INTERNATIONAL
AYURVEDIC
MEDICAL JOURNAL

IAMJ

Research Article ISSN: 2320 5091 Impact Factor: 4.018

MANAGEMENT OF LYME DISEASE WITH A POLYHERBAL COMBINATION OF 'OUT OF LYME' AND 'DIVINE 9 ADAPTOGEN' IMMUNOPROTECTOR

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ABSTRACT

Objective: This was an open labeled, non *comparative*, single arm, prospective study to evaluate the efficacy and safety of polyherbal combination of '*Out of Lyme*' and '*Divine 9 Adaptogen'* Immunoprotector manufactured by Somalata Ayurveda India Pvt. Ltd. in the treatment of Lyme disease. **Methods:** Subjects from the outpatient department of Ashvin Rural Ayurvedic College and Hospital fulfilling inclusion and exclusion criteria were enrolled in the study. ELISA for IgG antibody was a confirmatory assessment criterion. ELISA was performed at the screening visit (baseline) and at the end of study visit (at week 8). Change in the subjective and objective result from baseline to week 8 assessed the efficacy of the polyherbal combination. During each visit, subjects were assessed for rash, fever, chills, fatigue, body aches, headache, joint pain, neck stiffness among other symptoms specific to Lyme disease. **Results and Conclusion:** Out of 32 enrolled subjects in the study, 28 subjects showed ELISA negative for IgG at the end of study visit. The Symptom score also showed significant results. The study showed that a polyherbal combination of '*Out of Lyme*' and '*Divine 9 Adaptogen'* Immunoprotectorare very much effective in the treatment of Lyme disease. Overall this *clinical experience has* established a good *curative treatment* useful for Lyme diseasewithout causing any unwanted side effects.

Keywords: Lyme disease, Out of Lyme, Divine 9 Adaptogen Immunoprotector

INTRODUCTION

Lyme disease is a tick-borne systemic infection caused by spiral-shaped bacteria, Borrelia burgdorferi, characterized by neurologic, joint, and cardiac manifestations. Lyme disease bacteria are transmitted by ticks. It begins with a bite from an infected tick and sometimes a rash that can be so slight, it might not be noticed.[1,2] However, the consequences can be serious, sometimes even fatal. Lyme disease can create symptoms that mimic a wide variety of other diseases, ranging from juvenile arthritis to multiple sclerosis to Alzheimer's disease. Lyme disease has a worldwide distribution including India. Warmer weather is expected to increase the emergence of common vector-borne diseases worldwide. Thousands of cases are reported each year. In the USA, according to CDC, each year,

more than 30,000 cases of Lyme disease are reported nationwide, while studies suggest the actual number of people diagnosed with Lyme disease is more likely about 300,000.[3]

Symptoms of Lyme disease can be highly variable from one person to another and also can vary dramatically over time in one person. Although there is a classic pattern of illnesses in Lyme disease, it is not expressed in nearly half of all subjects. This can make spotting the disease extraordinary difficult and living with it frustrating and painful. The disease progresses in three stages. In the first stage the symptom most commonly experienced by people with Lyme disease is a distinctive rash. This rash is called EMC, which means a "red, chronic, migrating rash". It is most likely to appear a week after the tick bite but may occur from two to thirty days after such a bite, if not treated the rash will disappear on its own, usually within about three weeks. Along with the rash, or often in its absence, the subject often experiences a flu-like illness. About 60 to 80 percent of those who have the rash will experience flu-like symptoms simultaneously. The symptoms may include: headache, fever, chills, aching muscles, stiff neck, loss of appetite, sore throat, nausea, and vomiting. Months later the second stage will kick in which includes various neurologic, cardiac, and joint manifestations. The third stage which eventually occurs in some untreated subjects is characterized by chronic arthritis and various neurologic problems. Some subjects do not experience any of these symptoms. In these cases, doctors wonder if the subjects will ever experience any symptoms of Lyme disease.[4,5]

