Efficacy of Rituharitaki (seasonal adjuvant of Haritaki) on disorders of Varsha Ritu (monsoon) w.s.r. to quality of life: An open labelled randomized controlled clinical trial

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Abstract

Background: Monsoon epidemics are always a serious concern in the public health sector. Administration of Haritaki with suitable vehicle as per season (Rituharitaki) is a simple, cost-effective preventive measure which can be used for such conditions. Aims and Objectives: Study objectives were to assess the effect of Rituharitaki in preventing the diseases in Varsha Ritu (monsoon) and its effect on the WHO quality of life BREF (QOL BREF), total leukocyte count (TLC), differential count (DC) and erythrocyte sedimentation rate (ESR) in healthy volunteers. Materials and Methods: From 82 participants, based on inclusion criteria, 60 participants were selected and randomly allocated into trial and control group of 30 each using a computer generated random number table. Intervention given was Rituharitaki (Terminalia chebula Retz) in tablet form-3 tablets of 1g each and Saindhava (rock salt) 1g with lukewarm water at 6.30 am on empty stomach to the participants of trial group for 60 days in Varsha Ritu in Kerala and were observed during this period. Results: The results were analyzed using Chi-square test and paired t-test. Significant results were obtained in the trial group in reducing the severity and frequency of common cold (p < 0.001), cough (p < 0.05), and fever (p < 0.001). In the WHO QOL BREF domain 1 & 4 showed significant result in the trial group (p < 0.05). Among the haematological parameters - total leukocyte count (TLC), eosinophil count and erythrocyte sedimentation rate (ESR) were statistically significant reduced (p < 0.05) in the trial group. Conclusion: Rituharitaki is found to be effective in reducing severity and frequency of diseases in Varsha Ritu and had effect on quality of life of patients.

Keywords: Agni, Rasayana, Rituharitaki, Saindhava, seasonal diseases, Varsha Ritu

Introduction

Due to tremendous changes in the mode of living as well as seasonal variations, human beings are prone to various infections and lifestyle ailments. The infectious diseases once thought to be under control, are re-emerging with increased virulence.[1] The outbreak of the seasonal epidemics during the last few monsoons has affected millions, and this has been a serious concern in the public health sector. The data on communicable diseases prepared by the Directorate of health services, Kerala State 2019 reported that there were nearly 2,862,375 cases of fever, 4,651 cases of dengue fever and 5,44,027 cases of diarrheal diseases and all these illnesses were reported to be more in the monsoon time.[2] So, the present situation requires critical health concern to prevent the outbreak of various diseases.

In Ayurveda, it is mentioned that when seasonal variations occur, the Dosha (bioelements) get imbalanced in the form of Chaya and Prakopa (accumulation and aggravation).[3] As Varsha Ritu (monsoon) is the season with least Bala (strength), Tridosha vitiation, and weakened Agni (state of digestion and metabolism), human beings are susceptible to many diseases.[4] Various modalities are mentioned to alleviate this Dosha vitiation and to improve the Agni by improving

Access this article online

Quick Response Code:  
Website: www.ayujournal.org  
DOI: 10.4103/ayu.AYU_243_18

How to cite this article: Smitha AV, Dilipkumar KV. Efficacy of Rituharitaki (seasonal adjuvant of Haritaki) on disorders of Varsha Ritu (monsoon) w.s.r. to quality of life: An open labelled randomized controlled clinical trial. AYU 2019;40:223-9.

Submitted: 09-Apr-2018 Revised: 19-Feb-2019
Accepted: 05-Mar-2020 Published: 14-Jan-2021
the Vyadhikshamatva (immunity). One among those is the seasonal usage of Haritaki (Terminalia chebula Retz), which is mentioned in one of the Laghuatrayi-Bhavaprakasha, in the Haritakaayadi Varga as Rasayana (anti-aging). This Rituharitaki is a simple and cost-effective Rasayana that is easy to administer, and this will be socially relevant if proven as a preventive drug in seasonal outbreaks in Varsha Ritu.

