Contents lists available at ScienceDirect

Journal of Ayurveda and Integrative Medicine

journal homepage: http://elsevier.com/locate/jaim



AYURVEDA

COVID-19 patient with B cell lymphoma co-morbidity managed with co-administration of ayurvedic formulation



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ARTICLE INFO

Article history: Received 30 June 2020 Received in revised form 16 July 2022 Accepted 1 August 2022 Available online 12 August 2022

Keywords: COVID-19 Cancer Immunocompromised Lymphoma Host immune response Antiviral

ABSTRACT

'Renaissance took place in Chaos and plague'. It was COVID-19 pandemic, when world realized ayurveda co-interventions are praiseworthy even in acute, infective and fatal conditions like COVID-19. We report perhaps first case of COVID-19 patient with cancer managed with poly-herbal ayurvedic formulation and integrated approach. In the first wave of COVID-19 (June 2020), a 47 year old male with history of Chronic kidney disease and active B Cell Lymphoma complained of fever, malaise, cattarah and ageusia. He was found positive on RT-PCR which was done promptly and was later treated in home quarantine with antipyretics, Vitamin C and Madhav rasayan a polyherbal preparation containing Piper longum, Glycyrrhiza glabra, Eclipta alba, Achyranthes aspera, Embelia ribes and Aloe vera designed to modulate host response. It was challenging to treat a patient with cancer with immunocompromised status as he had recently finished his chemotherapy cycle (R-CHOP regimen). Patient well tolerated the intervention and recovered symptomatically. He did not developed any respiratory complications and oxygen saturation remained maintained. On 7th day RT-PCR was found to be negative. Plethora of literature is available on anti-viral and immunomodulatory efficacies of Ayurveda herbs based on in vitro studies. Such efficacies can be replicated at patient's level if supported with wisdom of Ayurveda epistemology. Early diagnosis on RT-PCR and early inception of ayurveda medicine and diet interventions might be crucial element for better recovery.

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1. Introduction

There is no gold standard therapeutic agent proven for COVID-19 and world is still facing health emergency of COVID-19 pandemic/endemic. Cohort studies have reported higher mortality rates in COVID-19 patients with cancer [1,2]. Increased mortality is observed in COVID-19 patients with lymphoma because of immune-compromised status due to the disease and/or its treatment with immune-chemotherapy [3]. Here we report a mild COVID-19 case with lymphoma treated in home quarantine with integrated treatment. Ayurvedic understanding of COVID-19 is reported as 'exogenous fever' later resulting in systemic involvement with vata-kapha dosha profile and pitta dosha as adjuvant [4]. Case reports and trials of Ayurveda interventions in mild to severe

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Peer review under responsibility of Transdisciplinary University, Bangalore.

COVID-19 cases are published [5,6]. This is perhaps the first reported case of COVID-19 with cancer (B Cell lymphoma) treated with integrated approach and Ayurveda medicine and resulted RT-PCR negative in a week.

2. Patient information

2.1. De-identified patient specific information

A 47 year old shopkeeper patient from Mumbai started fever and Malaise on 12th June 2020. It was early first wave of COVID-19 pandemic in Mumbai. He was asked for RT-PCR examination of nasal swab and was found to be infected with SARS Cov-2.

2.2. Primary concerns and symptoms of the patient

Patient had high fever (Fever 103 $^{\circ}$ F), catarrh, malaise/bodyache. There was also loss of smell (anosmia) and loss of taste (ageusia). There was no sore throat or cough and other any upper respiratory

https://doi.org/10.1016/j.jaim.2022.100632

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Table 1

Patient presentation with interventions.

