

Patients' Compliance in Pulmonary Drug Delivery Systems in Mirpur

By

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A thesis submitted to the Department of Pharmacy in partial fulfillment of the
requirements for the degree of
Bachelor of Pharmacy

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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

The project titled “Patients’ Compliance in Pulmonary Drug Delivery Systems in Mirpur” submitted by Abdullah Al Faruqe (14346026) of Spring, 2020 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy on 2nd March, 2020.

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Ethics Statement

No harm to any animal was done on this survey. All the surveys were collected from individuals with their full consent and willingness.

Abstract

Patients' compliance in pulmonary drug delivery system is an important factor, which reflects the disease management and affects the overall therapeutic outcome of the medication. The objective of this study was to evaluate the patients' compliance in pulmonary drug delivery systems in Mirpur. This study was conducted with 150 patients in Mirpur who were suffering from pulmonary diseases and using inhalation dosage forms such as MDI, DPI or nebulizers as their medication. All the preferences were measured regardless of age, marital status or gender. It was found that the highest number of patients (34%) are using the MDI as their current inhalation device followed by DPI (30%) and nebulizer 6% respectively. Moreover, many patients were prescribed to use combination of different type of devices. Moreover, based on the ease of use and cost effectiveness patients prefer the MDI over any other type of inhalers.

Keywords: Patients compliance; Pulmonary Disease; COPD; MDI; DPI; Nebulizer.

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List of Acronyms

WHO World Health Organization

COPD Chronic Obstructive Pulmonary Disease

QOL Quality of life

MDI Metered Dose Inhaler

pMDI Pressurized Metered Dose Inhaler

DPI Dry Powder Inhaler

USA United States of America

UK United Kingdom

GENEBI AIPO Gruppo Educazionale for NEBulizers and Inhalers

Chapter 1

INTRODUCTION

1.1 Background

Patients' compliance on pulmonary drug delivery system has high influence on disease control. Asthma is preventable cause of morbidity but leading cause of mortality and economic burden which affect around 235 million people and COPD affects 65 million people worldwide. World Health Organization (WHO) estimated that chronic respiratory diseases represent 5% of total disease burden and 8.3% of chronic disease burden that estimates more than 4 million deaths per year. Chronic respiratory diseases can affect the ability and quality of life (QOL) in individuals. COPD is awaits to be the third leading cause of death within 2030 (Mäkelä, Backer, Hedegaard, & Larsson, 2013).

Pharmacological management of asthma and COPD (Chronic Obstructive Pulmonary Disease) mainly depends on inhaled therapy (Melani et al., 2011). Although the cost of those medication is considerable, it plays an important role in the prevalence of the condition. For asthma, cost varies but depending of the severity of the condition it might increase. An analysis shows that industrialized nations spends 1-2% of total healthcare expenditures on asthma. But there are very few information about the low and middle income countries (Mäkelä et al., 2013).

Pneumonia is another death-causing pulmonary disease which is a form of lung infection. Around 90% death occurs by this disease in the developing country like Bangladesh. Community. 52% mortality is caused in the children aged less than 5 years old. However, it has been shown that rural and urban areas have higher rate of pneumonia in

children (Naheed et al., 2009). Pneumonia treatment is mainly based on antibacterial medications. Those drugs are available in different dosage forms such as tablets, capsules, injections or solutions for nebulizers.

Patient compliance means the degree of following medical advice or instructions associated with the medical device, therapy sessions or exercises. In other words, patient compliance means the willingness or willingness to follow medical advice, following scheduled appointments, taking medications or to complete the advised courses. (Murphy & Coster, 1997). Non-compliance, on the other hand, means the irregularities to maintain physicians or professionals' advice of taking medications, performing instructions (Kardas, 2002).

There is more than one definition of adherence. Non-adherence can be divided into 2 categories. Primary Non-Adherence can be examples of failing the prescription, which leads to discontinuation of prescribed drugs. In addition, Secondary Non-Adherence can be example of underuse, overuse, forgetfulness, and alteration of doses and schedules. Another form of non-adherence can be the ineffective inhaler techniques. For example, patients may take 50% of the prescribed drugs, relying on fast acting drugs instead (more than 100% adherence) and attending the clinical visits regularly (100% adherence). So there is no universal definition of adherence. Moreover, definition of adherence can vary depending on the outcomes (such as hospitalization, exacerbation etc.) or the process involved (such as medications, number of exercise session attended etc.) (Bourbeau & Bartlett, 2008). There are differences between Patient Compliance and Adherence. Adherence is the active choice of the patient to follow the treatment and taking responsibilities for their own well-being.

Whereas, compliance is the passive behavior of the patient to follow the instructions that were given to them.

Non-adherence is a significant risk factor for high morbidity and mortality. Conservative estimates indicate that half of the prescribed drug has never been taken (Rand, 2005). It has been found that, therapeutic responses of a drug are directly linked to the patient compliance. Treatment failure may arise because of non-compliance. Although Non-compliance is not the only reason for treatment failure. Right choice of medication, proper dosage are some of the main factors for achieving proper treatment. In the cases of acute respiratory tract infections (symptoms includes fever, cough, malaise and aches), doctors unexpectedly found non-compliance among the patients even in acute infections which included the basic medications for specific diseases (Kardas, 2002).

Patient satisfaction and preference in specific devices has become known recent years because of potential positive outcome in long run. Inhaler device preference is now considered as an important factor as it can affect the outcome. Now a days patients expresses their preference to a particular type of device which is more convenient for them to use correctly. Patients who get to use their preferred inhalers are more likely to get more satisfaction in the treatment. Moreover, increased satisfaction with the device may even lead to more adherence, better outcome and less expenditures (Lavorini & Fontana, 2014).

1.2 Aim of the Study

As we have discussed before, patients' compliance in pulmonary drug delivery system is directly linked to the clinical outcome of the medications given to the patients. There are 3 major aim to this study:

1. With this study we want to find the best dosage form according to the patients' preference. By this we will be able to find out the most convenient inhalation device for any kind of patients and the efficacy of the devices they are using.
2. Secondly, we will try to find the most popular problems they face in their daily life of the device and the drug that can directly affect the compliance and adherence to the medications.
3. Last but not least, we will try to find the use of DPI (Dry Powder Inhaler) rate for pulmonary disease in Mirpur area.

1.3 Rationale

The reason to perform this study is to find if the patients are getting their preferable inhalation device(s). Because of the significant relationship between patient compliance and clinical outcome. Numerous studies that showed that if the patients are compliant to their medications, they are more likely to follow the instructions and adherence to the medications they were given in a period of time. As patients are more likely to use their own preferred devices for pulmonary dosage they are more likely to follow the guidance and that helps to get better therapeutic results. With this study we will find their compliance and will be able to find the relationship between the therapeutic effect and the compliance that is directly interlinked to each other. Moreover, this study will help to find the possible improvement of the devices they are using on regular or irregular basis.