In many previous studies, liver function tests, cholesterol levels etc., showed seasonal variations, in healthy individuals. These findings point out that physiological imbalance occurring in Tridosha can be reflected in various objective parameters. In Varsha Ritu, Haritaki is mentioned to be taken with Saindhava (rock salt) As Varsha Ritu is the season with least Bala, intense hypofunctioning of Agni and Tridosha vitiation, the present study focussed on the intake of Haritaki with Saindhava as both possess Agnivardhana (appetizer) and Tridosha Shamana properties.

Aims and objectives
1. To assess the effect of Rituharitaki (Haritaki along with Saindhava) in preventing diseases of Varsha Ritu in the participants
2. To evaluate the effect of Rituharitaki (Haritaki along with Saindhava) on WHO quality of life bref (QOL-BREF) and hematological parameters (total leukocyte count [TLC], differential count [DC] and erythrocyte sedimentation rate [ESR]) in the participants in Varsha Ritu
3. To monitor the incidence of diseases in Varsha Ritu in trial group & control group.

Materials and Methods
The study was conducted as a randomized controlled trial (preventive trial) in healthy volunteers in the Varsha Ritu. Before starting of the study, a newspaper announcement was given and a total of 82 participants were screened. From those based on inclusion and exclusion criteria, 60 participants were selected, and they were randomly allocated in to trial group and control group of 30 each using computer generated random number table.

After randomization based on the random number table, participants were allocated in to trial group and control group of 30 each. On the first day initial assessment of parameters of the subject of both groups was taken and daily assessment sheet was given to mark the ailments they experience during the study period. Trial drug was given to the study group. On every 20th day they were called to evaluate any ailments in between. On 61st day, reassessment of the parameters and the disease incidence, frequency and severity during the intervention period was recorded.

Inclusion criteria
1. Healthy individuals (those without any physical and mental ailments and the parameters below mentioned to be in normal range) of either gender in age group 20–40 years
2. Participants with physical (weight, BMI) and bio-chemical parameters (TLC, DC, ESR, FBS, Lipid profile) in concern within the normal range
3. Participants willing to give informed consent [Annexure 1].

Exclusion criteria
1. Participants with any systemic illness
2. Participants classically contra-indicated for Haritaki administration.

Intervention
Before the starting of the actual study, a pilot study was conducted and the dose (6 g Haritaki powder and 1 g Saindhava) as per the Ayurveda pharmacopeia of India was observed to cause severe purgation and vomiting. On the basis of the observations, the dose was reduced to half (3 g Haritaki powder and 1 g Saindhava). The study was approved by the Institutional Ethics Committee (IEC/ DOC/014/2011 dated 07.04.2011), and clearance obtained. Informed consent was taken from participants in document form after being informed regarding the study, intervention and duration.

- Kala: Varsha Ritu: Rituharitaki: Rasayana
- Drug: Haritaki in tablet form-3 tablets of 1 gm each
- Prakshepa: Saindhava (rock salt) 1 g dissolved in 5 ml water.

[Due to the deliquescent property of Saindhava this was given in liquid form– 20 g dissolved in 100 ml water– 5 ml given daily with tablet. Haritaki tablet and Saindhava liquid was prepared from the Pilot plant of Vaidyaratnam P.S.Varier’s AryaVaidyasala, Kottakkal. Tablet was prepared with starch as binding material with a disintegration time of 30 seconds]
- Anupana: Ushnodaka (lute warm water -For easy dissemination of the tablet)
- Time of administration: 6.30 am on an empty stomach
- Intervention period: 60 days.

Assessment criteria
1. A pre-designed validated questionnaire (face validity taken) was used to assess the status of Agni and Tridosha vitiation in Varsha Ritu before intervention
2. Daily assessment sheet was given to the participants to record disease incidence, severity and frequency during the Varsha Ritu in the year 2011(Kerala) during the intervention period
3. WHO QOL (BREF) before and after intervention
4. Hematological parameters: TLC, DC, ESR (before and after intervention).