Date/Day	Symptoms	Test/Result	Medication	Dietary Intervention
12/6/2020, Day 1	Catarrh ++, Fever 104 °F, Malaise +++. Anosmia, Ageusia present.	Swab Test for CoVID-19 RT- PCR done.	Tab Madhav Rasayan 250 mg (Twice a day) Tab Paracetamol 500 mg (Twice a day) Tab Viewice 6500 mg (Twice dw)	Green gram soup in the dinner.(Roasted green gram + 14 parts of water, cooked until semisolid consistency)
			Tab Vitamin C 500 mg (Twice a day)	Drinking hot water. Hot water steam and gargles.
13/06/2020, Day 2	Catarrh ++,	Swab Test for CoVID-19 RT-	Tab Madhav Rasayan 250 mg	Green gram soup in the dinner.
	Fever 100 °F,	PCR Positive.	(Twice a day) Tab Vitamin C 500 mg (Twice a day)	Drinking hot water. Hot water steam and gargles.
	Malaise +++. Anosmia, Ageusia present.	Positive.	Tab Paracetamol 500 mg (Twice a day)	HOL WALEI SLEAIII AILU GAIGIES.
	Allosillia, Ageusia present.		day)	
14/06/2020, Day 3	Catarrh +,		Tab Madhav Rasayan 250 mg	Green gram soup in the dinner.
1 1 2	Fever 99 °F,		(Twice a day)	Drinking hot water.
	Malaise ++.		Tab Vitamin C 500 mg (Twice a day)	Hot water steam and gargles.
	Anosmia, Ageusia present.		Tab Paracetamol 500 mg (Twice a	
			day)	
15/6/2020,	Catarrh +,		Tab Madhav Rasayan 250 mg	Green gram soup in the dinner.
Day 4	Fever 99 °F,		(Twice a day)	Hot water steam and gargles.
	Malaise ++ Anosmia,		Tab Vitamin C 500 mg (Twice a day)	
16/06/2020 Day 5	Ageusia present. Catarrh,		Tab Madbay Pacayan 250 mg	Croop gram coup in the dipper
16/06/2020, Day 5	Fever 99 °F,		Tab Madhav Rasayan 250 mg (Twice a day)	Green gram soup in the dinner. Hot water steam and gargles.
	Malaise Anosmia Ageusia		Tab Vitamin C 500 mg (Twice a day)	not water steam and gargies.
	present.		rub vitanini e 500 mg (rwiee a day)	
17/06/2020, Day 6	Catarrh,	Swab Test for CoVID-19 RT-	Tab Madhav Rasayan 250 mg	Green gram soup in the dinner.
	No Fever 97.8 °F,	PCR done.	(Twice a day)	Hot water steam and gargles.
	No Malaise,		Tab Vitamin C 500 mg (Twice a day)	
18/06/2020, Day 7	No Catarrh,	Swab Test for CoVID-19 RT-	Tab Madhav Rasayan 250 mg	Green gram soup in the dinner.
	No Fever 97.8 °F,	PCR was resulted	(Twice a day)	Hot water steam and gargles.
	No Malaise,	Negative.	Tab Vitamin C 500 mg (Twice a day)	
	Anosmia and Ageusia			
10/00/2020	restored partially. No Catarrh, No Fever,		Teh Madhay Basayan 250 mg (On as	Demulan dist near med
19/06/2020 Day 8	No Malaise, Anosmia and		Tab Madhav Rasayan 250 mg (Once a day)	Regular diet resumed.
Day 0	Ageusia restored partially.		Tab Vitamin C 500 mg(Once a day)	
20/06/2020	No Catarrh, No Fever		Tab Madhav Rasayan 250 mg (Once	Regular diet
Day 9	No Malaise, Anosmia and		a day)	Regular alec
	Ageusia Resolved.		Tab Vitamin C 500 mg(Once a day)	
21/06/2020	No Catarrh, No Fever		Tab Madhav Rasayan 250 mg (Once	Regular diet
Day 10	No Malaise, Anosmia and		a day)	-
	Ageusia Resolved.		Tab Vitamin C 500 mg(Once a day)	
The following treat	ment was continued till 28/06/2	020		
	No Catarrh, No Fever, No		Tab Madhav Rasayan 250 mg (Once	Regular diet
	Malaise,		a day)	
			Tab Vitamin C 500 mg(Once a day)	

symptom. It was first wave of COVID-19 and lockdown in the city and patient opted telephonic video consultation. He was recommended RT-PCR Nasal swab test.

2.3. Medical, family, and psychosocial history including relevant genetic information

He had a history of CKD (chronic kidney disease) and active diffuse large B cell lymphoma with recently (in May 2020) finished 3 cycles of chemotherapy for the same. There was no other comorbidity like diabetes mellitus, hypertension. Family history included father's cerebro-vascular accident and hypertension. His lifestyle was sedentary and he used to eat madhura (sweet) food items in large quantity and frequency. Doshaja prakriti of patient was identified to be pitta-kapha dominant.

2.4. Relevant past interventions and their outcomes

Patient was diagnosed with B Cell lymphoma and was recently underwent 3 cycles of chemotherapy. Protocol included R–CHOP regimen containing rituximab, cyclophosphamide, doxurubicin, vineristine and prednisolone.

