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Study on the Preventive Effects of Chitraka Haritaki Avaleha in Recurrent Upper Respiratory Illness in Children: A Randomized Controlled Clinical Trial

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Recurrent Respiratory Infections, Chyavanprash Avaleha, Chitraka Haritaki Avaleha, Upper Recurrent Respiratory Tract Illness.

Abstract

Background: Upper respiratory illnesses are the most frequently occurring illness in childhood and it can decrease quality of life for children. The cause of recurrence of these illnesses is linked to relative immaturity of the immune system. Increasing bacterial resistance in recent years has shifted focus more on prevention of recurrent upper respiratory illness in children. The aim of study is to evaluate the immune modulator effect of Chitraka haritaki avaleha and its preventive effects of recurrent upper respiratory illness in children. Objectives - To evaluate and compare the immune-modulator effects of control and trial drugs in children suffering from recurrent upper respiratory tract illness through AEC, IgG, IgE levels. Methodology- The patients attending the OPD and IPD of the department of Kaumarbhritya, MahatmaGandhi Ayurved College, Hospital and Research Centre, Salod (H), Wardha will be diagnosed as Upper Recurrent Respiratory Illness on the basis of diagnostic criteria and after fulfilling inclusive criteria, randomly such patients will be enrolled for the study. The enrolled patients will be divided into two groups, patients of one group will be received Chitraka Haritaki Avaleha and other group will be received Chyavanprash Avaleha for 60 days. Follow up of 60 days will be done and after that the effects of the therapy will be assessed for IgG and IgE. Expected Results- Chitraka haritaki avaleha is a preventive in recurrent upper respiratory illness in paediatric patients. Conclusion- Preventive focus in Recurrent Upper Respiratory Illness in children will help to restore the health of the children and improve the quality of life. Children with impaired immune responses may benefit from chitraka haritaki avaleha. There is need to gain more data insights in Indian children from larger studies.

1. Introduction

In the paediatric age group, upper respiratory tract disease is the most common cause for hospital admissions, resulting in missed schoolwork. These illnesses can happen at any time .Viruses are responsible for the vast majority of upper respiratory illnesses. Cough, sneezing, nasal discharge, nasal congestion, runny nose, fever, and sore throat are the most common signs of upper respiratory illness... [1] The recurrence of these illnesses is hazardous to the general health and educational performance of the child. Recurrent Respiratory Illness is characterized by the recurrence of infection within a short period and the prevalence of recurrent respiratory illness is highest in children[2]. Common cold and cough in children is the most common recurrence. Dealing with these recurrent respiratory problems and ensuring to parents that their child's comfort and quick recovery is a challenge for the paediatrician. It is a significant matter of concern to parents and creating a dilemma for the paediatrician as well. In such conditions, there is the main role of the defence mechanism of the body and herbal medicines have a good potential to

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modulate the immune system and also used as curative as well as preventive medicine in upper respiratory tract illness [3].

Anatomical and physiological variations of the respiratory system in children-

*Tatra Balam Nama Aparipakva Dhatu, Asampurna Balam, Virya, Prayaha Shleshma Bahu*m[4]

Ayurveda mentioned clearly, that the childhood period is a period of immaturity so rightly the terminal bronchioles and conducting Airway is grow very slowly by the age of 8 years, elastic recoiling is less and more resistant, intra luminar mucus production is more and it causes more airway obstruction due to these reasons child get recurrent respiratory infections[5]. These are the immunological considerations mentioned in Ayurveda childhood is Kapha dominant period and immune system under continuous risk and target for causative organisms; due to immaturity of immune system infections organism bypass the defence barrier easily.

Recurrent Conditions of upper respiratory illnesses are common in paediatric practice and account for 20-40% of OPD and 12 to 35% IPD attendance and a majority (90%) of these are viral[6]. There is no single answer to this illness but it's an important problem that needs to be worked out carefully to set in motion the correct actions, the correct plans to overcome what may be the studies posing factors, and the causes of the recurrent respiratory problems to come out with best plans for recurrent respiratory infections it is a significant matter of concern to parents as well as paediatricians.

Available treatment like antibiotics, antihistamines, and analgesics use may relieve symptoms but not prevent recurrence of the illness.

Relevant studies: Various searches regarding the topic are found in Google Scholar, MESH.

1. Nayan Kumar Subramanya, Kalpana Shanthi Bhai Patel and Rajagopala Shrikrishna. 2013, "Role of Kasahara Dashemani Vati in Kasa and Vyadhikshamatva in Children". https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3902595/

Findings – Kasahara Dashemani vati was more effective in Vata pradhana and Pitta pradhana Kasa, showed better action on RRTI with primarily allergic etiology and marginally better than Indukanta vati in improving Vyadhikshamatva/ Bala[7].