Even though there are no disease conditions similar to Lyme disease described in Ayurveda, several references are scattered in various texts. If we take a look at the pathogenesis of Lyme disease according to the principles of Ayurveda, we find that it is caused by bacteria subverting the immune system, leading to persistent infection. This results in decreased immune system response in fight against the disease. *Vyaadhiksamatva* (immunity) in Ayurveda is not immunity against a specific infectious agent or disease such as polio or rubella for which Western medicine provides "Immunizations". Rather, *Vyaadhiksamatva* implies a resistance against the loss of the integrity, proportion, and interrelationship amongst the individual's bio-energies (*doshas*) and tissues (*dhatus*). This homeostasis among the supporting elements of the mind and body is known as *dhaatusaamya*, and is the true meaning of immunity in the Ayurvedic system.[11] It follows then that the Ayurvedic concept of immunity is intricately interwoven with the concepts of nutrition, *agni* (digestive fire), and tissue formation.

In spite of many advances, the modern management of Lyme disease still remains unsatisfactory. Looking to the pathogenesis and complications of Lyme disease, it requires a systemic and radical therapy for which Ayurvedic treatment provides a way of hope through its holistic approach. Therefore, we critically reviewed the cases/subjects treated to find an effective and feasible management for Lyme disease.

Materials and Methods:

Enrollment of the Subjects: This study was carried out in Ashvin Rural Ayurvedic College and Hospital, Manchi Hill, Sangamner, Maharashtra, India. The subjects attaining the OPD and fulfilling the criteria of selection were enrolled in the trial irrespective of their religion, cast etc.

Ethical Considerations: The study protocol was in compliance with the Declaration of Helsinki (1989 revision), ICMR guidelines and GCP guidelines and approved by the Local Ethics Committee of Ashvin Rural Ayurvedic College.

Inclusion Criteria:

1. Subject must provide written informed consent prior to the conduct of any study-related procedures.
2. Male or female subjects who are at least 18 years of age.

3. Subjects are suspected to have active early or late stage Lyme disease based on the following criteria: Signs, symptoms and clinical history consistent with early-stage Lyme disease. Subjects must have a medical practitioner-diagnosed erythema migrans (EM) rash and should have systemic symptoms indicative of disseminated infection. Symptoms may include fever, headache, fatigue, myalgias, arthralgias, and stiff neck. Paired acute and convalescent titers will be drawn (first draw at time of initial visit and second draw 4 weeks later) or,
4. Clinical diagnosis of active Lyme disease at the time of the initial screening based on the CDC case definition. Study physician will review history to confirm probable cases.[7]
5. Seropositive controls: For the purposes of this study, a seropositive control is defined as an otherwise healthy male or female aged 18 and above who has positive serum IgG antibody to B. burgdorferi by ELISA and are asymptomatic and who recall no episodes of disease compatible with Lyme infection and have not received antibiotic therapy for Lyme disease.
6. Subjects are suspected to have late Lyme disease based on the following criteria: Signs, symptoms and clinical history consistent with late stage Lyme disease, including but not limited to disseminated rash, arthritis, meningitis, facial palsy, or carditis.
7. Subjects must be willing and have the ability to safely have the required quantity of blood drawn for the study at the discretion of the investigator.
8. Women who are able to conceive children must have a negative pregnancy test within 2 weeks before the procedure.

Exclusion Criteria:

1. Early Lyme disease: Subjects without an EM rash or do not have symptoms recognized as being associated with Lyme disease.
2. Exposure to antibiotics of any type during the 6 weeks prior to the initial blood sample collection.
3. Immune deficiency significant enough to render serological tests less reliable.
4. The subject is unwilling or unable to safely have the required quantity of blood drawn for this study.
5. Subjects who are not able to understand all of the requirements of the study or unable to give informed consent and/or comply with all aspects of the evaluation.
6. Subjects that have any other condition or situation which, in the opinion of the investigator, would make the subject unsuitable for enrollment or could interfere with the subject participating in and completing the study.

