

NEBULIZATION THERAPY - A NOVEL APPROACH TO DRUG DELIVERY SYSTEM IN AYURVEDA

Kajaria Divya Kumari*, Tripathi J.S., Tiwari S.K.

Faculty of Ayurveda, Department of Kayachikitsa, IMS, BHU, Varanasi, India

Article Received on: 12/08/11 Revised on: 25/10/11 Approved for publication: 14/11/11

*Dr. Divya Kumari Kajaria, Ph.D Scholar & Senior resident, Faculty of Ayurveda, Department of Kayachikitsa, Institute of Medical Sciences, B.H.U., Varanasi- 221005

ABSTRACT

Several route of administration of drug have not only been described in Ayurvedic texts but also practiced for several millennia. Depending upon physical property of the drug it can be rubbed on the skin like lotion or it can be instilled in the form of drops like nasal (nasya)/ ear (karnapurana) drop etc. It can be swallowed in the form of tablets and also it can be injected directly into the bloodstream. Similarly the medicines can also be administered through nasal route using nebulization technique or through meter dose inhalation.

The process of Nebulization involves a suspension of fine vaporized liquid droplets--otherwise known as aerosol--to administer fluids, oxygen and liquid medication directly to the respiratory system. Nebulizers are commonly used for treatment of cystic fibrosis, asthma, COPD and other respiratory diseases. Breakthroughs in the treatment of Asthma came in light with the introduction of Inhalation therapy (Nebulization / Aerosol mode of drug administration) in the conventional medicine. There are several plus points for through-the-lung delivery of medication. The lungs have a large surface area, so that absorption is fast and ample. Lungs are quite tolerant to foreign substances like powders of tobacco, smoke, and fragrances of a hundred types by common men. Lungs are much more permeable than skin, nasal mucosa or the gastro-intestinal tract. This mode of administration proves to be highly beneficial in saving life in acute life threatening condition such as "Status Asthmatics". But wide range of toxic side effects of modern medicine confines its use as permanent remedy. Administration of drug through nasal route is highly prevalent also in Ayurveda. Since ancient time Acharays very well knew the importance and effectiveness of this route as they had said that "Nasa hi Shirsodvaram". There are numerous variety of drugs mentioned in Ayurvedic text which can be administered through Nasal route, namely Nasya and Dhumrapana. There is no direct evidence that drug given through Nasya and Dhumrapana acts similar to that given through Nebulization technique. According to the demand of time Ayurvedic science also requires some modification to become more permissive and harmonize with ever-increasing diseases and their various presentations. Thus there is need to search Ayuurvedic formulations to be used for inhalation which are as effective as modern inhalation therapy and have least side effect and that can be useful in emergency condition. The clinical study was planned in two parts. The first part deals with preparation of drug, its standardization and antimicrobial study and second part deals with assessment of its efficacy in acute attack of Bronchial Asthma, and its comparison with the efficacy of modern medicine. The paper will discuss the method and material use for the preparation of Ayurvedic Nebulizer drug and its standardization.

Key Words: Inhalation Therapy, Nebulization, Bronchial Asthma, Hot percolation.

INTRODUCTION

In this era of globalization, rapid industrialization and urbanization has become endemic globally. The above trend leads to ever increasing air pollution which is contributing significantly for steady growth incidences of respiratory tract diseases like bronchial asthma. This etiological factor along with other factors including junk food habits and rampant habit of smoking in general population has helped in transformation of bronchial asthma as health menace. Worldwide asthma cases are increasing at the rate of 50% every decade and according to WHO by the year 2020, asthma along with COPD will become third leading cause of death. The social and economical burden associated with the increasing prevalence of asthma and related mortality makes it necessary to form a permanent strategy for the management of Asthma. Asthma is a reversible obstructive airway disease, but due to its chronic nature it causes permanent damage to the airways. Thus it is told that Asthma cannot be cured it can only be prevented. Asthma possesses great challenge to the medical world from the beginning and scientists have been continuously working to search an enduring solution of this life threatening disease.