2.5. Clinical findings

Relevant clinical examination and other findings: Patient started fever (104 $^{\circ}$ F) on 12th June 2020. There was also severe malaise, catarrh and anosmia. His consultation was done on a video call and was recommended to stay in home quarantine. The treatment was started early and thus patient did not landed in stage of lower respiratory complications. Oxygen levels were asked to be examined meticulously and to report in case of any deterioration and no fall in oxygen below 95% was observed during whole course. Patient was obese with height 168 cm, weight 96 kg with BMI of 34. It was a vatakaphasannitpata jwara with pittanubandhatva. There was decline in agni (metabolism), utsaha (enthusiasm) and bala (energy) evident clinically.

2.6. Diagnostic assessment

Diagnostic Testings: As patient had classical presentation of fever with anosmia, he was advised RT-PCR for COVID-19 and was found to be positive. Oxygen saturation was 96%. Hemoglobin level was 13.4 gm/dl and platelets were 2.15 million/cmm. CRP level was 13. Neutrophil/Lymphocyte ratio was not altered and leucocytes

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Day	Day 1	Day 2 Day 3 Day 4 Day 5 Day 6	Day 3	Day 4	Day 5		Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 7 Day 8 Day 9 Day 10 Day 11 Day 12 Day 13 Day 14 Day 15 Day 16 Day 17 Day 18	Day18
Date	12/06	13/06 14/06 15/06 16/06 17/06	14/06	15/06	16/06		18/06	19/06	20/06	21/06	22/06	23/06	24/06	25/06	26/06	27/06	28/06	29/06
Symptoms																		
Catarrh	++	++	+	+	+	+	Resolved	Resolved	Ι	Ι	Ι	I	I	Ι	I	I	I	Ι
Temperature	104 ∘F	$100 \circ F$	99 ∘F 99 ∘F	99 ∘ F	99 ∘F	Afebrile	Afebrile	Afebrile	Afebrile	Afebrile	Afebrile	Afebrile	Afebrile	Afebrile	Afebrile	Afebrile	Afebrile	Afebrile
Malaise	++++	+ + +	+++	+++++++++++++++++++++++++++++++++++++++	+	Resolved	Resolved	Resolved	Resolved	Resolved	Resolved	Resolved	Resolved	Resolved	Resolved	Resolved	Resolved	Resolved
Loss of Smell	>	>	>	>	>		Partially	Partially	Fully	Fully Restored	Fully							
							Restored	Restored	Restored	Restored	Restored	Restored	Restored	Restored	Restored	Restored		Restored
Loss Of Taste	>	>	>	>	>	>	Partially	Partially	Fully	Fully Restored	Fully							
							Restored	Restored	Restored	Restored	Restored	Restored	Restored	Restored	Restored	Restored		Restored
Average Oxygen Saturation	95%	95%	86%	%96	86%	96%	96%	98%	98%	88%	88%	88%	88%	98%	98%	98%	98%	98%
Investigation	RtPCR for CoVID 19	Tested Positive				RtPCR for CoVID 19	Tested Negative											

ment chart

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value was 8000/cmm. Urine report were within normal limits. Patient responded well to management and oxygen saturation remained above 95% for whole course of disease.

Diagnostic Challenges: It was first wave of COVID-19 and national lockdown in India. Patient was in home isolation and thus thorough physical assessment was not possible.

Differential Diagnosis: Patient presented with fever with anosmia and ageusia. RT-PCR confirmed the diagnosis of COVID-19. Possibility of dengue was ruled out by normal Neutrophil count and normal platelet counts observed in hemogram. Ayurveda diagnosis was vata kapha pradhana jwara.

Prognosis: Patient was in immune-compromised state as he was on chemotherapy for his B cell Lymphoma. His ECOG score was 1. Early confirmation of COVID-19 on RT-PCR and early commencement of treatment helped in better prognosis of COVID-19. Oxygen levels remained maintained above 95% during the disease course. There were no any respiratory symptom like dyspnoea, sore throat, cough or any other symptoms associated with COVID-19 till eighteenth day. On third day temperature was at peak. This was perhaps indicative of 'pachyamana jwara' (ayurvedic concept referring a last surge in temperature before its decline) which was followed by sweating. On fifth day all the symptoms subsided except anosmia and ageusia and patient was found negative on RT-PCR on seventh day. Patient's agni (metabolism), utsaha (enthusiasm) and bala (energy) returned to normal by tenth day.