The data obtained from the Indian Meteorological Department from 2005 to 2010 showed that in Kerala rainy season is observed mostly in the month of June and July. Hence, the clinical study was carried out in June and July and the study parameters (3&4) were assessed before and after intervention (0th day and 61st day). Two patients in clinical trial dropped out and three from the control group.
Data analysis
The analysis was performed on the basis of intention to treat analysis. From the data obtained, the association between the disease incidence and intervention was analyzed using the Chi-square test. The WHO QOL BREF and laboratory investigations were analyzed using paired t-test. All the statistical analysis was performed in Graphpad Instat v 3.05 software. Manufacturer: Graph Pad Software, 2365 Northside Dr. Suite 560, San Diego, California, USA.

Observation and analysis
Status of Agni
Before starting the intervention, the status of Agni was assessed based on amount of food intake, nature of belching etc., [Figure 1]. The observations were in favor of the classical references that there will be Agnimandya in the beginning of Varsha Ritu.[14]

Status of Dosha
The status of Dosha was assessed with their Chaya Prakopa Lakshanas (accumulation and aggravation) and Vikrita Karmas (pathological symptoms) before the intervention. As per the classics, during Varsha Ritu, Tridosha vitiation is expected. However, in this study, instead of Vatakopa (aggravated Vata Dosha), Kapha Pitta vitiation was present in the majority of the participants [Figure 2].

Disease incidence
On observation, it was found that common cold, cough, fever, throat pain, and headache were the common diseases seen in the participants during the intervention period [Figure 3].

To find out the association between the intervention and incidence of diseases in the participants, Chi square test was applied separately to each disease after intervention.

Common cold
The statistical significance ($P < 0.001$) shows that there is an association between the intervention and the incidence of the common cold. As the Odds ratio is $< 1$, the chance of getting common cold to the control group is more than the trial group during the assessment period of 60 days [Table 1].

To find out the nature of association, the severity and frequency were analyzed separately based on curability [Figure 4].

Among the diseased in the trial group, all participants were cured by itself and in the control group 60% of them got relief without taking medication and 40% needed medication.

The frequency of common cold during the intervention period was also observed, and a reduction was noted. Compared to the control group reduction in the incidence was more in the trial group, which may be due to the intervention [Figure 5]. As the values were very small Chi square test and Fisher’s exact test could not be applied to prove the statistical significance.

Cough
In the case of cough also the obtained Chi-square value was greater than the table value showing statistical significance ($P < 0.05$) and so an association is present between the intervention and disease incidence. Here also, as the Odds ratio is $< 1$, the chance of getting disease to the control is more than the trial group during the intervention period [Table 2].

Fever
Among those who suffered from fever, 67% in the trial group recovered from fever without taking any medication. Nearly 94% of participants in the control group needed medication during the intervention period [Figure 6].

WHO QOL BREF
In the WHO QOL BREF, paired t-test was applied among the four domains, domain 1 and 4 were significant in the trial group after the intervention.
The mean score in the study group increased from 66.19 to 69.52 with a mean difference of 3.33 and standard deviation of 8.64 ± 1.58. The t value was 2.11 which was statistically significant (p < 0.05) [Table 3].

**Table 3: Effect of intervention on domain 1**

| Group   | Mean score | Mean difference | SD   | t     | P   |
|---------|------------|-----------------|------|-------|-----|
| Trial   | 66.19      | 69.52           | 8.64±1.58 | 2.11  | <0.05 |
| Control | 70.36      | 72.38           | 8.47±1.55 | 1.31  | >0.05 |

SD: Standard deviation, BT: Before intervention, AT: After intervention

7.97 ± 1.46, which was statistically significant at the level of P < 0.05 [Table 4]

**Hematological parameters**

**Total leukocyte count**
In hematological assessment, there was a decrease in the TLC in the trial group with a mean difference of 760 and SD of 1498 ± 273.49. The t value was 2.78 which was statistically significant (P < 0.01). In the control group, the mean difference was 383.33 and SD was 1349.1 ± 246.31 and it was not significant [Table 5].