Study Drugs:

In this clinical study of 2 Polyherbal formulations manufactured by Somalata Ayurveda India Pvt. Ltd. were administered –

1. **'Out of Lyme' (*Krimi Hara Shakti* 555)** in a dose of 1 caplet of 1500mg BD which is composed of standardized extracts (5:1) of Acasia catechu (*Khadira*) 150 mg, Achyranthus aspera (*Apamarga*) 75 mg, Aegle maemelos (*Bilva*) 75 mg, Albizia lebbeck (*Shirish*) 300 mg, Azadiracta indica (*Nimb*) 75 mg, Casia fistula (*Aragwadh*) 150 mg, Curcuma longa (*Haldi*) 75 mg, Hemidesmus indicus (*Anantmool*) 150 mg, Holarrhena antidysenterica (*Kutaj*) 150 mg, Plumbago zeylanica (*Chitrak*) 75 mg, Tinospora cordifolia (*Guduchi*) 75 mg, Vitex negundo (*Nirgundi*) 150 mg.
2. **'Divine 9 Adaptogen' Immunoprotector** in a dose of 1 caplet of 1500mg BD composed with standardized extracts (5:1) of Asparagus racemosus (*Shatavari*) 240 mg, Boerhaaviadiffusa (*Punarnava*) 240 mg, Ocimum sanctum (*Tulsi*) 240 mg, Plumbagozeylanica (*Chitraka*) 240 mg,

Withania somnifera (*Ashwagandha*) 240 mg, Phyllanthus niruri (*Bhumiamla*) 112.5 mg, Emblica officinalis (*Amalaki*) 67.5 mg, Tinospora cordifolia (*Guduchi*) 45 mg, Curcuma longa (*Haldi*) 30mg

Study Design:

This was an open labeled, non comparative, single arm, prospective, efficacy study conducted after taking prior informed consent of the subjects. Total 39subjects were enrolled in the study out of which 32subjects completed the 8 week treatment period. In this period all subjects were advised to take the caplets in a dose of '*Out of Lyme*' - 1 caplet along with '*Divine 9 Adaptogen'* Immunoprotector 1 caplet two times a day after meal for 8 weeks. Subjects were called up for follow up after every 2 weeks for 8 weeks.

Assessment Criteria:

ELISA for IgG antibody was a confirmatory assessment criterion. ELISA was performed on screening visit (baseline) and at end of study visit (at week 8).Change in the result from baseline to week 8 assessed the efficacy. During each visit subjects were assessed for Rash, Fever, Chills, Fatigue, Body aches, Headache, Joint pain, Neck stiffness among other symptoms. Symptom score from 0 to 3 depending on severity was assessed for all symptoms.0 = No Symptom, 1= Mild, 2 = Moderate and 3 = Severe. Reporting of adverse events as safety criteria was done at each visit. However, for statistical analysis the data of week 0, week 4 and week 8 was considered.

Investigations:

IgG antibody to Borrelia burgdorferi was detected by commercial ELISA kit along with general Hematological investigations - CBC, Serum Biochemistry, Urine Routine and Microscopic.

Statistical Analysis:

The prevalence and 95% binomial exact confidence intervals (CI) were calculated for the results using graph pad instat-3. Continuous data was analyzed using one-way analysis of variance (ANOVA). All the other data was analyzed by using appropriate statistical tests by considering $p<0.0001$ as a highly significant, $p<0.001$ as significant and $p<0.05$ as non significant.

Observation and Results:

In present study, out of total 39 IgG ELISA positive subjects, 32 subjects were enrolled for the study and completed the study successfully. 28 subjects (87.50%) were found Negative for IgG at week 8 i.e. end of treatment of the study (Table 1).

Table 1: ELISA for IgG

	Week 0		Week 8
POSITIVE	32		4
	100%		12.50%
NEGATIVE	0		28
	0%		87.50%

Most of the subjects belong to the age group 20 to 60. In which65.63% were females (Table 2).