Chapter 2 LITERATURE REVIEW

2.1 History

The delivery of therapeutic drug by inhalation has been used for around 4000 years. Around 2000BC in India people inhaled substances for therapeutic purpose (asthma and other lung diseases) in traditional therapies like Ayurveda. The substances they used were datura species which contained alkaloids having the property of bronchodilation. Ginger, pepper and datura roots were mixed and made into a paste then dried and smoked by a pipe which gave the therapeutic effects (Anderson, 2005).

Later on, in around 1554 BC therapeutic aerosol delivery reference was discovered between the legs of a mummy in the Assassif district of Egypt. The papyrus described that, patients who were struggling to breathe were supposed to inhale black henbane (*Hyoscyamus niger*). Black henbane was placed into hot bricks. After that, a jar with a hole was placed on the herbs and the patients inhaled the fumes with a reed.



Figure 1: schematic diagram of therapeutic aerosol delivery system described in the oldest known reference (1554 BC) (Stein & Thiel, 2017).

One of the earliest inhalation device was designed by Hippocrates which was consisted of a pot with a reed in lid. Moreover, Central and South American native culture used inhalation devices that were used to inhale tobacco and other plant materials. Ancient people use different types of inhaler devices and ingredients such as pepper, honey, scruples, bayberries etc. They also inhaled ingredients which contained anticholinergic properties i.e. datura, balsam, gum resins etc (Anderson, 2005).

Inhalers from middle Ages to Industrial Revolutions:

Therapeutic vapors and aerosols delivery were highly practiced before fifth century AD, which included datura, opium or burning herbs into the patients' lungs. In the seventh century Greek physician Paulus Aegineta enlisted the ingredients for cough treatment. This included a complex plant mixture onto coals then inhaled. The ingredient was describing as "To be inhaled for a continued cough: storax, pepper, mastic, Macedonian parsley, of each one ounce; sandarach, 6 scruples; 2 bayberries; mix with honey; and fumigate by throwing them upon coals so that the person affected with the cough may inhale the vapor through a funnel." (Stein & Thiel, 2017).

Arabian physician Rhazes, from Baghdad had proposed an innovative idea for pulmonary drug delivery system. Rhazes used sponges that were soaked in narcotic plant solutions and dried. Then the sponge was moistened before surgery and placed over the patients' nose and mouth which acted as anesthesia during surgery.

After that, Spanish physician named Maimonides designed a device which had the greatest influence on inhalation of therapeutic aerosol. Maimonides fled Spain and became the personal physician of the sultan of Egypt, Saladin and his asthmatic son. Maimonides

recommended many dietary instructions including chicken soup, inhaling herbs burnt on fire, abstaining from sex etc.

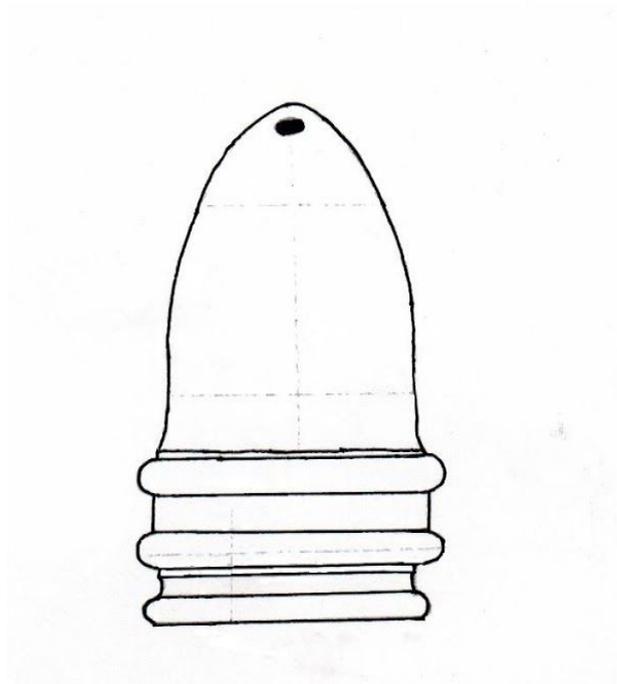


Figure 2 Oldest known illustration was done by Christopher Bennet in 1654 (Stein & Thiel, 2017)

The advancements of understanding asthma and drug delivery system was limited from Maimonides to industrial revolutions. In this time most contribution was from an Indian physician named Yogaratnakara who modified the datura smoking therapy for asthma. The oldest known illustration of inhalation device was done by an English physician named Christopher Bennet in 1654 (Stein & Thiel, 2017).

Early DPI Devices

Dr. John Mudge is considered as the first person who used the term “INHALER” in his book named *A Radical and Expeditious Cure for a Recent Catarrhus Cough* in 1778 which indicated the use of Opium to cure Cough. He described his invention based on pewter tankard in his book “A Radical and Expeditious Cure for a Recent Catarrhus Cough” in

1778. Many inhalers later followed this model in 18th century. One of the other famous designs was Nelson's inhaler which was later recognized for its cleanliness, portability and cheapness.

Inhalation of Datura for asthma was recorded by Dr. Sims who learned this technique from General Gent. General Gent adopted that practice for his own use when he was posted in Madras. But General Gent was the victim of his own therapy which caused his death. Toxic substances could be the cause of his untimely death.

Early Atomizers and Nebulizers

Atomizers (also called nebulizers) were developed in France in mid 1980s. Nebulizers was discovered by Dr Auphon Euget-Les Bain in 1849. The first portable nebulizer was invented by Jean Sales-Girons and won the silver price of Paris Academy of Science in 1858 for his invention. This mechanism included a pump that draw liquid from a reservoir and forced through against a plate. Therapeutically used liquids contained minerals, bicarbonate and arsenicals or even harmful ingredients such as petroleum and turpentine. Sales-Girons design was later improved by Bergsen of Berlin. Bergsen's design is the early example of Venturi system which influenced today's jet nebulizer.

Hand-Bulb Nebulizer and Early Electric and Compressor Nebulizers

Physicians used Adrenalin chloride solution as a bronchodilator which was nebulized through glass-bulb nebulizers in 1930s. Later plastic-bulb nebulizers were replaced in 1940s. In early 1930 pneumostat, a compressor nebulizer was manufactured in Germany. Pneumostats used rheostat as a power supply that allowed electrical voltage powering as a power supply.

Early MDIs, pMDIs and DPIs:

The first aerohaler was developed in 1948 by Abbot Laboratories to inhale Penicillin G powder. This contained 100000 units of penicillin powder which was inserted into the inhaler. The air intake caused a metal ball to strike the cartridge and shook the powder into the airstream. This was also applicable for nasal inhalation. The instruction was not to exhale back into the device.

In 1955, Dr. George Maisson stimulated the pressurized Meter Dose Inhalers (pMDIs). This revolutionary idea came from his asthmatic daughter who got her idea from perfume spray devices. Riker Labs researchers developed meter dose valve and with DuPont they manufactured propellant and produced alcohol based solution MDI. In 1956 Medihaler-Epi (Epinephrine). The first pMDI oral suspension for epinephrine and isoproterenol were produced in 1957. Although there were different types of inhalers such as Spinhaler (by Fisons, 1971), Rotahaler (by Glaxo, 1977) they were not successful in the market as a jet nebulizer (Anderson, 2005).