Nebulization / Inhalation Therapy

Breakthroughs in the treatment of Asthma come in light with the introduction of Inhalation therapy (Nebulization / Aerosol mode of drug administration). There are several plus points for through-the-lung delivery of medication. The lungs have a large surface area, so that absorption is fast and ample. Lungs are quite tolerant to foreign substances - otherwise how can one take powders of tobacco, smoke, fragrances of a hundred types? Lungs are much more permeable than skin, nasal mucosa or the gastro-intestinal tract. And lungs have substances that inhibit the enzymatic breakdown of proteins, so that the through-lung delivery of proteins is more attractive than through the stomach. This has led to much research into the pulmonary delivery of protein drugs.

This mode of administration proves to be highly beneficial in saving life in acute life threatening condition such as "Status Asthmatics".

But wide range of toxic side effects of modern medicine confines its use as permanent remedy. Thus in order to search an Ayuurvedic formulation to be used for inhalation which is as effective as modern inhalation therapy and have least side effect. It is decided to make some Ayuurvedic formulation for inhalation and evaluate its effectiveness in this clinical condition.

Background Description

The Indians dried the tobacco leaves and chewed them. They rolled the dry leaves, lit them and inhaled or smoked them - calling this practice "Sik-ar" (hence cigar/cigarette). When Christopher Columbus landed on the American coast in 1492, he found that some Indians took in powdered tobacco leaves through the nose and enjoyed the effects. He or his fellow sailors tried it, found it mildly intoxicating and brought it back to Europe. And this was how practise of cigarette came in practise.

"The nose, according to Charaka, is the "gateway" to the head¹. The nasal route for the administration of drugs was widely used in Ayurveda for treating a variety of ailments.

Nasal administration of drugs was indeed one of the chief procedures under the Panchakarma therapy of Ayurveda. Charaka prescribed a number of herbal formulations as powder, paste, ointment and so on for nasal application. They were used as snuff, blown into the nose through a special pipe, rubbed in the cavity as a paste or ointment, or used in the form of medicated smoking through another special pipe. The underlying principle of nasal therapy or nasya was that the medication would pervade the head region through innumerable channels and clear them of disturbed dosha. So Inhalation therapy is not new to Ayurveda, as from very ancient time Ayuurvedists are using this route of drug administration in various diseases.

On the basis of clinical features, Bronchial Asthma is similar to Tamaka Shwasa.

The classical description for the use of Dhumrapana and Nasya in Tamaka Shwasa are as follows-

1. Ayurvedic Aerosols (Dhumrapana) In Bronchial Asthma

Acharya Charaka told that after Vamana if Dosha remain stick to Srotas then for proper elimination of Doshas Dhumrapana is required. Acharya suggests different medications for Dhumrapana as Haldi, Yava, Eranda, Manashila, Devadaru, Hartal, Jatamansi, Guggulu, Agar² etc. Manashiladidhuma Dhumrapana is also widely used in other respiratory tract disorders such as in Kasa (Cough) eg Manashiladidhuma³, Vartidhuma⁴, Mustadidhumavarti⁵ etc. Acharya Sushruta has also advised other drugs to be used for Inhalation therapy as- Manashilla, Devadaru, Haridra, Guggulu, Laksha, and Eranda⁶.

2. Nasal Medications (Nasya) In Bronchial Asthma

The use of Lahsuna (*Allium sativa*) swarasa and Grinjanaka swarasa (*Daucus carota*) and milk mixed with Candan (*Santalum album*) has been advocated in acute stages of Tamaka Shwasa⁷.

Inhalation through Nebulization can be correlated with Avapidaka Nasya in which Swarasa or Kalkaras are given through nostril. Aerosol can be correlated with Pradhan Nasya in which fine powder form of drug is snuff into nostril with the help of a pipe. In Avapidaka Nasya drug is administered in the form of solution (liquid) whereas in Pradhan Nasya drug is administered in the solid form. Now question arises if Inhalation Therapy is already given in Ayurveda what is need to introduce the drug with the help of nebulizer machine? The answer for this question hidden in the fact that if we use classical mode of administration then for every dose we have to arrange fresh extract of drug (as swarasa get deteriorated in 24 hour), which is very difficult in daily outdoor practise and also all drug are not available every time and everywhere. All these facts limit the use of drug in liquid form through Nasya. These limitations necessitate the development of effective Ayurvedic formulation for inhalation therapy, which can be administered through nebulisation.

