobic exercise for at least 150 min a week, preferably 30 min a day³³. Diet and aerobic exercise showed improvement in liver fat assessment and/or liver enzymes with 3-6 months of follow-up³⁴. Those who lack the time for exercise,

High-intensity interval training (HIIT) is an attractive exercise modality for treating patients with NAFLD, also it reduces visceral adipose tissue, intra hepatic fat, and fibrosis³⁵. The American Gastroenterological Association, the American Association for the Study of Liver Diseases, and American College of Gastroenterology all recommend physical exercise as a treatment for NAFLD³⁶. Moderate intensity of physical activities for a duration of 6 months helps in improvement in hepatic steatosis, serum transaminitis, glycemic and lipid profiles as well as IR, as compared with low intensity exercise³⁷.

LANGHANA (FASTING)

Langhana (fasting/less food intake) is the topic of discussion many research activity are done about the impact of *Langhana* on many diseases. *Langhana* can be considered here as one of the *Adravyabhuta Chikita* where it is the procedure or the *Dravya* which creates the lightness in the body “*Langhanam Laghavay Tai*”³⁸. According to *Acharya Charaka* there are *Dashavidha Langhana* Among that *Vyayama* and *Upavasa* may be considered as useful.

The *Upavāsa* may be taken as complete or partial restriction of food intake³⁹. By the complete or partial food restriction, *Agni* which is previously busy with digestion becomes free hence it digests the undigested food which is already present in the body. Then it digests the *Sāma Doṣas*, *Dhātus* and *Malas*. The fundamental cause of all the diseases in human being is improper food habits which leads to impairment of *Jatharāgni* and *Ama* is formed⁴⁰. According to six studies in which 417 patients with NAFLD were included. In the meta-analysis, there were significant differences in BW (body weight), body mass

index (BMI), alanine aminotransferase (ALT), and aspartate transaminase (AST) between the control and fasting group. But there was no significant difference in triglycerides (TG), total cholesterol (TC), and other metabolic parameters between the two groups. Intermittent fasting is beneficial for weight management and liver enzyme improvement, but long-term feasibility and safety of intermittent fasting should be conducted in further studies⁴¹.

LIFE STYLE INTERVENTIONS

First-line strategy in NAFLD management is non-pharmacological⁴². life style modifications consisting of diet, exercise, and weight loss has been advocated to treat patients with NAFLD. Decreasing calorie intake of at least 30% or approximately 750-1000 kcal/day helps in IR and HS⁴³. Therefore it is recommended for all patients to change their eating habits. Given the high prevalence of overweight/obesity and diabetes in NAFLD patients, attention should be paid to the glycemic index (IG) and the energy value of products. Favorable effects were also observed in patients on a Mediterranean diet and a diet based on the healthy food pyramid, including low and medium IG product⁴⁴.

Discussion

NAFLD/NASH is a metabolic multi factorial disease the risk factors of NAFLD/NASH are type 2 diabetes mellitus, dyslipidemia, obesity, metabolic syndrome etc. in view of *Ayurveda Medoroga Nidana*, *Prameha Nidana* and *Santarpana Roga Nidana* will fit into the cause of the disease NAFLD/NASH. The *Aharaja* and *Viharaja Nidana* of all these disease is more are less similar. Indulging with *Aharaja Nidana* like *Atimatra*, *Atisnigdha* and *Atimadhura Ahara* which will leads to *Dravyata* and *Gunata Vruddi*

of *Kapha Dosh*a and *Medodhatu*. *Viharaja Nidan*as like *Aasya Sukha*, *Swapna Sukha*, *Diwaswapna* etc which all leads to *Karmata Vruddi* of *Kapha Dosh*a and further *Dusti* of *Medodhatu*. The *Chikitsa* explained for these condition comprises of both *Dravyabhuta* and *Adravya Bhuta Chikitsa*. *Dravya Bhuta Chikitsa* comprise *Kapha Medoharachikitsa* and *Adravya Bhuta Chikitsa* comprises *Vyayama*, *Langhana* etc best result can be obtained if both go hand in hand.

Conclusion

By following proper diet and physical activity the process of progression of NAFLD/NASH can be prevented. The *Ayurvedic* and contemporary method of management of NAFLD/NASH will follow the same track.

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