2.7. Changes in interventions with rationale

The patient was recommended: 1) Madhav Rasayan (250 mg twice a day) for a week 2) Tab. Paracetamol 500 mg twice a day for first three days. After seventh day as RT-PCR was negative, it was continued for ten more days one tablet a day. Paracetamol in 500 mg dosage was used twice a day for first three days. Patient was also was asked to take vitamin C tablets in 500 mg dosage twice a day for first seven days and once a day for next 10days. Patient was recommended to take green gram soup by boiling roasted green grams in 14 parts of water till it obtains semisolid consistency for dinner. He was also asked to drink hot water for first three days. After seventh day patient was asked to resume his regular diet. Hot water steams and gargles were advocated for a week (Table 1).

3. Follow-up and outcomes

3.1. Clinician and patient assessed outcome

Body ache was relieved on second day with medication. Cattarah and malaise were not there after 3rd day of medication. Green gram soup and hot water helped in restoring agni (metabolic fire). On sixth day fever was completely relieved and taste and smell restored partially. On seventh day nasopharyngeal swab RT-PCR was found negative. Oxygen saturation remained maintained above 95% during whole course of disease. Details are mentioned in Table 2.

3.2. Important follow up diagnostic tests

Telephonic follow-up was taken every day. Outcomes were good as symptoms were relieved and no form of deterioration or complication was observed. Patient visited the clinic on 8th day and was found to be healthy on clinical examination.

3.3. Intervention aderehence/tolerability

Intervention was well tolerated by patient. Ayurveda formulation was in tablet form and thus palatable. Patient was already on ayurveda medicines and hence was compatible with the prescribed medications and pathya (dietary dos and donts) food regimes.

3.4. Adverse effects

No adverse effects were not observed.

4. Discussion and remarks

4.1. Strengths and limitations of case

Patient was in home guarantine and thus daily charts of vitals and biochemistry reports are not avaliable. Among inflammatory markers only CRP was evaluated. As patient was responding well, we did not evaluate more inflammatory markers like Interlukin-6. Thorough physical examination was not possible as patient was in home isolation. Apart from these limitations, this is perhaps the first reported case of COVID-19 with active cancer and treated with integrated approach. Immunosuppression (whether caused by the disease itself or the treatment) can lead cancer patients to serious complications requiring hospitalizations and affected disease prognosis [7]. Patients with cancer are more susceptible to COVID-19 and also show increased mortality as reported in systematic review [8]. Another meta-analysis reports higher risk of severe disease and death outcomes from COVID-19 infection as compared with general COVID-19 populations [9]. Thus treating a patient with such prominent co-morbidity like cancer is a strength of this case report.

In this case integrated management helped in better outcomes and did not necessitate hospitalization. Patient was in Home isolation and we repeated RTPCR on 7th day (instead of a repeating it after 14 days as per trend in first Covid-19 wave). Interestingly we found it negative implying anti viral effects of treatment and also early clearance of viral particles. RT-PCR was found to be negative on seventh day implying anti-viral effects of treatment and also early clearance of viral particles. In this case initial CRP value was 13. According to another systematic reviews and metaanalysis raised CRP is associated with poor prognosis in COVID with cancer cases [10]. CDC reports that immunocompromised patients need twenty days for recovery and are infectious for same period (https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html). Median time for recovery in mild COVID-19 patients according to WHO document is two weeks (Complete clinical recovery and Negative RTPCR) [11,12]. The patient recovered in 7 days as well as swab RT-PCR test was negative. This early recovery can be attributed to integrated approach and poly-herbal ayurveda medication.

4.2. Discussion on medical literature

COVID-19 is still health emergency as there is no gold standard therapeutic agent available. Although the disease presentation remains minimal in 80% cases, immune-deregulation can lead to cytokine storm, COVID-19 pneumonia and hypoxemia and even in Acute Respiratory Distress and death [14]. Ayurveda formulations with antivirals, anticoagulant, anti-fibrotic and immune Restoring herbs are relevant in present context. 'Conservation of agni-bala', 'attainment of rakta-pitta-prana homeostasis' and 'protection of tri-marma i.e. vital organs' are suggested as management strategies for better clinical outcomes and reduction of mortality in COVID-19 [15]. This was a COVID-19 case with active B cell lymphoma. Now there is enough evidence that Gut—Brain axis is not mere bidirectional but a cluster including immune, endocrine and metabolic components [37]. Concept of Agni is pivotal in Ayurveda pathophysiology and deepana (medicines enhancing 'agni' including appetizers) and pachana (medicine improving metabolism) are pivotal in practise of Ayurveda medicine.