2.2 Mechanisms of different types of devices

2.2.1 Mechanism of MDIs:

A Metered Dose Inhalation device contains a canister which contains the drug, a metering valve and valve stem. When the valve stem is actuated, the device delivers the drug to the patient. The greatest disadvantage of MDI is it requires large force to compress the spring that helps to actuate the valve of the device. This problem is slightly overcome by the patient by compressing large spring with a sufficient force to release the drug. This spring is

compressed by patient which works by “positive clocking” or works automatically when the mouthpiece removed. (Simpson & Us, 2019) Although there are various types of MDI in modern technology. We will discuss about a typical MDI inhaler in this study.

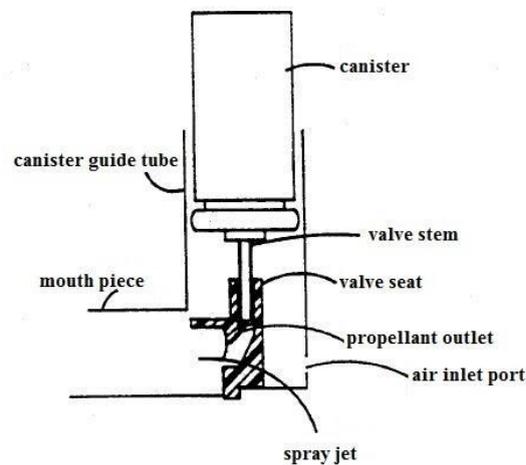


Figure 3A Typical MDI inhaler device. (Jan, 1943)

A typical MDI inhaler device consists of:

1. Canister
2. Valve stem
3. Valve seat
4. Propellant outlet
5. Air inlet port
6. Spray jet
7. Mouth piece

8. Canister guide tube

The canister contains the drug and the propellant which helps to deliver the drug. The canister is positioned in the device through the canister guide tube that helps the canister to keep it in place and helps in the actuation process. The mouth piece is the extension of the canister guide tube through which the drug goes into the mouth. Patients put the mouthpiece into the mouth and actuate the valve that delivers the drug into their body. The valve stem is placed on the valve seat that supports the stem. By pressuring the canister the device allows the propellant mixture to move through the propellant outlet and the spray jet in a precise manner. When the canister is released air enters through the inlet port into the device.

2.2.2 DPI (Dry Powder Inhaler):

DPI or Dry Powder Inhaler is an alternative to the MDI which does not contain propellant unlike MDI. DPI usually contains the drug or drug mixture that is directly inhaled by the patients from the device. Although this type of device has its own disadvantage such as patients who has poor capability to inhale the drug because it varies patients to patients. Moreover, patients who is undergoing asthmatic attack might find difficulties to inhale the drug.

There are 2 generalized types of DPI devices based on the design:

1. Single dose (pre-measured) use: such as single capsules containing the powder is inserted into the device.
2. Bulk powder reservoir: drug powder or powder mixtures are reserved into the device which delivers fixed amount of drug when inhaled.

The delivery of the drug of DPI solely depends on the inhalation of the patients. The device intends to deliver the drug in a physical form into the patient's airway system. That's why particle size is a very important factor in the DPI. When the drug is inhaled, drug particles are directly deposited on the desired site. But if the patient is unable to provide sufficient effort, drug particles might prematurely deposit on the throat or the mouth.

2.2.3 Challenges during developing DPI Devices:

There are number of challenges during developing a DPI. One problem can be the agglomeration of the powder within themselves due to the cohesion forces between the particles. There are certain types of drugs or powders that can cause agglomeration which affects the flow property of the drug. Reduces flow property can significantly affect the therapeutic effect by binding the drug or deposition of the drug at the wrong site when inhaled.

Moreover, there can be a significant amount of drug retention inside the device itself. When drug is retained into the device it may require thorough cleaning to avoid drug delivery problems in the long run (Groaning & Johnstoston, David A Gabel, 2007).

Thirdly, there are certain types of drugs that can retain moisture from the environment that might cause coagulation and can affect the drug delivery by blocking the outlet of the drug. This may result in poor delivery and the amount of the dose. Although there are certain types of devices that overcomes these problems by using de-agglomeration rod, rotating carrier disk etc.

2.2.4 Mechanism of DPI:

Different types of DPI devices are found in the market. A basic DPI device contains:

1. Mouthpiece
2. Cap
3. Actuator (typically buttons)
4. Reservoir / capsule holder

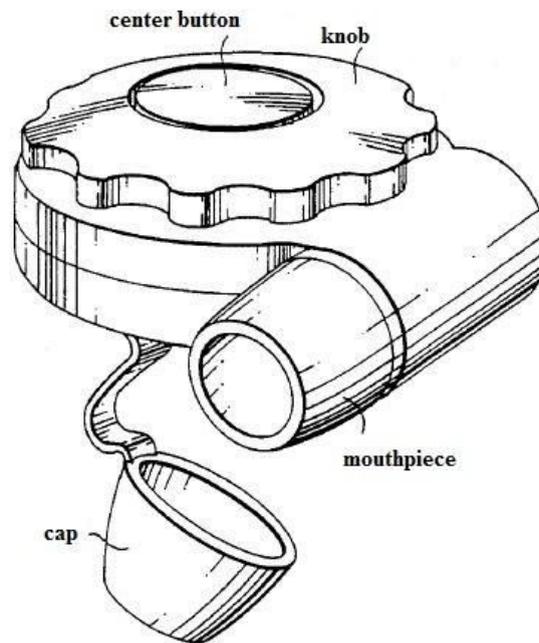


Figure 4 Dry Powder Inhaler Device. (Hosoda, Imai, Okatani, Nishio, & Takahashi, 1996)

Single dose DPIs are mainly based on the respiratory flow of the patients. This type of devices use single capsule containing the drug powder in which the capsule is pierced with a needle placed in the device. After perforation of the capsule patients inhales the drug powder from device. Single dose DPIs strictly rely on the inhalation of the patients to insure the efficacy of the device (Rogliani et al., 2017).

The Multi-dose/ bulk powder reservoir DPI has reservoir that contains the bulk powder. By pressing the button the device mechanically delivers specific amount of drug

powder through the mouthpiece. The generalized mechanism of DPI is much simpler than the pMDIs and nebulizers.

2.3 Factors that affect the therapeutic outcome during inhalation process

There are several factors that can severely affect the outcome of the medication. Factors might be related to the device related or the actual inhalation steps that are performed by the patients. As we have discussed previously, there are several studies that found that most of the patients who use MDI inhaler makes most mistakes in the process, followed by the DPI inhaler users and nebulizer inhaler respectively.

There are 8 main steps where patients makes mistakes as studies suggest:

1. Reading the dose indicator correctly to ensure the medication process
2. Loading the device correctly
3. Removing the cap/lid
4. Shaking the inhaler
5. Holding the device in horizontal or upright position (depending on the device)
6. Proper actuation and inhalation
7. Restriction of the air vents
8. Sealing the lips around the mouthpiece so that all the particles are inhaled properly.