Drug Selected For The Preparation Of Aerosol

The selected drugs were divided into two groups of three ingredients each. Group Ist contains- Bharangi (*Clerodendrum serratum*), Sati (*Hedychium spicatum*), Pushkarmoola (*Inula racemosa*), & Group IInd contains Shirisha (*Albizia lebeck*), Nagarmotha (*Cyprus rotundas*), Kantakari (*Solanum surratence*).

Scientific Background And Principle For Selection Of Drug

Sati, Bharangi & Pushkarmoola has been selected in the present study because of their action on Pranavaha Srotas. Avapidaka Nasya and Pradhan Nasya come under the heading of Sirovirechana Nasya according to Susruta. Whereas according to Acharya Charaka Avapidaka Nasya are of two type Sodhana & Stambhana. For Stambhan Nasya Acharya advocate use of Kashaya Skandha drugs⁸, Shirisha, Bharangi and Pushkarmoola belong to this group so their use in inhalation therapy is according to classical literature. Moreover Sati, Kantakari & Pushkarmoola are described in Shwasa & Hikkahara Mahakashaya⁹. Shirisha has also been described under the heading of Sirovirechana so it can also be used in Aerosol form¹⁰. Shirisha Swarasa Nasya is indicated in Sarpadarsta¹¹, Shirisha is said to be Vishaghnam¹², Shirishpushpadi yoga is indicated in Shwasa roga¹³. Kantakari is enormously used in the treatment of Shwasa roga and it is main ingredient of various Ayurvedic formulations such as Kankasava, Devadarvadi kwatha, Vasadi kwatha etc. Sati, Nagarmotha, & Pushkarmoola are main ingredient of Satyadi Churna¹⁴ and Satyadi Yoga¹⁵. Similarly Bharangi is the main ingredient of Vartidhuma¹⁶ i.e. for inhalation and musta is main ingredient of Mustadidhuma¹⁷.

Bharangi (*Clerodendrum serratum*)-Saponin and D-mannitol in Bharangi are found to have the **Antihistaminic** and **antiallergic** effect. Apigenin-7-glucoside (**flavonide**) was obtained as yellowish brown amorphous solid has demonstrated anti-inflammatory¹⁸,

antimicrobial¹⁹, hepatoprotective²⁰ and antidiarrheal properties²¹. The compound also showed significant protection against Alzheimer's disease in mice²².

Sati (*Hedychium spicatum*) -The crude ethanolic extract of rhizomes possesses antiinflammatory and analgesic activity. The antiinflammatory activity was mainly localized in the hexane fraction, from which 1% of pure active constituent hedychenone a terpene has been isolated. The analgesic activity was more prominent in the benzene fraction²³. The root stalk is useful in local inflammation, nausea, asthma, bronchitis and in pain. The rhizome of the plant is carminative, stimulant and tonic. Clinical study proved that rhizome of *Hedychium spicatum* has antiasthmatic effect. Clinical trial proves its efficacy in the treatment of Tropical pulmonary eosinophilia. After 4 weeks of treatment with the powder of *H. spicatum* in the dose of 6 gm b.i.d. there was 60.54% reduction found in the eosinophil count.

Pushkarmoola (*Inula racemosa*)- Preliminary studies with the ethanolic extract of roots of *Inula racemosa* exhibited antiallergic and antiasthmatic properties, the later being more pronounced. Specific studies for bronchodilator properties on isolated trachea were performed and found it a potent bronchodilator. The extract also protected guinea-pigs against various experimental asthma, plant pollen etc. It possessed antihistaminic as well as anti-5-HT activity, suggesting its use in bronchial asthma²⁴. Alcoholic root extract of *I. racemosa* found to exert anti-histaminic as well as antiserotogenic effect²⁵.

