# COST EFFECTIVE ANALYSIS OF DRY POWDERED INHALERS AND METERED DOSE INHALERS OF SALBUTAMOL FOR ASTHMA IN A SECONDARY CARE HOSPITAL OF SOUTH INDIA

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## ABSTRACT

**Objectives:** To estimate the cost effective treatment option between salbutamol dry powdered inhalers and metered dose inhalers. **Methodology:** It is a prospective comparative study conducted among subjects those who were newly diagnosed with asthma. The patients were divided into two groups, based on the type of inhaler used. Patients were counseled about the usage of both the inhalers during their first visit before they use. Data regarding the quality of life was collected by using mini asthma quality of life questionnaire and FEV 1 was measured by using peak flow meter. Medication adherence was also measured to decrease the bias. Direct costs like medical, lab and re-hospitalization costs were measured. Similar data was collected during their follow up. **Results:** Baseline characteristics were similar between two treatment groups and effectiveness was measured by using quality of life and FEV 1. After the treatment there is a significant difference in both QOL and FEV 1 between two different treatment groups. Average cost effectiveness ratio for metered dose inhalers was found to be less when compared to dry powdered inhalers. **Conclusion:** Both the inhaler devices are equal in terms of cost but effectiveness which was measured using QOL and FEV 1 gives an affirmative suggestion towards selecting metered dose in halers of salbutamol.

## Introduction:

Asthma is a chronic inflammatory disease of the air ways precise cause of which is incompletely understood. In susceptible individuals inflammatory symptoms are usually associated with widespread variable airflow obstruction and an increase in airways response to a variety of stimuli. Obstruction is usually reversible either spontaneously or with treatment.[1]

The estimated statistics as on 2019 states that, approximately 300 million individuals are currently suffering from Asthma worldwide including 10% (i.e. 30 million) in India.[2]The annual death due to asthma is estimated to be 250,000 and the majority of deaths occur in low and middle income countries.[3-6]Asthma accounts for 1.6% of ambulatory care visits (13.7 million physician office visits and 1.0 million hospital outpatient visits) and results in more than 497,000 hospitalizations and 1.8 million emergency department visits per year.[7] Aerosol delivery of drugs for asthma has an advantage of being site-specific and thus enhancing the therapeutic ratio.[8,9] Inhalation of shortacting β2-agonists provides more rapid bronchodilation than either parenteral or oral administration, as well as the greatest degree of protection against exercise induced bronchospasm and other challenges.[10]

Asthma is a chronic disorder requires continuous and long term management thus it makes the patient economically week and produces more burden on to patient. Emergency department visits also takes a major share in terms of economics burden to the patient. Economic burden includes direct and the indirect medical costs such loss of working days, loss of wages, loss of school days and loss of productivity secondary to asthma. The present study site is rural district of Andhra Pradesh (Anantapuramu), where socio economic status of common public is very low. Asthma patients from this resource limited settings are expected to suffer with lack of continuity in the management of Asthma due to low socio economic status. Cost effectiveness analysis identifies economically most efficient way to fulfill an objective of providing maximal therapeutic outcome with minimal cost. The present study aims to investigate and to select appropriate cost effective device to deliver salbutamol. Hence there are only fewer studies have documented the cost effectiveness various Salbutamol delivery devices. Among that most of the studies have reported in Indian urban settings.[11]

As India is a developing country financial burden among people is more and asthma is predominantly seems to affecttheeconomic status of the people by loss of wage of the patients, increase in emergency visits.[12, 13, 14] Our study concentrated on specifying the best cost effective drug to the patientsto improve the economic status of the patientsand decreasing other negative clinical outcomes.In this study we used to study two delivery devices of salbutamol having a potential cost difference. Selected patients are categorized in those two devices. Predicting the response can contribute to minimizing unnecessary drug exposure and health care costs to the patients. Drug response from the patient is done by using the following data such as hospitalization history and forced expiratory volume in one second (FEV1) values, these parameters have the most significant impact on the QOL of asthmatics.