(Mahon et al., 2017)

There could be other cautions that should be kept in mind:

1. holding the breath if needed
2. ensuring sealing of the spacer used along with the inhaler device

3. checking and cleaning the powder blockage (in case of dry powder inhaler)
4. timing of the breathing during the inhalation process
5. Cleaning the mouth after using inhaler as the particles might deposit between the teeth and gum.

2.3.1 Importance of Particle size associated in patient's compliance

Particle size is an important factor that can affect the efficacy of the drug delivery system. In vitro experiments and mathematical modeling shows that particle size influences the respiratory tract and lungs deposition when it is inhaled. Although in vitro, experiments cannot represent the in vivo experimental results. Studies have demonstrated that patients who have severe pulmonary obstruction prefers the particle size around 3 μ m.

When inhaled, drug particles are deposited into lungs by impaction, sedimentation and diffusion. If the drug particles are too big (>5 μ m) they get deposited into the walls and surface when it crosses the retropharynx due to its 90° angle bend. For this reason, majority of the particles cannot cross the retropharynx due to its size. If the particle size is smaller than 5 μ m it can cross the retropharynx and reach to the trachea. Particles having 2-5 μ m diameter are deposited in the upper respiratory tract (trachea and tracheal bifurcation). When it crosses this area, it can settle down due to the gravitational force of earth. For this reason breath holding is important to hold the breath if the particle size is too fine. If the particle size is less than 0.5 μ m, the sedimentation rate due to gravitational force gets slower due to Brownian motion. Hence, if the particles encounter the airway lining, they are deposited otherwise they are exhaled back into the outer environment (Rogliani et al., 2017).

2.4 Reasons of Non-Compliance in the Treatment of Pulmonary Disease

Studies have showed that children and elderly patients are more likely to non-compliance.

There are certain factors that affect the compliance in the treatment. The reasons could be:

1. Adverse effect
2. Increased or decreased pharmacological action
3. Financial situations such as high medication cost or low income
4. Social acceptance
5. Inconvenience to take the medication or carrying problem
6. Lack of awareness and knowledge

2.5 Available Studies on Patients Compliance in Pulmonary Drug Delivery Systems.

Few studies have been done specifically on patient compliance on pulmonary disease. Furthermore, very few studies has been conducted on patience compliance in Bangladesh specifically. However, there is no data found on patients' compliance in pulmonary drug delivery systems in Mirpur specifically.

One of the earliest study was done in 78 outpatients at a medical center in the south region of USA. This study showed that the patients were prescribed 6 different medications on average. 31% of them had poor pMDI technique and more than 50% reported under usage of the medication. The study's author did not mention the demographic variables with adherence. Moreover, patients did not report the overuse reports when they were experiencing respiratory distress.

In 2008, another study was carried out by the GENEBI in 24 chest clinics in Italy. 1664 patients aged more than 14 participated in the study who were diagnosed with asthma and COPD. According to the result, 1113 patients were using DPIs and 843 were using MDIs where most of them were diagnosed with COPD. 37% patients were using more than type of inhaler. (Melani et al., 2011)The data did not show any relationship between the compliance and inhaler mishandling while using the device. Moreover, this report did not include the patients who were under 14 years old. Although the report showed the relationship between the inhaler handling and the therapeutic outcome.

Another research has conducted with 679 healthcare professionals in Spain, Germany, France, Italy and UK in 2009 in which 2922 patient record form were submitted. Of those, 1718 patients returned a patient self-completed form and 1443 patients were included in the analysis. 275 patients were excluded as they were missing data. According to the result, 10% patients were very satisfied with the inhaler they were using and 1% patients were not satisfied at all. Moreover, one third of the patients were fully compliant and 1% patients were not compliant at all (Chrystyn et al., 2014). This data did not considered the patients below age 40. Thus, it did not reflect the age based compliance.

Another study was done with 300 patients from Lala Ram Sarup Institute of Tuberculosis and Respiratory Diseases, New Delhi, India who were aged 15-40 to measure the possible mistakes done by the patients while using the devices. Majority of the patients (82.3%) had at least one mistake. Only 17.7% patients were using the devices with no mistake. This study showed that maximum error occurred when patients were using MDI, which is around 94.3%. 82.3% patients made mistakes who were using DPI. 70% nebulizer users made mistakes when they are using their devices. Although this study suggested that proper education might reduce the errors rate but this study did not focus any device

modification that might help to reduce the errors and increase the compliance of the users. Moreover many studies showed that patients who gets to use their preferred devices are more likely to use correctly thus higher positive clinical outcome (Arora et al., 2014).

Chapter 3 METHODOLOGY

An observational study was conducted in known or diagnosed cases where patients with pulmonary diseases participated. Randomized patients were selected to participate in this study from different hospitals and clinics in Mirpur, Dhaka, Bangladesh. We conducted this research by direct interview to the patients who were diagnosed with any type of pulmonary disease. The patients were asked to participate in this study and consent form were given to each of them after they have agreed to participate in the study. Then the patients were asked relevant questions about their medication and the devices they are using in the treatment of the pulmonary disease.

3.1 Selection

A total 150 patients regardless of their age and gender participated in the survey who were using inhalation devices for their diseases. Patients before adolescent age were considered as not eligible in order to eliminate possible confusion and outcome due to lack of knowledge and information about their disease and the drug or the devices.

Patients who were eligible were then asked to review the consent form and were interviewed about their name, gender, age, disease, drug name, preferred inhalation device, side-effects/

adverse effects, frequency, preferred modification to the device, and acceptance of the device based on ease of use, efficacy and cost. This study was performed from December 2019 to February 2020.

3.2 Challenges

As Bangladesh is a developing country, there are many people who are not aware of different types of medications and devices available in the pulmonary diseases. The challenges we faced during this study are as follows:

1. There are many people do not know about different devices that are available in the market. For this reason, they might prefer only the current drug device they are using in the medication process. This problem was overcome by using physical demonstration of the devices to the patients.
2. Some people are unaware of their disease name due to lack of education on their disease. Thus, they only describes the symptoms of their disease even they are already in the medication process. Although almost all of the patients knew their drug name (brand name in most of the cases) or the prescription.
3. Some people might not differentiate between different types of devices (i.e. DPI inhaler, MDI inhaler or Nebulizers). Physical demonstration of different types of inhalation device helped to overcome this problem.
4. The participation to the survey was based on the willingness of the patients. As a result, number of people refused to participate in this survey.

Chapter 4 ANALYSIS

The analysis of the data was done by the Microsoft Excel (2013). The statistical relationships between different data were shown in pie chart where we can observe and analyze the compliance towards the medication and the device they are using. Moreover, we can observe the preference, difficulties and the modifications they prefer.

4.1 Results

From November 2019 to February 2020, 150 patients participated in the study where 52% (78) were male and 48% (72) were female who visited different hospitals, pharmacies and clinics in Mirpur, Dhaka, Bangladesh for their pulmonary disease. In addition, 88% patients diagnosed with pulmonary disease were adults (more than 18) and only 12% patients were below age 18. The data demonstrates that majority of the patients diagnosed with pulmonary disease were adults. Figure 5 and Figure 6 describes the gender ratio and the age variation among the patients.