Ayurvedic understanding of cytokine storm can be inflammation involving vitals is Dhatu-paka (histological and functional deregulation of body tissue) according to ayurveda. Anti-inflammatory, immuno-modulatory evidences of Ayurveda herbs and their actions on particular cytokines are well documented [16]. Ayurveda Classical literature obviously do not mention Cytokine storm. However the phenomenon of inflammation is referred as Dhatupaka (histological and functional derangement of body tissue) in Ayurveda. Many ayurveda herbs are proven anti-inflammatory, immunomodulatory and also having effects on cytokines [17]. Madhav Rasayan is a formulation with most of ingredients having rasayana, Anti-inflammatory and immuno-modulatory efficacies.

5. Scientific rationale for conclusions

Use of immunomodulators achieving Th1/Th2 equlibrium and immune homeostasis for COVID-19 is reported in literature [18,19]. Madhav Rasavan is such formulation aimed at immune homeostasis. Along with immunomodulatory, it is mixture of herbs with anti-viral, anti lung fibriotic, anti coagulative activities. There are evidence of designer drugs involving safer, curative and synergistic combinations as multiple immune-modulating strategies are necessary to achieve clinical success owing to complex interplay between pathways [20]. Madhav Rasayana is a formulation with such synergy with ingredients as Piper longum, Glycyrrhiza glabra, Eclipta alba, Achyranthes aspera, Embelia ribes and Aloe vera. Glycerezine in Glycyrriza glabra is reported to neutralize SARS CoV 2 [21]. Phytochemicals from all ingredients have shown immunomodulatory efficacies in silico/in vitro models [22-29]. Phytochemicals from Glycyrriza glabra, E. alba, P. longum and A. vera are having efficacies for lung damage/fibrosis [30-33]. Embelin in emblia ribes is a PKC inhibitor and possesses antiplatelet and antithrombotic effects [34].

In Ayurvedic viewpoint, *P. longum* and Glycyrriza glabra is the combination to be used in infective respiratory conditions. *E. alba* is the key herb aimed at minimizing complications of COVID-19 which are result of inflammatory and coagulative pathologies. *E. alba* helps in maintaining 'Rakta-Pitta-Prana' homeostasis and for reducing Dhatu-paka i.e. inflammatory pathologies which are attributed to pitta dosha [35]. *E. alba* helps in maintaining Rakta (body tissue resembling and inclusive of Blood) - Pitta (Dosha required for digestion and tissue and molecular level metabolism)-Prana (vitality element and oxygen) homeostasis as it reduces Dhatu paka (inflammation in vital tissues) by alivating pitta which is reported to cause all inflammatory pathologies.

5.1. Patient perspective

On 12th June I started feeling running nose, fever and was unable to sense smell and taste. It was pandemic first wave in Mumbai and I suspected as loss of smell was COVID symptom. I consulted my Ayurveda doctor. I also had telephonic opinion from my allopathic physician. I opted to get tested for COVID-19 and was found positive. I was frightened as there was chaos and strict lockdown in the city. There was a good amount of fear factor, but at the same time I had belief in my Ayurveda doctor as I was his patient for CKD and Lymphoma in earlier times. I had personal experiences that ayurvedic treatment is effective. The doctor recommended me to take Vitamin C, Paracetamol and Ayurveda preparation Madhav Rasayan tablet. He confirmed if I had sore throat or cough or dyspnea which was not there. I was also recommended hot water steams and gargles and a specific ayurveda diet. I was keeping records of my oxygen levels which never dropped below 95% fortunately. After 3rd day of taking the medicine I started feeling almost well. On 7th day I repeated RTPCR test and it turned out to be negative. Thankfully no complications like cough or breathing issues happened and I got my illness resolved in almost a week. Thanks to Ayurveda treatment and my doctors.

5.2. Take away lesson

Immune dysregulation is key component in both inflammatory pathologies like COVID-19 and cancer for which ayurveda interventions are reported to be effective [35,36]. This was a COVID-19 case with B cell lymphoma. Early diagnosis on RT-PCR and early inception of ayurveda interventions and ayurveda diet recommendations might be crucial element for better recovery. Immunomodulatory efficacies of many herbs are reported using many in vitro models, but if supported with ayurvedic understanding of disease and Ayurveda principles of internal medicine, the results can replicated on patients level. This is perhaps first reported case of COVID-19 with cancer managed with Ayurveda and thus underlines importance of integrated approach for preventing COVID-19 patients from bad prognosis.

Informed consent

Informed written consent was obtained from the patient for publication.

Author contributions

Dr. Prasad Pandkar and Dr. Santosh Deshmukh were physicians treating patient and wrote the manuscript. Dr. Vinay Sachdev was assistant physician and also contributed in writing the manuscript.

Conflict of interest

None.

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