2. Vd. Thakur Jitesh Yadav, Vd. Chitte Sanjay Tukaram. 2017, "A Randomized Controlled Clinical Study on the Efficacy of Chitraka haritaki Avaleha in Vataj Pratishyaya wsr to Allergic Rhinitis in Children". www.pijar.org

Findings – Chitraka haritaki avaleha has given positive results because statistically, it is significant in Nasasrava, Nasakandu, Nasavrodha, and Shirshoola. Statistically less effective in Kshavathu[8].

3. MF Cotton, "Management of upper respiratory tract infections in children". https://www.ncbi.nlm.nih.gov/pmc/articcles/PMC3098742/

Findings – The clinician's ability to make clinically appropriate decisions would be aided by knowledge of the natural history of rhinovirus infection and understanding of URTI management[9].

4. Gopikrishna S, G Shrinivas Acharya. Randomized Comparative Clinical Study To Evaluate The Effect Of Chitraka Haritaki Avaleha And Kantakari Ghrita In Different Types Of Tamaka Swasa. http://www.iamj.in/posts/images/upload/2329_2337.pdf

Finding – After observations; it is found that both formulations are safe; Chitraka haritaki avaleha has an edge over Kantakari Ghrita. During the intervention of these drugs, no adverse reactions were noted[10].

5. Poonam gaur, Professor K. S. Patel, Dr. V. K. Kori. "A Comparative Clinical Evaluation Of Chitraka Haritaki Avaleha And Bharangyadi Avaleha In The Management Of Tamaka Swasa(Bronchial Asthma). http://ctri.//nic.in

Findings - Both the groups have shown significant improvement individually but the difference between effects of therapy of both the groups was statistically significant. Overall Citraka haritaki avaleha is more effective than Bharangyadi avaleha in most of the parameters [11].

AIM: To study the Immunomodulatory effects of Chitraka Haritaki Avaleha and compare its efficacy with Chyavanprash Avaleha on recurrent upper respiratory tract illness in children.

2. Objectives

1. To evaluate and compare the immune-modulatory effects of control and trial drugs in

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children suffering from recurrent upper respiratory tract illness through AEC, IgG, IgE levels[12].

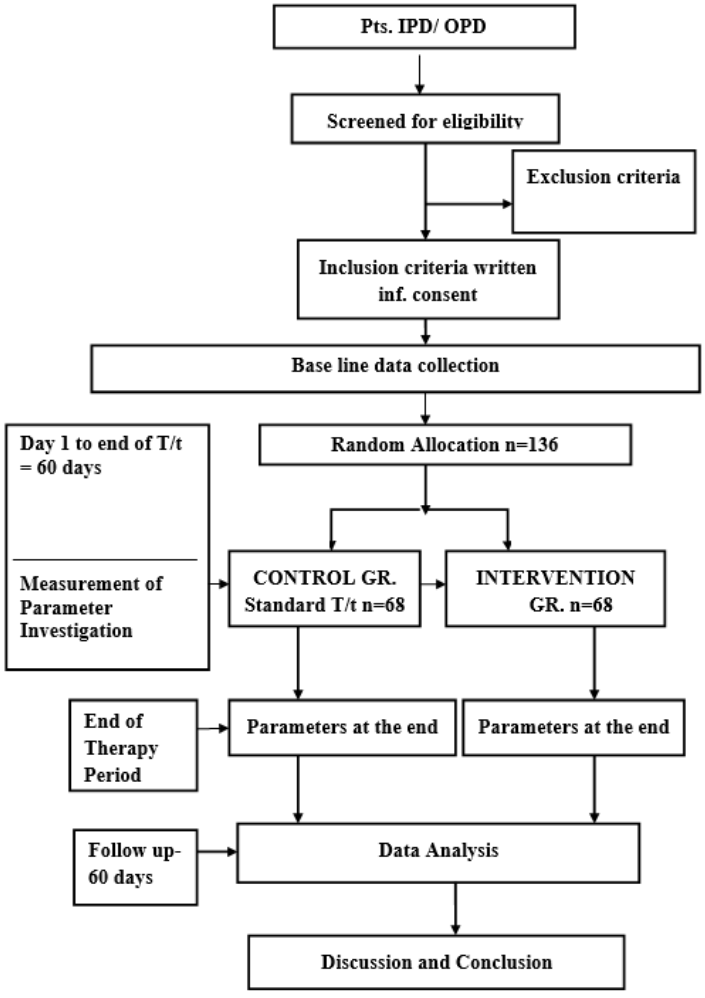
2. To evaluate and compare the effects of Chitraka Haritaki Avaleha and Chyavanprash Avaleha in reduction of the episodes of recurrent upper respiratory tract illness in Children.