Table 2: Demographic data of the Subjects

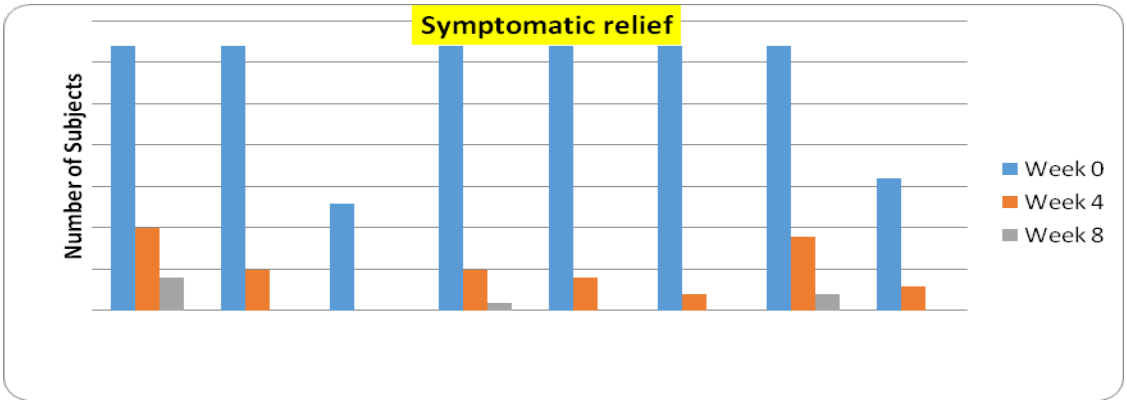
		No. of pt.	**%**
Age group	18 to 30	11	31.25%
	31 to 40	12	37.50%
	40 to 50	6	18.75%
	50 and above	3	9.38%
Gender	Male	11	31.25%
	female	21	65.63%

All the 32 (100%) subjects were suffering from Rash, Fever, Fatigue, Body aches, Headache and Joint pain at screening visit. The symptoms Fever, Body aches and Headache were completely relieved in all the subjects at week 8 visits (Table 3). There was marked reduction in the rash (erythema migrans) at week 8 visit. 87.5% subjects show no rash at end of treatment visit. 31 subjects (96.87%)felt no fatigue and 30 subjects (93.75%) got relief in joint pain at the end of treatment visit. 13 subjects (40.63%) were having chills at baseline screening visit however the symptom was completely relieved in all the subjects at week 4 visit and was not recurred till the end of the study.

Table 3: Symptomatic relief to subjects

	Week 0		Week 4		Week 8	
	No of Pts	%	No of Pts	%	No of Pts	%
Rash	32	100%	10	31.25%	4	12.50%
Fever	32	100%	5	15.63%	0	0%
Chills	13	40.63%	0	0%	0	0%
Fatigue	32	100%	5	15.63%	1	3.13%
Body aches	32	100%	4	12.50%	0	0%
Headache	32	100%	2	6.25%	0	0%
Joint pain	32	100%	9	28.12%	2	6.25%
Neck stiffness	16	50.00%	3	9.38%	0	0%

Graph 1: Symptomatic relief to subjects

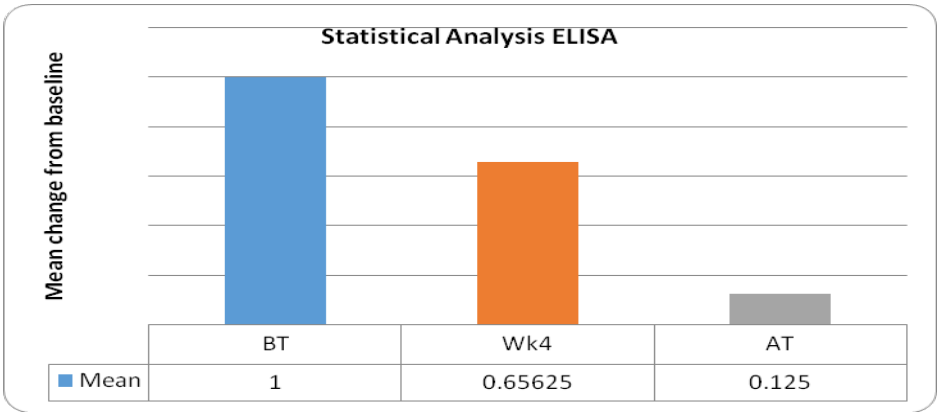


All the hematological parameters were within limits Results of ELISA test were analyzed using one-way ANOVA, Kruskal-Wallis test with Dunn's multiple comparison test was applied. Statistical analysis also supports the results showing p value <0.0001 which is considered as extremely significant, considering the confidence interval of 95%. Variation in column means is significantly greater than expected by chance. ANOVA assumes that the data are sampled from populations with identical Standard Deviations. Results of ELISA test were analyzed using one-way ANOVA, Kruskal-Wallis test with Dunn's multiple comparison test was applied.