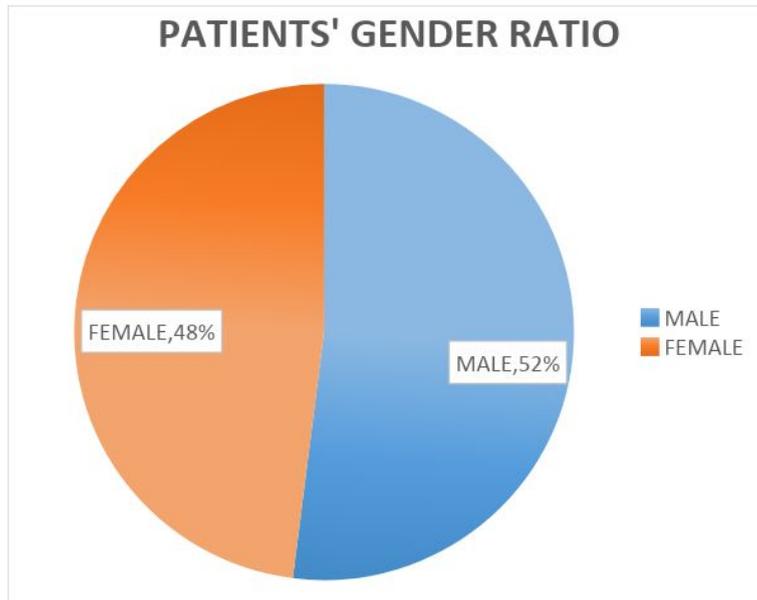


Figure 5 patients' gender ratio

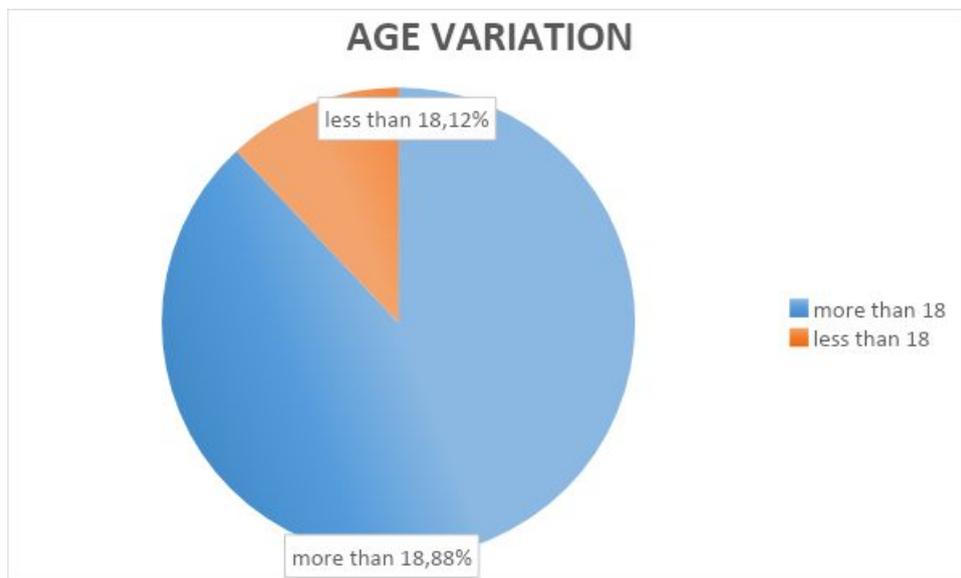


Figure 6 Age variation among the patients

All of the patients out of 150 were diagnosed with asthma or COPD. 63% (95 out of 150) of the patients were diagnosed with asthma and 37% (55 out of 150) were diagnosed with Chronic Obstructive Pulmonary Disease (COPD). Note that no patients were diagnosed associated with other pulmonary diseases in the given population. Figure 7 illustrates the diseases among the patients.

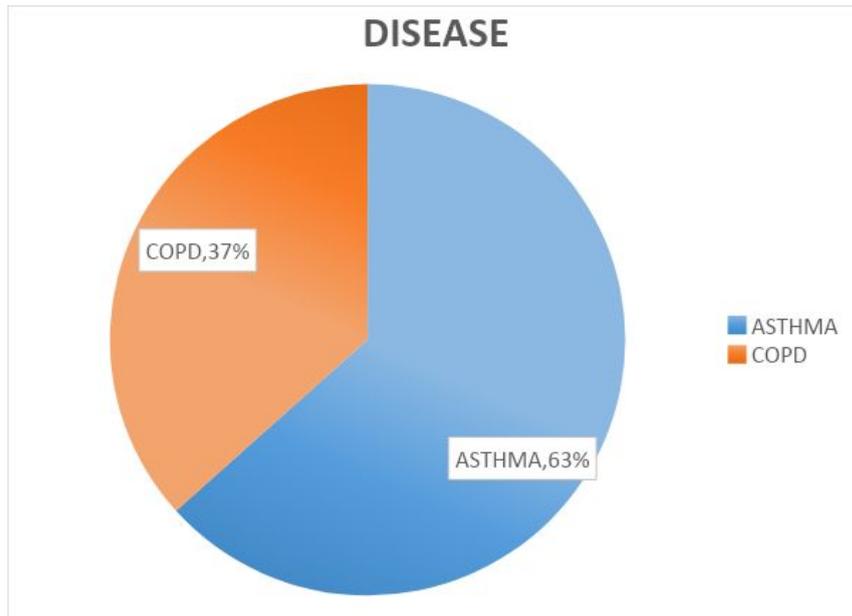


Figure 7 Illustration of diseases among the patients

This study shows that majority (59%) of the patients were using drugs for their pulmonary disease and 41% patients have never used any kind of pulmonary drugs. We categorized the timeline into three segments. It can be seen that 62% of the patients are using pulmonary drugs more than 12 months, 19% patients were using pulmonary drugs 6-12 months and 19% patients were using under 6 months.