Shirisha (*Albizia lebeck*)- *Albizia lebeck* is found to have anti-inflammatory, analgesic, antihistaminic & mast cell stabilizing effect²⁶.

Mustaka (*Cyprus rotundus*)

Cyprus rotundus is also found to have Anti-Inflammatory, Anti-Pyretic and Analgesic activities along with antioxidant activity^{27,28,29}.

Kantakari (*Solanum xanthocarpum*)- Similarly *Solanum* is also found to have anti-inflammatory and anti asthmatic activities in clinical trials³⁰. The above mentioned facts favour the selection of drug for preparation of Ayurvedic Nebulization.

Preparation Of Nebulization Fluid

The following methods are employed for preparation of nebulization drug-

- ▶ Though classical Ayurvedic decoction preparation method.
- ▶ Through Soxhlet by hot percolation method.
- ▶ Extraction of volatile oil through steam distillation.

Decoction Method

50gms of raw Bharangyadi mixture was taken and 16 times of water was added and boiled on heater till one fourth remains. The extract was filtered and the remaining mixture was again mixed with 16 times of water and boiled to obtain one fourth of decoction. The procedure was repeated till the mixture was totally exhausted (i.e. till the color of mixture lost). The final extract (800ml) was then put in water bath to evaporated water content completely. Net volume of the drug after complete evaporation of water obtained was 22ml. According to Ayurveda principle of drug formation, 5% of alcohol i.e. 3ml of ethanol was added to final volume of drug.

Similarly the water extract of Shirishyadi mixture was obtained. Net volume of drug was 22ml to which 3ml of alcohol was added and stored.

Soxhlet Process Of Drug Extraction

The drug was made by continuous hot percolation process known as **Soxhlet process** in which small volume of hot menstrum was passed over the drug by the time, as gain and again to dissolve out the active constituents until the drug was exhausted. 100 gm of crude drug in fine powdered form was taken in extraction chamber of soxhlet and moistened with water & alcohol in the ratio of 2:1 for few hours until the drug was totally moistened. Thimble made of filter paper was then placed into the wider part of the extractor.

Thimble is used to prevent chocking of the lower part of the extractor by drug particles.

The vapors are allowed to pass through the side tube to the condenser where they are condensed and fall on to the packed drug through which it percolates and extract out the active constituents. As the volume of menstrum in the extractor increase, the level of the liquid in the siphon also increase till it reaches the maximum point from where it is siphoned out into the flask. On further heating, the menstrum vaporizes while the dissolved active constituents remain behind in the flask. The alternate filling and emptying of the body of the extractor goes on continuously till the drug is exhausted. Thus the same quantity of menstrum was made to percolate repeatedly, about 14 to 15 times through the drug and the active constituent were collected in the flask.

The extract carried out by this method was then dried to know the solid mass. Out of 100 gm of crude drug, 30 gm of dried solid extract was obtained. This extract was then dissolved in 2 liter of distilled water & 1 liter of absolute alcohol.

CONCLUSION

This paper has been prepared with an objective of presenting the broad based approach for the preparation of Ayurvedic Nebulization medication, where herbal drugs can be given in the form of Aerosol through Nebulization apparatus. An effort to manage acute asthma through herbal drugs mainly in conditions where respiratory distress leads to loss of consciousness and no other route of drug administration except Nasal and I.V. is available for drug delivery necessitates formulating drug in Aerosol form. It is also an approach to expand the knowledge of Ayurveda with the help of available modern techniques. Yet lot of work has to be done for standardization of drug, understanding its mode of action through pharmacodynamic and pharmacokinetic studies. Few of these scientific studies have already been done by the authors, results of which are yet to be interpreted. The details of all the studies will be presented before the scientific community after the completion of the above work.

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Fig. 1, Patient taking Ayurvedic Drug through Nebulizer



Fig.2, Soxhlet Appratus For Extraction



Fig.3, Distillation Process



Fig. 4,Centrifugation Process



Fig.5, Prepared Drug



Fig.6, Extract Of Drug