Table 4: Statistical Analysis of ELISA results

	BT	Wk4	AT
Mean	1	0.65625	0.125
Median	1.000	1.000	0.000
Sample Size	32	32	32
Minimum	1	0	0
Maximum	1	1	1
Range	0	1	1
Std. deviation	0	0.48256	0.33601
STD Error	0	0.0853	0.0594
P value summary		<0.0001	<0.0001

Graph 2: Statistical Analysis (ELISA)



DISCUSSION

The study has provided interesting new information about Lyme disease, but further investigation using larger numbers of population from more localities is necessary in order to gain a truly comprehensive understanding of the distributions of this disease in India.

Lyme disease occurs in stages, with different clinical manifestations that reflect the immune response to *B. burgdorferi*. The stage I, early localized infection, is characterized by EM accompanied by systemic viral-like symptoms, including fever, malaise, headache, and joint pain. Stage II, early disseminated infection, develops within 1–9 months following an untreated infection, and is due to hematogenous spread of bacteria to sites distant from the original EM lesion. Early disseminated infection affects the skin, heart, and the nervous system.[6,7]

Most of the times subjects with Lyme disease are treated with antibiotics, but in some cases this

treatment produce only a temporary relief and the disease persists in the form of chronic infection. So treatment for Lyme disease should be holistic in curing all associated disorders.

The selection of the herbs for the formulas was based on traditional Ayurvedic medicines. The combination of herbs in '*Out of Lyme'* proved excellent in the context of relieving all the associated symptoms of Lyme disease and in majority of cases healing disease completely. The results are very encouraging in the first 4 weeks itself. Albizia lebbeck (*Shirish*) from '*Out of Lyme*' is the main and the best herb described in Ayurveda as an antitoxin.[9] Of all the herbs that are useful to treat toxicosis, Shireesha - Albizia lebbeck is the best. *Shothahara* - relieves inflammation; *Visarpaghna* - relieves herpes, spreading skin disease; *Vranahara* - brings about quick wound healing; *Vishapaha* - Useful in treating toxins; *Varnya* - Good for skin, improves complexion; *Kushtaghna* - Useful in skin diseases; *Kandughna* - relieves itching, pruritis; *Twak Doshahara* - detoxifies skin[8]; Cassia fistula (*Aragvadha*) is used in skin diseases. It is slightly purgative which helps in reliving toxins from the body. It described as a *vatahara* that relieves pain.[10]Acacia catechu (*Khadira*) acts as a blood purifier, Hemidesmus indicus (*Anantmool*)is used for the treatment of fever and inflammation, Curcuma longa (Haldi) is a potent anti-inflammatory herb, Hollarhena antidysenterica (*Kutaja*) restores gut and directly acts on blood thereby detoxifying liver; Vitex negundo (*Nirgundi*) is a natural purifier, a good muscle relaxant and pain reliever; Aegle marmelos (*Bilva*) is hepatoprotective and detoxifies. Achyranthes aspera (*Apamarga*), Azadirachta indica (*Neem*), Plumbago zeylanica (*Chitrak*) and Tinospora cordifolia (*Guduchi*) are the other immunomodulatory, antioxidant and anti-inflammatory herbs in '*Out of Lyme*' which are very effective in the treatment of Lyme disease.

Lyme disease affects Immune, Nervous and Endocrine systems. '*Divine 9 Adaptogen'* Immunoprotector is a perfect blend of adaptogenic herbs which naturally boosts Immune, Nervous and Endocrine Systems and improves endurance and stamina. The herbs in '*Divine 9 Adaptogen'* Immunoprotector like Asparagus racemosus (*Shatavari),* Boerhaaviadiffusa (*Punarnava*), Ocimum sanctum (*Tulsi*), Plumbagozeylanica (*Chitraka*) and Withania somnifera (*Ashwagandha*) are proven immune boosters. Phyllanthusniruri (*Bhumiamla*), Emblica officinalis (*Amalaki*), Tinospora cordifolia (*Guduchi*) and Curcuma longa (*Haldi*) act as antitoxins, and they also improve digestion.