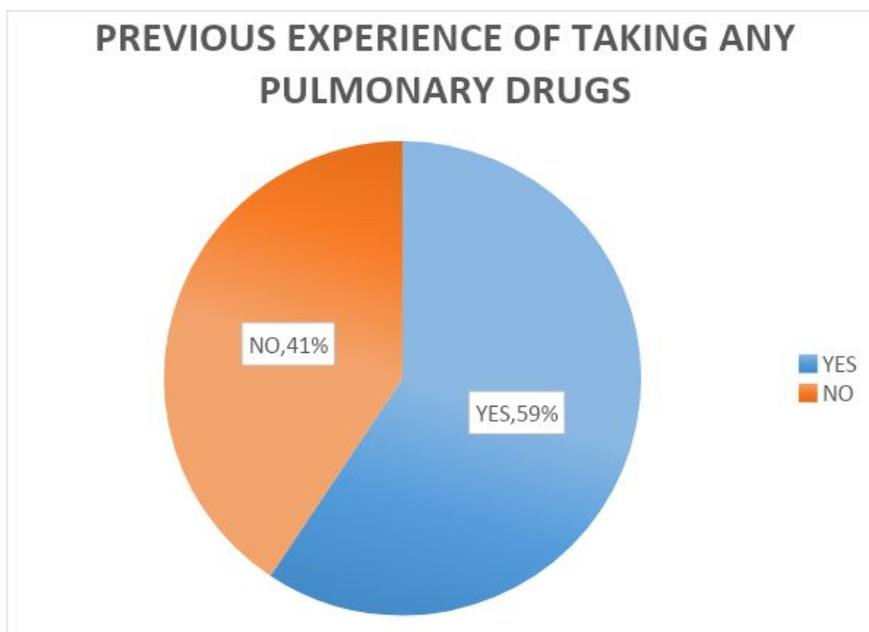


Figure 8 Previous experience of taking any pulmonary drug

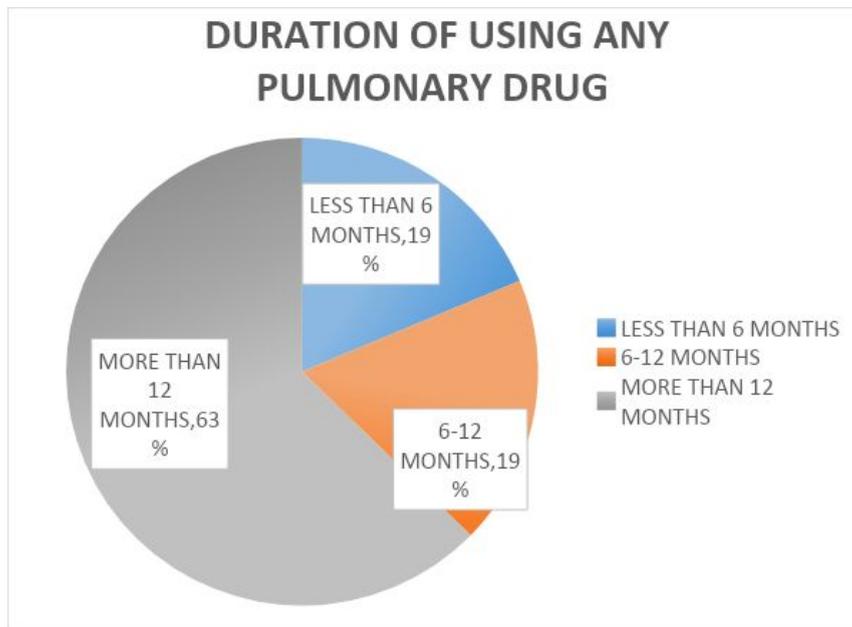


Figure 9 Duration of using any pulmonary drug

This statistical data shows different types of devices patients are currently using for their medications. Although there are several types of devices available in the market, MDI, DPI and nebulizers are considered as major types in this study. The highest number of patients (34%) are using the MDI as their current inhalation device followed by DPI (30%) and nebulizer 6% respectively. Moreover, many patients were prescribed to use combination of different type of devices. Both MDI and DPI users were 12% (17), MDI and nebulizer combination users were found to be at 19% (29), and 2 (1.34%) users were found to be using all of the three devices.

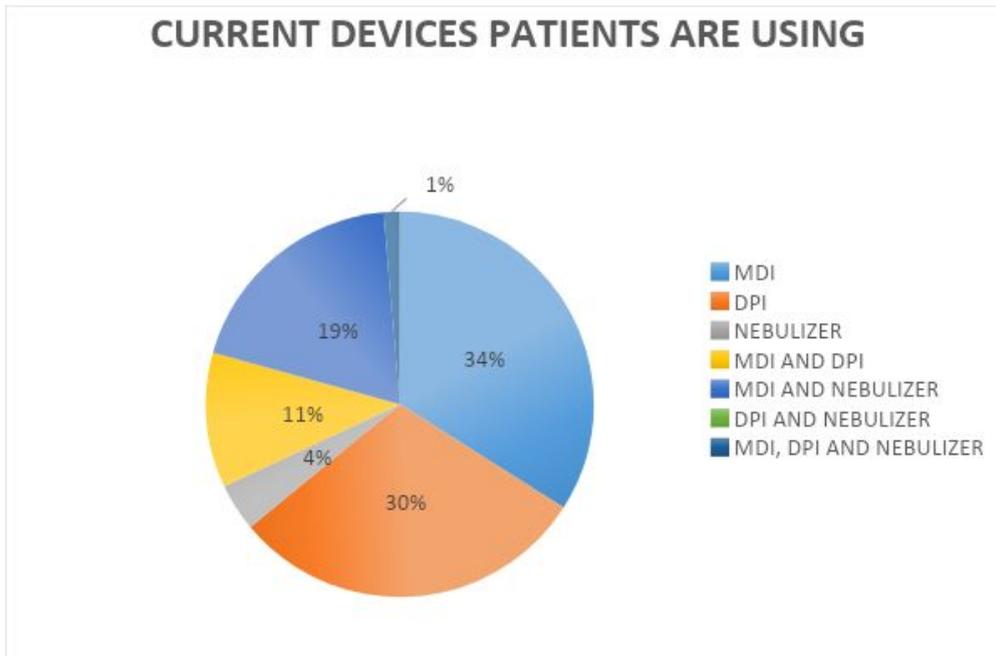


Figure 10 Current devices patients are using

Patients were asked about their knowledge of different types of devices. 68% of the patients had basic idea or known different types of drug or devices available in the market. 32% of the patients had no idea about the diversity of devices. Most of that 32% could not differentiate the devices that are available in the market (Figure 11).

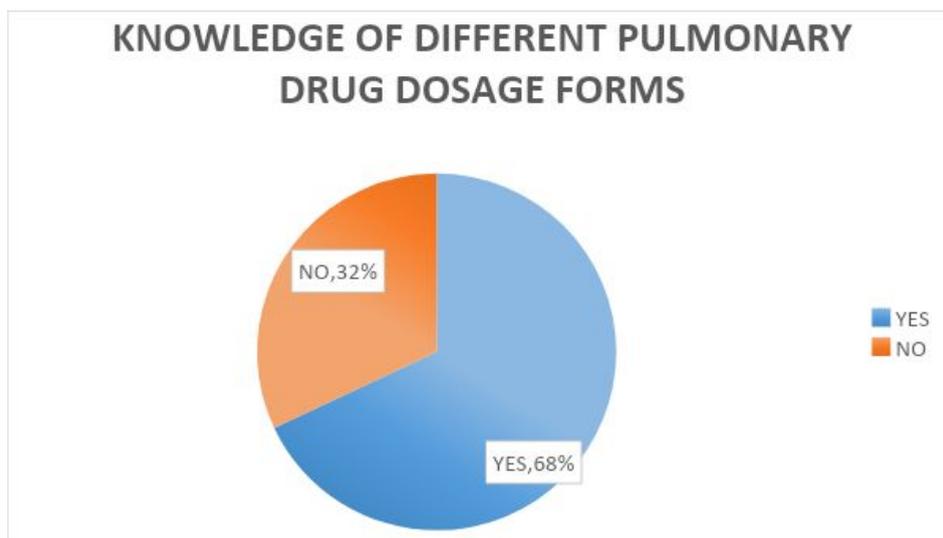


Figure 11 Knowledge of Different pulmonary drug dosage forms

Among 150 patients, 53% patients (80) preferred the MDI based on the efficacy and the convenience about using the device. 24% patients (36) preferred the DPI and 23% (23) patients preferred nebulizer as drug delivery system. Here, we can observe that most of the patients are using the MDI and prefers the MDI as their device. This higher rate of acceptance can lead to greater adherence to the medication. Although other factors can affect this rate such as cost, effectiveness, and ease of use/comfort (Figure 12).