## Aims and objectives:

**Aim:**To estimate the cost effective treatment option between salbutamol dry powdered inhaler and metered dose inhaler.

## Objectives:

- To assess the effectiveness of salbutamol dry powdered inhaler and metered dose inhaler.
- To assess the direct medical costs of the patients using salbutamol dry powder inhalers and metered dose inhaler.

## Methodology:

It is a prospective comparative study conducted at a secondary care referral hospital belongs to non-governmental organization situated in one of the resource limited settings in south India known as Anantapuramu, Andhra Pradesh.

A non-probabilistic convenient sampling was done to recruit study subjects. Both male and female adult subjects recently diagnosed with asthma and prescribed with salbutamol dry powdered or pressurized metered dose inhalers were included in the present study. Children, pregnant women, subjects with other respiratory disorders, and subjects who are exposed with anti-asthmatic medication for the past four months were excluded from the present investigation.

60 days of initial time period was taken to recruit the study subjects from outpatients of general medicine department. All the study subjects are clearly explained with study protocol and purpose to produce a written consent to participate in study. The recruited study subjects were divided into two groups such as salbutamol dry powdered inhaler and salbutamol metered dose inhaler based on their prescription (intention to treat analysis) and the doses were decided by the physician based on subject's requirement. Their prescriptions were filled and dispensed with an appropriate counselling and training about the proper usage of devices by the pharmacist.

After providing appropriate counselling and training, subjects were interviewed to estimate the quality of life by using mini asthma quality of life questionnaire. In addition to that forced expiratory volume in one second (FEV1) values are estimated thrice by using peak flow meter and best value was taken and considered for evaluation. Hospital patient records were also used to obtain the data such as cost of laboratory investigations, consultation fees and etc. Follow up was done for all the patients based on their physician visit. Patients were also reminded through phone for their follow up physician visit. During follow up once again variables like QOL and FEV1 were estimated.

To avoid bias due to medication adherence, medication adherence between both treatment groups, was measured using local medication adherence measuring scale which was validated by local experts. Medication adherence was measured every month up to whole study period.

Quality of life was measured by using a mini asthma quality of life questionnaire (MAQOL). It showed a good responsiveness, reliability and construct validity as that of WHO - 32 item asthma quality of life questionnaire (AQLQ). Cost of the treatment was measured in Indian rupees (INR). Direct medical costs like consultation costs, medical costs, laboratory costs and re-hospitalization costs were also included. Cost of treating adverse drug reaction (if there) was also included. After collection of both effectiveness parameters and costs in monetary units average cost effectiveness ratio also calculated. Statistical analyses were performed by using instat-3.4 version.

## Results:

A total of 106 subjects were recruited in to the present study,among that 54subjects were included in metered dose inhaler group and 52subjects were included in dry powdered inhaler group. Gender distribution between both the inhaler groups is nearly similar and the difference of proportion of gender distribution between two study groups shows no statistically significant difference at 95 % confidence interval (Fischer's exact test). The mean age of the present study population was found to be 55.19±12.93 years. There was no significant difference between two treatment device groups based on age distribution.

The baseline evaluation reveals that both the groups are found to have same kind of severity in terms of FEV1 volume measurement. We found no significant difference between two different device groups regards to FEV1 volume based on student't' test. (Mean ± SD is 243.75±32.10 for metered dose inhalers and 241.14 ±31.35 for dry powdered inhalers). Comparison of baseline scores of various domains of mini asthma quality of life questionnaire between two different treatment device groups was found to have no statistical difference. The 'p' value of individual domains such as symptomatic, environmental, emotional activity and physical activity were found to that there is no significant statistical difference. The overall quality of life score found to have no significant difference among different study groups as the data are shown in the Table 1.

