Research Article

www.ijrap.net (ISSN:2229–3566)

NEBULIZATION WITH HARIDRA ARKA VERSUS METERED DOSE INHALER IN ACUTE EXACERBATION OF BRONCHIAL ASTHMA: AN OPEN LABEL, NON-RANDOMIZED, NON-INFERIORITY TRIAL

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Received on: 21/01/20 Accepted on: 18/06/20

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DOI: 10.7897/2277-4343.110486

ABSTRACT

Intranasal drug delivery especially in respiratory diseases has solemnly increased over past years owing to the pollution, especially in bronchial asthma. Advancements in treatment of Asthma came into light with the introduction of Nebulization. So if Āyurveda drug formulations can be used by incorporating modern technologies to manage acute exacerbations, it will help asthmatics to minimize their sufferings. On this line a study was designed to study the efficacy of Nebulization with Haridrā Arka versus Metered dose inhaler in acute exacerbation of bronchial asthma. The objectives of this study were to find out efficacy of Nebulization with Haridrā Arka in acute exacerbation of Bronchial Asthma and to compare efficacy of Nebulization with Haridrā Arka against Metered Dose Inhaler in acute exacerbation of Bronchial Asthma. Thirty participants satisfying the diagnostic criteria of Bronchial asthma, selected from the OPD of Panchakarma were equally divided into two groups by convenience sampling. Group A was given Nebulization with Haridrā Arka and Group B participants - Metered dose inhaler (Salbutamol). Assessments were done before and after treatment with the help of subjective and objective pulmonary parameters. Statistical analysis was done using SPSS 16 and Instat graph pad 3.1. In Group A improvement was seen in intensity of wheeze, sputum production, FEV1/FVC% whereas in Group B better results were obtained in parameters like cough, FVC, PEFR per sec. Equal effectiveness seen on breathlessness, chest tightness, FEV1 values. Nebulization with Haridrā Arka can be safely and effectively administered in providing instantaneous relief in acute exacerbation of bronchial asthma, both in OPD and IPD based settings.

Keywords: Haridrā Arka, Metered dose inhaler, Nebulization, Āyurveda

INTRODUCTION

In this era, ever increasing pollution has paved the way for hike in respiratory disorders. If the present situation continues Asthma will holds the 3rd position among non-communicable diseases by 2025. India has an estimated 15-20 million asthmatics.[1]

Management of acute exacerbation of Bronchial asthma is a serious threat confronting Āyurveda practitioners, where inhalation therapy stands best against oral therapy, as former has drug delivery directly to target area.[2] This drug delivery method arrived under the name of inhalation therapy in case of respiratory diseases has its origins date back to the name of Dhumapana in Āyurveda where fumes of drugs are inhaled for specific duration and with multiple frequency based on disease severity.[3]

Major revolution occurred in the treatment of Asthma after the introduction of inhalation therapy – Nebulization.[4,5] In Āyurveda proper Nebulization therapy has been not explained but the process of Dhumapana, Dhūpana and Nasya may be comparable in some extent. Nebulization uses liquid formulations for inhalation. Though clinicians have started using various liquid formulations, especially Arka Kalpana as nebulizer solutions, their actions on subjective and objective parameters of Bronchial asthma remain least explored.[6] These practices have not come to limelight of a hospital based setting and there is least knowledge of formulations which could be utilized in acute exacerbation.

Hence the study entitled as Nebulization with Haridrā Arka versus Metered Dose Inhaler in acute exacerbation of Bronchial Asthma – an open label, non-randomized, non-inferiority trial, was planned. Haridrā has got reference of usage in form of Arka Kalpana and is widely practiced in clinical practice in form of Dhumavarti in Tamaka Shwasa. Metered dose inhaler was kept as the control group being the most widely used modality in acute exacerbation of bronchial asthma.

MATERIALS AND METHODS

Nebulization apparatus: Nebulising instrument, Mask, Cleansing materials; Spiro meter, Peak flow meter; Haridrā Arka, Metered dose Inhaler

Case record form, Informed consent;
GINA criteria (2014), EPR – 3 (2005), Event evaluation scale, Acute AQLQ

Institutional Ethics Committee (IEC) clearance was obtained prior to the study with an approval number IEC/Cl/16/15 dated 17/04/2015. Consent form was in Malayalam and prior consent was obtained from all the participants with name and signature. A case record form with the necessary details was made to record the case. The study drug Haridrā Arka was prepared from Research and Development department, Aryavaidyasala, Kottakkal as per the general rule of Arka preparation. During the time of Nebulization a pinch of Saindhava was added to Arka to prevent irritation during inhalation.

Participants satisfying the diagnostic criteria (Primary screening by GINA 2014 and secondary screening by EPR-3) of Bronchial asthma were selected from the OPD of Panchakarma, VPSV Ayurveda College Hospital and Kottakkal. The participants were divided into 2 groups. Group A was given Nebulization with Haridrā Arka 3-6 ml for a period of 10 minutes (trial drug).[7] In Group B participants were advised to take 2-10 puffs of Metered dose inhaler (Salbutamol – control drug).[8]

Study Design

Open label, non-randomised, non–inferiority trial

Sample Size

15 each (Total 30)

Sampling Technique

Convenience sampling

Setting

IPD and OPD of VPSV Ayurveda College, Kottakkal

Study Duration

18 Months

Inclusion Criteria

- Patients with mild to moderate exacerbations of Bronchial asthma as per guidelines.
- Sex: No discrimination
- Age: 20 - 60 years
- Participants who have given informed consent.