**Eosinophil count**
There was a decrease in the eosinophil count in the trial group with a mean difference of 1.07 and SD of 1.36 ± 0.25 which was statistically significant at P < 0.001, whereas in the control group, mean difference was 0.01 and SD of 1.54 ± 0.28 and it was not significant [Figure 7].

**Erythrocyte sedimentation rate**
In the trial group, the mean score of ESR reduced from 14.3 to 8.5 with a mean difference of 5.80 and SD of 9.94 ± 1.81, the difference was statistically significant at P < 0.01. In the control group also there was a reduction (mean difference 5.50 and SD 16.5 ± 3.01) which was not significant [Figure 8].

**Discussion**

The health impact caused by seasonal variation includes not only physical problems but also physiological changes. A study conducted by Mallika K J, reported that the Tridosha Prakopa (aggravation of Tridosha) and Agnimandya are common in all Ritusandhi (seasonal junction), but not up to the pathological mark. Furthermore, a study reported in the American Journal of Public Health states that recent evidences indicate that seasonal variation of diseases depend to some extent on periodic changes in immunity caused by...
seasonal variations in the physiological activities of human body.\[25\]

Experimental studies carried out by Arnold Z on dogs indicated that the secretion of hydrochloric acid by the stomach was diminished when the external temperature was high. This in turn was found to disturb the acid base equilibrium of the upper part of the small intestine, with the result that the self-disinfecting power of the mucous membrane was reduced. In this instance also variation in immunity seems to be due to variation in physiological activity.\[16\] Although one cannot directly correlate hydrochloric acid with *Agni* (digestive power), the increased digestive problems by the end of summer and starting of monsoon very well goes in accordance with the concept that by the end of summer, the status of *Agni* declines.\[17\]

To correct this physiological imbalance, Ayurveda had explained in detail about the seasonal regimens along with seasonal purificatory regimen to prevent the onset of pathological process. In the *Brihattrayi* (Charaka Samhita, Sushruta Samhita and Ashtanga Sangraha) as well as *Laghutrayi* (Sharangadhara Samhita, Yogaratnakara and, Bhavaprakasa) these have been detailed. However as the years passed, change in the food habits and lifestyle would have made it difficult to follow the seasonal purificatory procedures and this may be the reason why in Bhavaprakasha which came later, i.e., in the 16th century AD, a simple and easier way of usage of *Haritaki* according to seasons was mentioned for prevention of seasonal diseases.

As the diseases are more in the rainy season as per the data of communicable diseases from Directorate of health services Kerala, which affected the health of many people, the present study was done for preventing the diseases of *Varsha Ritu*. This has been done as a phase one clinical trial in healthy volunteers.

*Rituharitaki* is the seasonal usage of *Haritaki* with different *Prakshepas* (vehicles) and the action is said to be as *Swasthasya Urjaskaram* (health promoting).\[18\] In each season *Haritaki* is advised to be taken with a specific *Prakshepa* which reduces the particular *Dosha* vitiation in that season. As this is mentioned as *Rasayana*, this will bring down the vitiation of *Dosha* and improve the *Vyadhikshamatva* in that particular season. According to Acharya Sushruta, *Rasayana* drugs not only arrest the ageing process but also develop resistance against diseases.\[19\] Acharya Sharangadhara has also claimed the *Rasayana* to be effective in increasing the immunity.\[20\] The imbalance of *Vata*, *Pitta* and *Kapha* at cellular level can be the precursor of a disease condition.\[21\] *Rasayana* has an important role in maintaining this homeostasis.