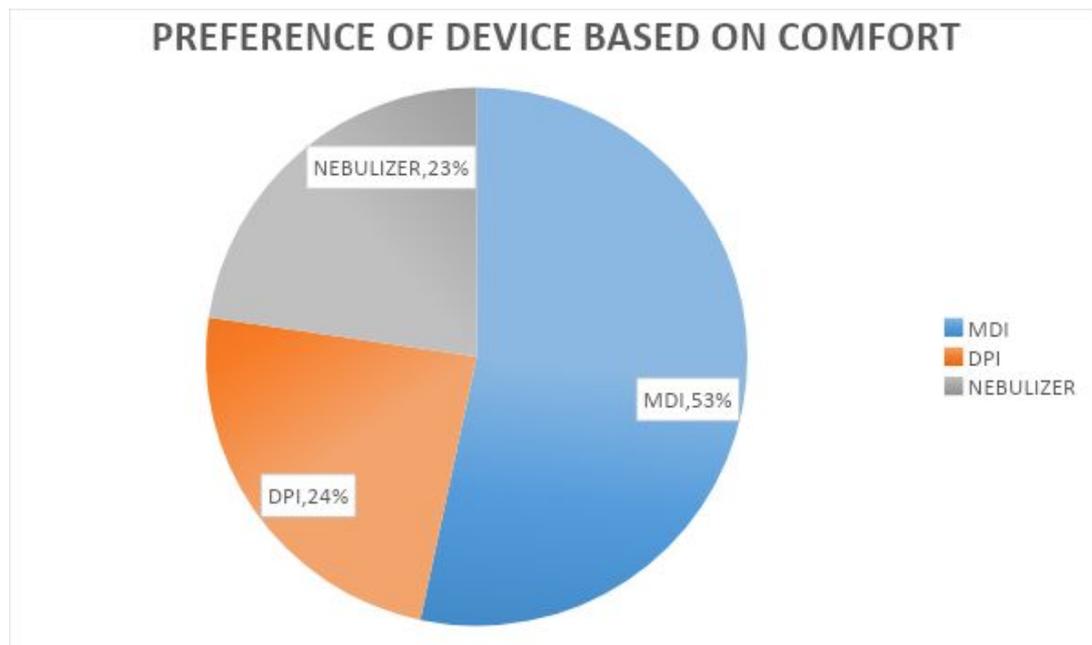


Figure 12 Preference of device based of comfort

In this study, we tried to find about the instructions given by the doctors or the pharmacists to the patients. Study findings showed that 93% patients were given instructions about using the device by the doctors/pharmacist and the patients understood each and every point. Other 4% (6) patients were instructed properly but did not understand the instructions and only 3% (4) patients did not get any instruction. Although high rate shows that patients were instructed correctly but this study demonstrated the lower rate of the tendency to follow the instructions they were given. 62% patients agreed to follow each and every steps they were advised while taking the medication or using the device. However, 29% patients do not follow all the

instructions they were provided. 9% patients did not know about their steps whether they were correctly using the device drug or not.