In this study, the results are very positive and encouraging in reliving symptoms of Lyme disease. In addition to this, there are marked improvements in CBC and Haemoglobin levels are increased as well.

This study showed that the combination therapy of' *Out of Lyme*' and '*Divine 9 Adaptogen'* Immunoprotector can have detoxifying, anti-inflammatory and immune boosting effect in the subjects with Lyme disease which was demonstrated by a significant reduction in the level of symptom scores in these subjects. It has also helped reduce levels of SGPT in subjects.

The combination therapy of traditional polyherbal formulations can increase the efficacy of the disease treatment and decrease the risk of adverse events such as loss of muscle tone and carditis. There is an increased interest in the research and development of combination therapies.

Author Contributions:

The work presented in this article was carried out through collaboration between all authors. SD and SRC made the initial hypothesis. All authors participated in defining the research theme and provided the proposal. SD, SRC, VSC and APM performed the experiments, collected the data, analyzed the data, and wrote the article. APM and SD conceptualized the study, critically analyzed and discussed the data, and corrected and reviewed the article.

CONCLUSION

The study showed a potential detoxifying, analgesic, anti-inflammatory and immune boosting effect of the two herbal formulations '*Out of Lyme*' and '*Divine 9 Adaptogen'* Immunoprotector which cause significant reduction in the symptoms of Lyme disease at week 4 and more compelling results were seen at week 8 of treatment. The formulation did not show any significant adverse effect in this study. Further studies with larger sample size should be done to confirm the observed effects.

Declaration of Conflicting Interests: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding: The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was supported by a grant from the Somalata Ayurveda India Pvt. Ltd., Bulandshahr, U.P. India and Ashvin Ayurveda College.

REFERENCES

1. Steere A.C. Lyme disease. N Engl J Med. 2001; 345:115–125.
2. Bethesda (MD): U.S. National Library of Medicine; c2013. Lyme disease; 2013 May 23 [cited 2012 Feb 27]; Available from: http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0002296/
3. http://www.cdc.gov/media/dpk/diseases-and-conditions/lyme-disease/index.html
4. Patial RK, Kashyap S, Bansal SK, Sood A. Lyme disease in a Shimla boy. J Assoc Physicians India. 1990; 38:503-504.
5. Handa R, Wali JP, Singh S, Aggarwal P. A prospective study of Lyme Arthritis in North India. Indian J Med Res. 1999; 110:107-109.
6. Murray TS, Shapiro ED. Lyme disease. Clin Lab Med. 2010; 30(1):311–328. [PMC free article][PubMed]
7. Meyerhoff JO. Lyme disease. 2013. [Accessed November 5, 2013]. Available from: http://emedicine.medscape.com/article/330178-overview.
8. Centers for Disease Control and Prevention (CDC) Summary of notifiable diseases – United States, 2010. MMWR Morb Mortal Wkly Rep. 2012; 59(53):1–111. [PubMed]
9. Triphathi R, Charak Samhita, Chaukhamba oriantalia Vol 2; 2013; 25
10. Triphathi R, Charak Samhita, Chaukhamba oriantalia Vol 2; 2013; 8
11. Agnivesha, Charaka Samhita with Ayurved Deepika commentary of Chakrapanidatta, Ed. Yadavji Trikamji Acharya, Chaukhambha Sanskrit Sansthan, Varanasi, Reprint, Chikitsasthana, 2014; 3/167: 413

Source of Support: Nil
Conflict Of Interest: None Declared

How to cite this URL: Deshpande Sarang et al: Management of Lyme Disease With A Polyherbal Combination of 'Out Of Lyme' And 'Divine 9 Adaptogen' Immunoprotector. International Ayurvedic Medical Journal {online} 2018 {cited November, 2018} Available from: http://www.iamj.in/posts/images/upload/2475_2482.pdf