Exclusion Criteria

- Known C/o Cardiac involvement, TB, emphysema.
- H/o Sensitivity to Haridrā.
- Uncontrolled Hypertension, Diabetes mellitus.
- Pregnant and lactating women.
- Upper respiratory tract infection, nasal polyps, nasal blockage.
- Any condition which the guide thinks may jeopardize the study

Assessment Criteria

Assessment was done before and after Nebulization and Inhalation with the help of subjective and objective parameters. All the vitals were checked before and after the treatment.

Subjective

Assessment of symptoms (by scoring) - Breathlessness, Cough, Wheeze, Chest tightness, Sputum production and Respiratory rate

Objective

Lung function tests–Spiro meter and Peak flow meter – FVC, FEV1, FEV1/FVC %, PEFR per sec

Statistical analysis

The tools used are excel sheet, SPSS software version 16 and Instat graph pad 3.1 version and the tests used were Paired t test, Man Whitney U test, Odds ratio

RESULT

Effects of therapy on subjective and objective parameters were studied and results obtained are as follows.

In Group A improvement was seen in intensity of wheeze, sputum production, FEV1/FVC% whereas in Group B better results were obtained in parameters like cough, FVC, PEFR per sec. Equal effectiveness seen on breathlessness, chest tightness, FEV1 values.

Breathlessness

In both the groups, all the participants complain of breathlessness before treatment which indicates that groups were comparable. After treatment, all the participants reported that breathlessness was relieved in both the groups which imply there was no difference between two groups.

Chest tightness

In both the groups, all the participants complain of chest tightness before treatment which indicates that groups were comparable. After treatment, all the participants reported that chest tightness was relieved in both the groups which imply there was no difference between two groups.

All other subjective parameters, namely Cough, Wheeze, Sputum production, Respiratory rate and objective parameters Forced Vital Capacity (FVC), Forced expiratory volume in first sec (FEV1), FEV1/FVC %, PEFR (Peak expiratory) per sec were subjected to statistical analysis and results are given in the tables (Annexure 1)

DISCUSSION

The trial drug Haridrā is mentioned under Śirovirechana by Acharya Charaka[9] and Kaphasamśamana varga by Acharya Sushruta[10]. It is having Tikta Ḳatu rasa, Uṣṇa Vīrya and Kapha Vatahara property. In Tamaka Śvāsa there is Avarana of Vāta by Kapha where Haridrā could act with its Guṇa and Vīrya. These properties helped in clearing the channels, there by relieving the obstruction in bronchioles and facilitating easy expectoration of sputum leading to Vāta Anulomana.

Subjective parameters

Breathlessness and Chest tightness

Nebulization helped in removing the obstruction to the passages of Prānavāyu and facilitating the Avyāhatagati of Vāta and to remove the Avarana caused by Kapha to the Cala Guṇa of Vāta. In metered dose inhaler, bronchodilator action and muscle relaxant activity reduced breathlessness and chest tightness.

Wheeze

Ghurghura Śabda is produced when there is no free movement of Vāta. There is narrowing of Prānavaha Srotas due to Sanga. Sanga is caused due to Kapha Avarana. In bronchial asthma, narrowing of bronchioles occurs due to secretion of mucus from the glands situated on the walls of bronchioles. The mucolytic action of Haridrā Arka helped in Kapha vilayana thereby reducing the intensity of wheeze, whereas bronchodilator action of metered dose inhalers helped in reduction in intensity.

Cough and Sputum production

Diminution of cough is possible only when there occurs liquefaction and expectoration of sputum. Both the treatments helped in liquefaction of sputum, thereby causing a reduction in cough. Thus, Kapha Cheda occurred and Srotas became clear.

The ingredients of Haridrā Arka are mucolytic in nature which helped in Kapha vilayana and Srotośodhana. Here Saindhava is used along with Haridrā Arka. Studies have shown that hypertonic saline is mucolytic in nature and it is mainly used in bronchial asthma for sputum induction. In case of metered dose inhaler, by bronchodilator action, airways open allowing free movement of mucus and facilitating easy expectoration.

Respiratory rate

In both groups, respiratory rate was compared before and after treatment and both were statistically insignificant. Here mild to moderate exacerbations is only taken which may be the probable reason for insignificant results.

Objective parameters

Pulmonary function shows slight increase which is due to easiness of respiration. Respiration in ease occurs when there is a decrease in obstruction to airways. The expectoration of sputum and reduction in cough may have facilitated this in both the groups.

The trial drug Haridrā Arka was given as per the dosage of Nebulizer solution and in control group the participants were allowed to inhale their regular dose (puffs) of inhaler. The dosages were sufficient enough to bring about desired effect in both groups. As they are of different forms and quantities, they may act as confounding factor which contributes to one of the limitations of the study.