Scores of various domains of mini asthma quality of life questionnaire between two different treatment device groups were compared after treatment.They were found to have a significant difference in all the domains. The overall quality of life score between both treatment device groups was found to have a significant difference (Mean ± SD is 70.91± 4.61 for metered dose inhaler group and 54.82 ± 4.61 for dry powdered inhaler group).Both the groups were found to have similar in terms of FEV 1 volume measurement with a little difference. We found there is significant difference between two different groups regards toFEV 1 value based on student t test(Mean ± SD is 278.98±14.80 for metered dose inhalers and 249.00 ± 26.50 for dry powdered inhalers).

Comparison of medication adherence between both treatment device groups were measured every month and found there is no significant difference. Over all medication adherence between both metered dose inhaler group and dry powdered inhaler group also found that there is no significant difference (Mean ± SD is 75.4±5.7 for metered dose inhalers and 75.00 ± 5.8 for dry powdered inhalers). (Described in table 5)

Table 3 shows that there is no significant difference between the costs of two different treatment device groups except laboratory costs. Direct medical costs such as cost for medication, laboratory costs and hospital re- admission costs were measured and the mean values were mentioned in the table. Total direct costs for both the treatment groups were compared and found to have no significant difference.

Average cost effectiveness ratio was measured to each effectiveness parameter and compared between both treatment device groups. The average cost per QOL for metered dose inhaler group and dry powdered inhaler group was 17.611 and 29.38 INR respectively. Average cost

per FEV 1 for metered dose inhaler group and dry powdered inhaler group was 4.47 and 6.46 INR respectively.

## Discussion:

Plenty of studies have published on the selection of various inhalation devices for delivering anti asthmatic drugs.[15, 17, 18, 20]Up to our knowledge this is the first study estimated the selection of cost effective treatment device among metered dose inhalers and dry powdered inhalers for delivering salbutamol to asthmatic patients in resource limited settings.

The present study results showed that before the initiation of treatment there was no differences in terms of demographic characteristics. It implies that the study populations in both the groups are similar in terms of demographic characteristics. In addition to that outcome variables such as quality of life and FEV1 values are also found to be similar in both groups.

These findings are similar to another study conducted among mild intermittent asthmatic patients, where they reported that, inhalation devices does not alter the dose of salbutamol, and clinical objective outcome (FEV1).[21, 22]  The efficacy of budesonide is depends on the inhalation device, and turbohalers are found to be more efficient than metered dose inhalers for delivering budesonide.[16, 17]

Required dose of terbutaline or budesonide were reduced to half of the actual dose for turbohaler when compared to metered dose inhalers to maintain same kind of clinical efficacy. Further it was found that salbutamol delivery in both the inhaler devices was found to have same kind of clinical and humanistic outcome.[19, 20]Whereas our study also found similar kind of results  in between two treatment device groups with regards to humanistic outcome (quality of life) and  clinical outcome (FEV1).

Salbutamol metered dose inhalers was found to be cost effective treatment option than dry powdered inhalers of salbutamol. Similar kind of results were observed in a study done at pediatric emergency department in a Canadian hospital that metered dose inhaler is cost effective treatment option than nebulizers and metered dose inhalers delivery system is expensive than nebulizer hospital admission costs are contributing as major portion making the nebulizers are very expensive.[15, 17, 18]

Direct medical costs were mentioned in the present study with physician's perspective after initiation of 6 months treatment for both treatment device groups. Medical costs were taken a major portion in total direct medical costs. Average medical costs, laboratory costs and hospital readmission costs per each patient using Salbutamol metered dose inhaler is less compared to dry powdered inhaler.

## Conclusion:

Over all this study reveals that both the salbutamol metered dose inhaler and dry powdered inhalers are equal in terms of cost.  But quality of life and FEV 1 in effectiveness measures showed a positive approach towards metered dose inhaler, to select an appropriate one among metered dose inhaler and dry powdered inhaler. Thus this study concluded that metered dose inhalers might be a better option than dry powdered inhalers.