In healthy human body, the generation of pro oxidants in the form of ROS (reactive oxygen species) and RNS (reactive nitrogen species) are effectively kept in check by the various levels of antioxidant defense.\[22\] However when seasonal variation occurs or when gets exposed to adverse physiochemical, environmental or pathological agents, this delicately maintained balance is shifted in favor of pro oxides resulting in oxidative stress and this oxidative stress disturbs the normal cell functions.\[23\]

As a part of seasonal variation also, there will be *Agnimandya* resulting in the formation of *Ama* (toxic substance/free radicals). This can be correlated with the role of free radicals in diseases manifestation. These free radicals interact with various nonradicals and the cumulative effect of multiple changes by free radicals is the proximate cause of cell death.\[24\] Membrane lipids are highly susceptible to free radical damage. This

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**Table 4: Effect of intervention on domain 4**

| Group | Mean score | Mean difference | SD   | T    | P   |
|-------|------------|-----------------|------|------|-----|
|       | BT         | AT              |      |      |     |
| Trial | 58.96      | 62.71           | -3.75| 7.97| <0.01 |
| Control | 63.54      | 62.92           | 0.63 | 8.14| >0.05|

SD: Standard deviation, BT: Before intervention, AT: After intervention

**Table 5: Effect of intervention on total leukocyte count**

| Group | Mean score | Mean difference | SD   | T    | P   |
|-------|------------|-----------------|------|------|-----|
|       | BT         | AT              |      |      |     |
| Trial | 8923.30    | 8163.30         | 760  | 1498| <0.01|
| Control | 7406.70    | 7023.30         | 383.33| 1349| >0.05|

SD: Standard deviation, BT: Before intervention, AT: After intervention

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**Figure 7: Effect of intervention on eosinophil**

**Figure 8: Effect of intervention on erythrocyte sedimentation rate**
chain reaction of lipid peroxidation has deleterious effect on cells.[25] The concept of Rasayana goes well with the concept of anti-oxidants which are substances that neutralize either free radicals or their actions.

In the present study, Haritaki has been used which may have acted as Rasayana which was found to be effective in breaking the chain reaction of free radicals and reduced the lipid peroxidation. Haritaki with its Tridosha Shamana (pacifies Tridosha), Agni vardinaha (increases digestive power) and Rasayana action might have reduced the incidence of common cold, cough and fever in the trial group compared to the control group.[28] As the trial drug is Tridosha Shamana even the Mithya Yoga (improper contact) of Dosha vitiation might have pacified by the Kashaaya Rasa (astringent taste) of Haritaki. The Ushnaveerya (hot potency) of the drug would have acted on Kapha Vata Dosha.[29] Saindhava is also Tridoshashamaka and Agni vardinaka.[30] The result obtained in the trial group may be due to the combined effect of these two drugs.

Evaluation of disease incidence in Varsha Ritu

This was one of the objectives of the present study. In the study group, the incidence of diseases were with less severity and no recurrence, showing an improvement in their general health condition. The trial drug was found to be more effective in the intervention period and maximum result was obtained during the last period of intervention. In the next Ritu also the diseases were with less severity, but not recorded as it was not the objective. Haritaki due to its Deepana Pachana (stimulates digestion) and Sroto Shodhana (purification of channels of circulations) property and Saindhava with its Agni vardinaha and Tikhnashuna (penetrating property), the intervention might have improved the Agni.[31,32] When the Agni is proper, naturally Bala (strength) will increase due to proper assimilation. This Bala is none other than Vyadhi Kshamatva.[33] Hence, the reduction in disease incidence and recurrence may be due to the improvement in Vyadhi Kshamatva (immunity).

Assessment of the WHO quality of life brief

Results of a study conducted by Skevington et al. on WHO QOL BREF indicate that overall the WHO QOL BREF is a sound, cross culturally valid assessment of QOL, as reflected by its four domains: Physical, psychological, social and environmental.[34] This is a questionnaire comprising 26 items which measure the health under four domains. Hence for the present study, WHO QOL BREF was used to assess the improvement on the perception on QOL among the volunteers.