1.5] **Hypothesis**

Generated Hypothesis - Chitraka haritaki avaleha is likely to prevent the Recurrent Upper Respiratory System illness in children.

3. METHODOLOGY:

Consort flow diagram



Study setting: Paediatric patients of recurrent respiratory conditions will be selected from OPD of Datta Meghe Ayurvedic Medical College Hospital and Research Centre Nagpur, and Mahatma Gandhi Ayurvedic College Hospital and Research Centre salod ,Wardha. Maharastra

Null Hypothesis

Chitraka haritaki avaleha does not prevent Recurrent Upper Respiratory System illness in children.

Trial design: Open-label randomized controlled clinical trial. Parallel group, Interventional study.

Eligibility criteria:

Inclusion Criteria:

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Children of age 2 to 6 years of either sex; The Child with upper respiratory illness- Common cold, Sinusitis, Pharyngitis, Upper Airway disease.; The Child having the atopic respiratory condition; The Child fulfilling the diagnostic criteria will be included in study.

Exclusion criteria:

The Child with acute respiratory conditions; as it needs emergency management like Oxygen supplementation; The child with congenital malformation; The child with lower respiratory illness; The child of congenital heart disease. Children with any life-threatening condition will be excluded from the study.

Intervention

Table-1 Intervention and grouping

Sr.no	Features	Group A Experimental group	Group B control Group
1	No. of Patients	68	68
2	Drugs	Chitraka haritaki avaleha	Chyavanprash avaleha
3	Dose	As per age	As per age
4	Timing	twice in a day	twice in a day
5	Duration	60 days	60 day
6	Route	Oral	Oral
7	*Anupana*	Water	Water
8	Follow up-	During Treatment: 0^{th}, $5^{th,}$ 15^{th}, 30^{th}, 45^{th} Day. 60^{th}, 90^{th}, 120^{th} day After treatment period	During Treatment: 0^{th}, $5^{th,}$ 15^{th}, 30^{th}, 45^{th} Day. 60^{th}, 90^{th}, 120^{th} day After treatment period

Withdrawal criteria:

- Develops any allergic reaction or any unpleasant symptom will be withdraw from the study
- If the patient refuses or denies to take medicine in between treatment course
- Patient /parent do not give written consent, in these conditions patient will be withdrawn from the study.

Concomitant care:

All the paediatric patients enrolled in the study will be directed to follow dietary restrictions as per history found in that particular patient. Apart from this patients will be restrained from taking other medicines. Cold drinks or fridge food, soured food will restrict to eat. Advice to prefer fresh food and avoid pack food for the child.

Outcomes:

Primary outcomes:

- **Preventive effects-** prevention of the recurrence of upper respiratory tract infections.
- **Immunological effects-** Promote host defence by enhancing immunity so that prevent recurrence of upper respiratory illness.
- **Weight gain-** Trial drug have Agni dipana(increase digestive fire) property, by increasing appetite weight gain will be achieved.

Secondary outcomes:

- **Quality of life**[13]**- (**will be assessed according to Ayurvedic protocol**)** Trial **drug** have a Rasanana (rejuvenation) property and by enhancing immunity that will be stave of illness and restore

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the health of the child and will be improve quality of life.

Intervention Period: 60 days.
Follow up Period: – 120 days. (3 follow up)
Sample size- Sample size is estimated on effectiveness of chitraka haritaki avaleha on recurrent upper respiratory conditions in children with following assumptions
1. % effective in standard treatment = 67.8% [14]
2. % effective in new/ trial drug = 85%
3. Observed/ Expected difference in proportion 17%
4. Superiority margin = 0.05 (5%)
5. Power (1-β) % =80

required sample size in each group is **68**.

Formula

$$\frac{(Z_{1-\alpha} + Z_{1-\beta})^2 \left[\pi_S (1-\pi)_S + \delta (1-\pi)_T \right]}{(\pi_T - \pi_S - \delta)^2}$$

Where,
π_T : Proportion in test treatment
δ : Superiority limit
π_S : Proportion in standard treatment
$\pi_T - \pi_S$: Expected difference in proportion
α : Significance level
1-β : Power

Sampling Procedure: – Allocation of the patients in two different groups will be done by random sampling using Computer generated random table. (Allocation ratio:- 1:1).