Table 1: Effect of therapy on cough

		Mean	SD	Percentage of relief	P value
Trial	BT	0.93	0.26		P < 0.01
	AT	0.40	0.50	57.14%	
Control	BT	0.80	0.41		P < 0.01
	AT	0.27	0.45	66.67%	
After Treatment	Trial	0.53	0.512		P > 0.05
	Control	0.53	0.52		

BT: Before treatment; AT: After treatment
P < 0.01: indicates strong evidence against null hypothesis, as there is less than 1% by chance; P > 0.05: no difference between two groups

Table 2: Effect of therapy on intensity of wheeze

		Mean	SD	Percentage of relief	P value
Trial	BT	0.67	0.49		P < 0.05
	AT	0.27	0.46	59%	
Control	BT	0.80	0.41		P < 0.05
	AT	0.40	0.50	50%	
After Treatment	Trial	0.40	0.51		P > 0.05
	Control	0.40	0.51		

BT: Before treatment; AT: After treatment
P < 0.05: indicates strong evidence against null hypothesis, as there is less than 5% by chance; P > 0.05: no difference between two groups

Table 3: Effect of therapy on sputum production

		Mean	SD	Percentage of relief	P value
Trial	BT	0.13	0.35		P < 0.01
	AT	0.67	0.49	40%	
Control	BT	0.13	0.35		P < 0.05
	AT	0.53	0.51	30%	
After treatment	Trial	-0.53	0.52		P > 0.05
	Control	-0.40	0.51		

BT: Before treatment; AT: After treatment
P < 0.01: indicates strong evidence against null hypothesis, as there is less than 1% by chance; P < 0.05: indicates strong evidence against null hypothesis, as there is less than 5% by chance; P > 0.05: no difference between two groups

Table 4: Effect of therapy on respiratory rate

		Mean	SD	P value
Trial	BT	20.13	2.20	P > 0.05
	AT	19.73	1.67	
Control	BT	21.20	2.80	P > 0.05
	AT	20.13	2.20	
After Treatment	Trial	0.4	1.88	P > 0.05
	Control	1.06	1.83	

BT: Before treatment; AT: After treatment
P > 0.05: no difference

Table 5: Effect of therapy on pulmonary function tests

Pulmonary tests			Mean	SD	P value
Forced Vital Capacity (FVC)	Trial	BT	2.03	0.74	P < 0.001
		AT	2.24	0.72	
	Control	BT	2.45	0.85	P < 0.001
		AT	2.72	0.85	
	After Treatment	Trial	-0.21	0.12	P > 0.05
		Control	-0.27	0.12	
Forced expiratory volume in first sec	Trial	BT	1.44	0.61	P < 0.001
		AT	1.70	0.60	
	Control	BT	1.73	0.66	P < 0.001
		AT	2.03	0.64	
	After Treatment	Trial	-0.25	0.11	P > 0.05
		Control	-0.30	0.13	
FEV1/FVC%	Trial	BT	70.4	5.15	P < 0.001
		AT	75.27	4.85	
	Control	BT	70.07	6.14	P < 0.001
		AT	74.13	5.15	
	After Treatment	Trial	-4.87	4.07	P > 0.05
		Control	-4.07	3.56	
Peak expiratory flow per sec	Trial	BT	3.65	1.24	P < 0.001
		AT	4.15	1.37	
	Control	BT	3.72	1.40	P < 0.001
		AT	4.25	1.65	
	After Treatment	Trial	-0.49	0.26	P > 0.05
		Control	-0.52	0.31	

BT: Before treatment; AT: After treatment
P < 0.01: indicates strong evidence against null hypothesis; P > 0.05: no difference

When a drug is given orally it may take at least 20-30 minutes to act while a medicine given through inhalation acts in 2-3 minutes thus relieving acute exacerbation. There is no need to cross the first pass metabolism. Asthma drugs are preferably inhaled, because this route minimizes systemic absorption and thus, improves the ratio of the therapeutic benefit to the potential side-effects. Here Haridrā Arka did not report any adverse reactions when used in the form of Nebulization.

CONCLUSION

Nebulization with Haridrā Arka was found to be safe and effective in acute exacerbation of bronchial asthma. Even though there is no much difference found clinically and statistically, considering the key indicator of bronchial asthma vis breathlessness, participant compliance, safety aspect and cost effectiveness, null hypothesis is rejected and alternate hypothesis is accepted, i.e. Nebulization with Haridrā Arka is non inferior to Metered Dose Inhaler in providing instant relief in acute exacerbation of Bronchial Asthma.

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Cite this article as:

Anusree D.*et al*. Nebulization with Haridrā Arka versus metered dose inhaler in Acute exacerbation of Bronchial asthma: An Open Label, Non-Randomized, Non-Inferiority Trial. Int. J. Res. Ayurveda Pharm. 2020;11(4):40-44 http://dx.doi.org/10.7897/2277-4343.110486

Source of support: Nil, Conflict of interest: None Declared