Table 1: Base line characteristics:

| S.No | Parameter | Metered dose Inhaler (Mean ± SD) | Dry powdered Inhaler (Mean ± SD) |
|---|---|---|---|
| 1. | Male n (%) | 28 (51.85) | 28(53.84) |
| 2. | Age in years | 51.137±12.97 | 52.037±12.34 |
| 3. | FEV1 in millilitres/min | 243.75 ± 32.10 | 241.14 ± 31.35 |
| 4. | Quality of life domains:<br>• Symptomatic<br>• Environmental<br>• Emotional<br>• Activity<br>• Over all QOL | 44.84 ± 8.39<br>46.62 ± 6.29<br>52.81 ± 13.69<br>51.29 ± 14.61<br>48.65 ± 6.34 | 44.25 ± 8.91<br>46.65 ± 9.63<br>53.61 ± 14.22<br>51.26 ± 14.33<br>49.14 ± 6.14 |

*p value < 0.05 considered significant (student't' test)

Table 2: Efficacy outcome of two different treatment device groups:

| S.NO | Outcome variables | Metered dose Inhaler (Mean ± SD) | Dry powdered inhaler (Mean ±SD) |
|---|---|---|---|
| 1. | Quality of life domains<br>• Symptomatic*<br>• Environmental*<br>• Emotional*<br>• Activity*<br>• Over all QOL* | • 64.75 ± 9.09<br>• 70.85 ± 9.53<br>• 74.83 ±7.92<br>• 73.22 ± 8.45<br>• 70.91 ± 4.61 | • 49.71 ± 8.24<br>• 64.75 ± 9.09<br>• 58.90 ± 10.77<br>• 57.96 ± 11.23<br>• 54.82 ± 4.61 |
| 2. | FEV1* | 278.98 ± 14.80 | 249.00±26.50 |

*p value < 0.05 considered significant (student't' test)

Table 3: Direct cost of two different treatment groups:

| S.NO | Type of cost | Metered dose Inhaler (Mean ± SD) | Dry powdered inhaler (Mean ± SD) |
|---|---|---|---|
| 1 | Medical costs | 811.79±289.71 | 859.44±466.31 |
| 2 | Laboratory costs* | 91.20±117.41 | 175.92±18.97 |
| 3 | Hospital re admission costs | 299.06±907.15 | 518.11±1148.3 |
| 4 | Total cost | 1248.86±1289.9 | 1610.92±1745.7 |

*p value<0.05 considered significant (Student't' test)

Table 4: Average cost effectiveness ratio:

| S.NO | Parameter | Metered dose Inhaler | Dry powdered Inhaler |
|------|-----------|----------------------|----------------------|
| 1 | Cost per patient ( INR) | 1248.86 | 1610.92 |
| 2 | QOL per patient | 70.91 | 54.82 |
| 3 | FEV1 per patient ml/min | 278.98 | 249.00 |
| 4 | Average cost per QOL(INR) | 17.611 | 29.38 |
| 5 | Average cost per FEV1(INR) | 4.47 | 6.46 |

Table:5 Comparison of medication adherence between two groups

| S.NO | Month | Metered dose inhalers (MDI) | Dry powdered inhalers (DPI) |
|------|-------|------------------------------|------------------------------|
| 1 | 1st month | 75.5 ± 1.5 | 73.2 ± 1.5 |
| 2 | 2nd month | 73.3 ± 1.4 | 75.1 ± 1.5 |
| 3 | 3rd month | 75.9 ±1.4 | 75.9 ± 1.3 |
| 4 | 4th month | 75.7 ± 1.3 | 74.2 ± 1.4 |
| 5 | 5th month | 78.5 ± 1.2 | 72.8 ± 1.3 |
| 6 | 6th month | 73.8 ± 1.4 | 78.4 ± 2.9 |
| 7 | Overall | 75.4 ± 5.7 | 75.0 ± 5.8 |

*p value<0.05 considered significant (Student't' test)

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