Data collection tools and process:

Diagnosis

Diagnosis of Recurrent respiratory illness will be done based on clinical symptoms.

For the diagnosis of Recurent Respiratory illness in children, at least one of the following criteria has to be Present:

1. ≥ 6 respiratory infections per year[15]
2. ≥ 1 upper airway infection per month. [16].

Patients having complained of common cold, cold with fever, cold without fever, cough, sore throat, running nose, recurrent respiratory illness and will be diagnosed based on clinical symptoms and history.

Statistical analysis - collected data will be entered in to excel spreadsheet. Continuous variables (objective parameters) will be presented as mean ± SD. Categorical variables (subjective parameters) will be expressed in frequency and percentages. An Independent t-test will be used to compare objective parameters. The subjective parameter will be compared before and after treatment by Wilcoxon sign rank test % of the effectiveness of therapy after drug between 2 graphs by performing Man –Whitney test.

ASSESSMENT CRITERIA:

Subjective parameters

Table- 2. Subjective Parameters [17, 18]

Parameter	1	2	3	4
1. Kasa (cough)	Coughing	Persistent cough, relieving with expectoration	Persistent cough, occasional repetition with expectoration	Persistent cough with fainting(darkness)
2. Shabda shwasa(wheezing)	Normal breathing	Localized wheezing	Wheezing at entire lung	Audible without stethoscope

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	sounds heard			
3. Running nose	Absent / dry	Wet nose	Intermittently running nose	Running nose
4. Throat congestion	No congestion	Mild congestion	Moderate congestion	Swelling, redness with pain
5. Swasa vega(breathing)	Normal breathing/ talk normally	Mild increase in resperation rate	Talk in words	Cant talk, severe
6. Cervical lymphadenopathy	Lymph node normal	Palpable at one side	Pain during day time, palpable at both sides	Continuous pain with large lymph nodes

7. **Weight** – will be taken with the help of weighing machine.

8. **Appetite** (As per Simplified Nutritional Appetite Questionnaire – SNAQ)[19]

9. No. of episodes of respiratory illness:

10. Nature of episode and persistent duration.

Objective Parameter:

1. Complete Blood Count

2. Serum IgE

3 Serum IgG

4. Absolute Eosinophills Count.

Ethical clearance: clearance from the institutional ethical committee of DMIMS, Sawangi Wardha is taken.

Consent: Well informed written consent will be taken from parents before enrolled the patient (child) for the study. Parents will be informed / explained about nature, purpose, duration of study & what they will be expected to do. They will be completely informed about the probable consequences and risks.

Confidentiality: Personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality, before, during, and after the trial.

EXPECTED OUTCOMES / RESULTS:

- **Preventive effects-** prevention of the recurrence of upper respiratory tract infections.
- **Immunological effects-** Promote host defence by enhancing immunity so that prevent recurrence of upper respiratory illness.
- **Weight gain-** Trial drug have Agni dipana(increase digestive fire) property, by increasing appetite weight gain will be achieved.
- **Quality of life-(assessed as per Ayurveda parameters)** Trial **drug** have a Rasayana (rejuvenation) property and by enhancing immunity that will be stave of illness and restore the health of the child and will be improve quality of life of the child.
- **Statistical Analysis:** collected data will be entered in to excel spreadsheet. Continuous variables (objective parameters) will be presented as mean ± SD. Categorical variables (subjective parameters) will be expressed in frequency and percentages. An Independent t-test will be used to compare objective parameters. The subjective parameter will be compared before and after treatment by Wilcoxon sign rank test % of the effectiveness of therapy after drug between 2 graphs by performing Man –Whitney test.

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- Group A participants (Experimental group) will be given Chitraka Haritaki Avaleha orally in the dosage as per age, with water as anupana for 60 days. Group B participants (Controlled group) will be given Chyavanprash Avaleha orally in the dosage as per age, with water as anupana for 60 days.

- **Implementation**
- The principal investigator will be enrolled and allocate to the participants. The data entry coding will be done by the principal investigator.
- **Consent or Assent**
- The written informed consent will be obtained from the participants before starting the study. The confidentiality of each participant will be maintained.
- **Dissemination Policy**
- The data will be disseminated by paper publication, authorship elidibility guidelines, and any intended use of professional writer.
- **Informed Consent Materials**
- The model consent form and other related documentations will be given to participants and authorised surrogates with all the information.

4. Conclusions

Preventive focus in Recurrent Upper Respiratory Illness in children will help to restore the health of the children and improve the quality of life. Children with impaired immune responses may benefit from chitraka haritaki avaleha. There is need to gain more data insights in Indian children from larger studies.

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