As the change in the physical domain was statistically significant in the study group at $P < 0.05$, there was a significant improvement in the physical activities. Reduced dependence on medicine is always a favorable factor for increase in physical activity. An increased level of energy, working capacity, mobility and reduced fatigue, pain and discomfort as well as proper sleep and relaxation were achieved through the intervention. The reduction in disease incidence can be attributed to the Rasayana property of the trial drug.

In the present study, domain (1) and (4) showed significant improvement in the study group at $P < 0.05$ which may be due to the improvement obtained by intervention in physical and environmental domains. Reduced dependence on medical services provides enough time for recreation, leisure, information, etc., Social Domain (3) also showed some improvement in the trial group, but it was not significant statistically. The change in the psychological domain (2) was not significant in both groups at $P < 0.05$ which indicates that Rituharitaki when given in Varsha Ritu is not having any effect on psychological parameters. As the study was conducted in healthy volunteers change in the psychological aspect will not be that much predominant before and after intervention [Tables 3 and 4].

Effect on hematological parameters

TLC, DC & ESR were included in the present study as these are said to be the base inflammatory indicators. In the trial group, there was a significant reduction in the TLC, but within the normal limits. In differential leukocyte count, there was a significant reduction in eosinophil count in study participants. The observations are suggestive of a low grade inflammation in the study participants. The significant change in the eosinophil count may be due to the anti-allergic property of Haritaki.[35] There was a significant change in the ESR in the study group. The antiarthritic activity of Terminalia chebula Retz is a proved one and the present study also supports this.[36]

As the study was conducted in healthy volunteers and also blood samples were examined with a gap of 2 months and hence, many factors might have affected the results.

Reasons for dropouts of subject

Two healthy individual dropped from study group. In one of the previous study with Haritaki Churna, the non-palatability was the main reason for drop out. Hence, in the present study, Haritaki was made in the tablet form (1 g tablet), but still due to big size of the tablet, some reported difficulty in swallowing. Furthermore, the less disintegration time and due to breaking of the tablet for swallowing along with water, the astringent taste of the drug was not comfortable to many. In the control group, there were three dropouts. As the study was conducted in the healthy volunteers and no intervention given to the controls, may be they opted out of study due to loss of interest.

Conclusion

The present study was an attempt to find out a simple cost effective measure for the prevention of diseases in rainy season. Rituharitaki was found to be effective in reducing the severity and frequency of diseases (common cold, cough and fever) among the participants during Varsha Ritu

- There was significant improvement in the Domain 1 and Domain 4 of WHO QOL BREF. The changes in the hematological parameters(TLC, DC, ESR) within the normal limits suggest an improvement in the general health which also can be concluded due to the intervention.
Limitations
1. Due to small sample size, many of the associations could not be evaluated.
2. The last objective of this study was to monitor the incidence of diseases in *Varsha Ritu* but with the present infrastructure, it was very difficult to carry out the aim fully

Recommendations
1. Cross sectional studies can be designed to observe the disease incidence in *Ritushandhi*, period and during the *Ritu*
2. In further studies of *Rituharitaki*, specific immunological assessment can be included
3. Study should be conducted in larger samples, to generalize the results of present study
4. The duration of *Rituharitaki* intake in each *Ritu* can be studied in larger sample and to assess the effect of *Rituharitaki* according to different geographical areas a multicenter study can be conducted.

Financial support and sponsorship
1. Financial support for biochemical investigation was received from the laboratory of college hospital, VPSV, Ayurveda college, Kottakal.
2. Drug for the trial was received from the pilot plant of Vaidyaratnam, P.S, Varier’s Aryavaidyasala, Kottakal.

Conflicts of interest
There are no conflicts of interest.

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