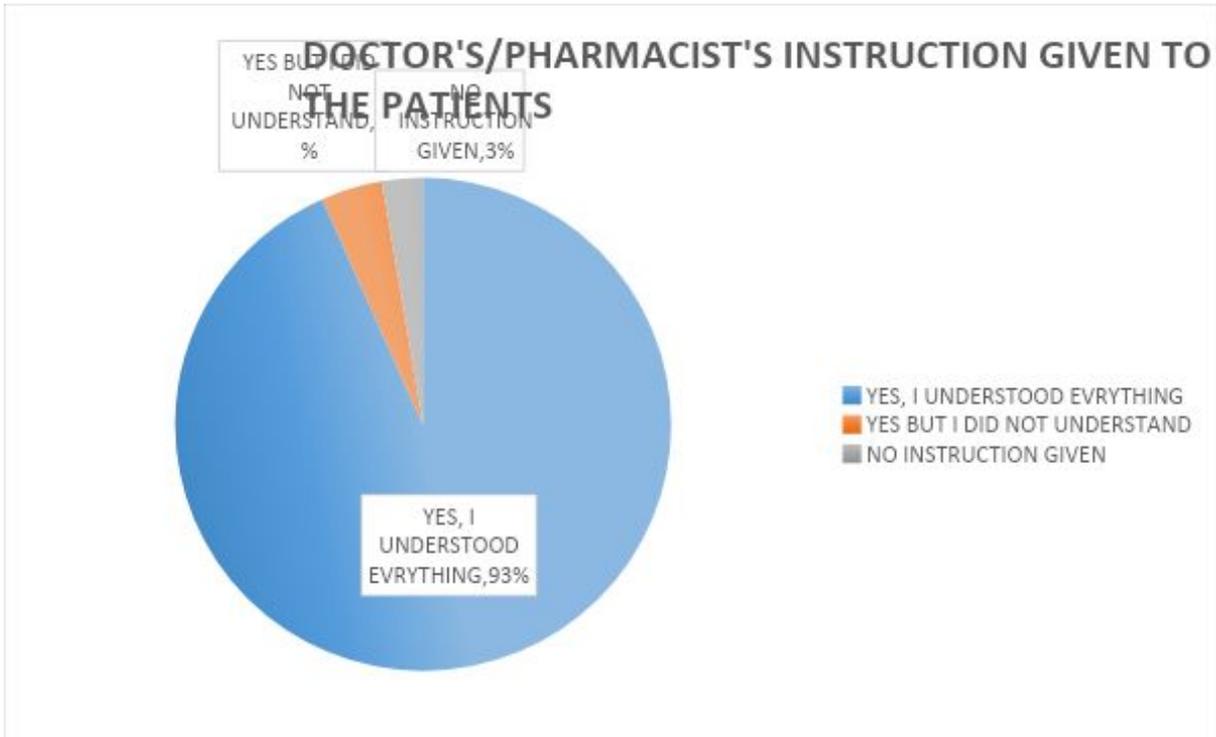


Figure 13 Doctor /Pharmacist's instruction given to the patients

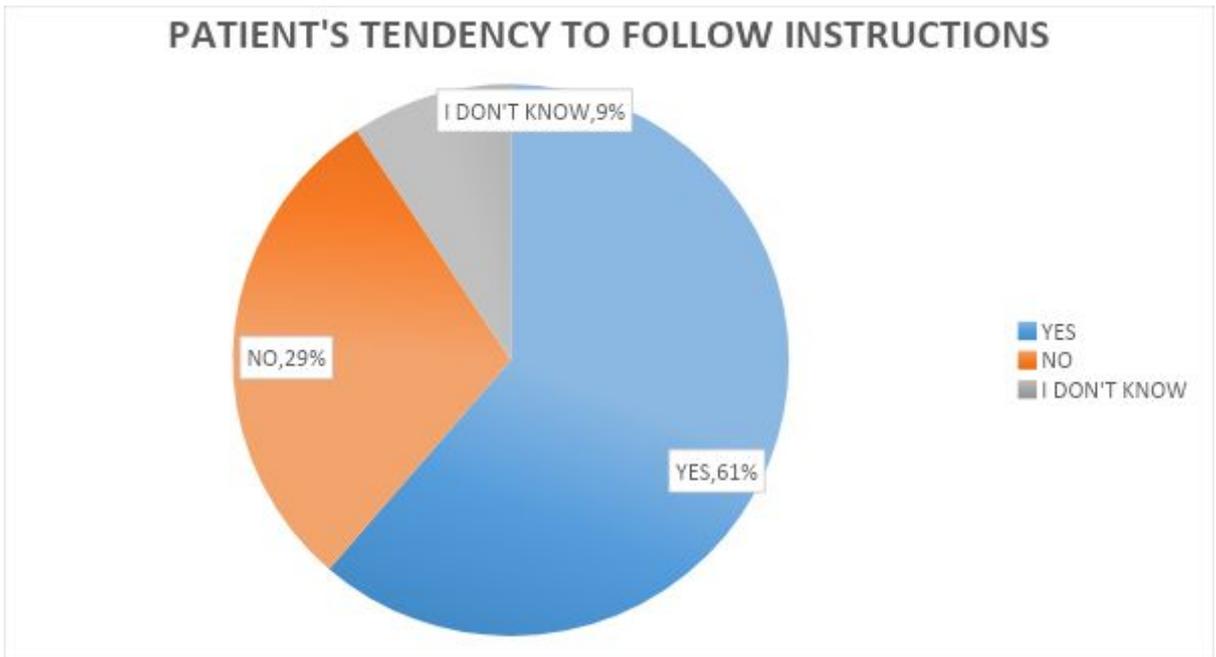


Figure 14 Patients tendency to follow the instructions

Most of the patients (93%) could administer the drug themselves. Only 7% of the patients could not administer themselves. Patients who did not have the nebulizer device could not administer themselves.

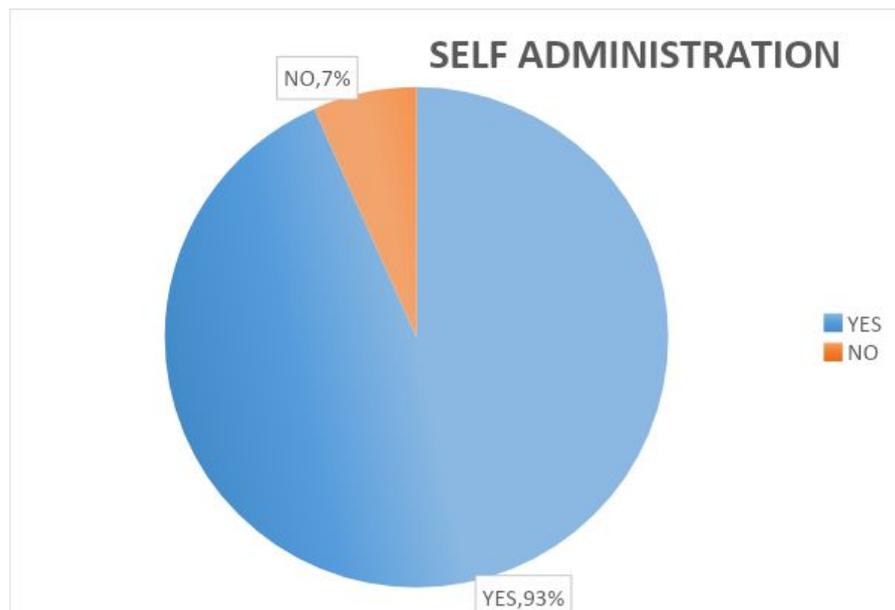


Figure 15 Self administration

Most of the Patients (96%) had no difficulties about using their drug or the device in their daily life. However, 4% patients had slight difficulties about their medications. 144 patients had no complication but 1 patient was having muscle contraction, and 1 patient was having slight dizziness after administrating the drug. Moreover, 4 patients (2%) were forgetful about their medication.

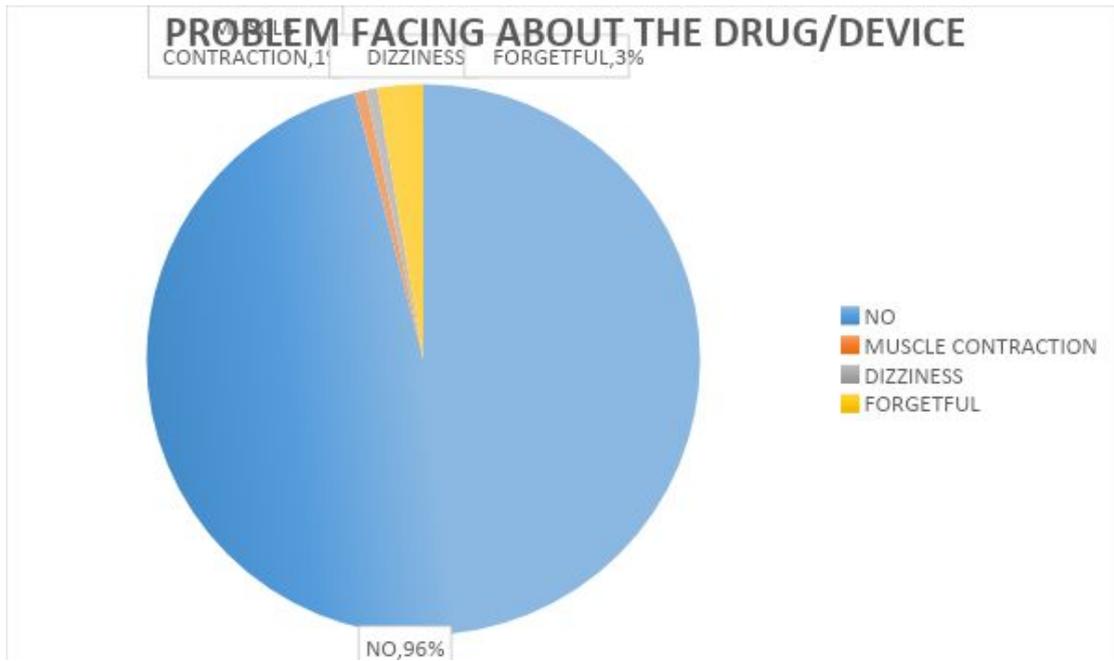


Figure 16 Problem facing about the drug/device

All of the 150 patients were asked if they wanted anything to be changed in their device. Majority of the patients (93%) suggested no change. 2% patients (3) suggested change in the nebulizer as nebulizer device is less portable as compared to MDIs and DPIs. In addition, 5% patients were not satisfied with the price of the drug including the device. Only one patient suggested making the nebulizer much faster process as it takes longer time compared to MDI and DPIs.

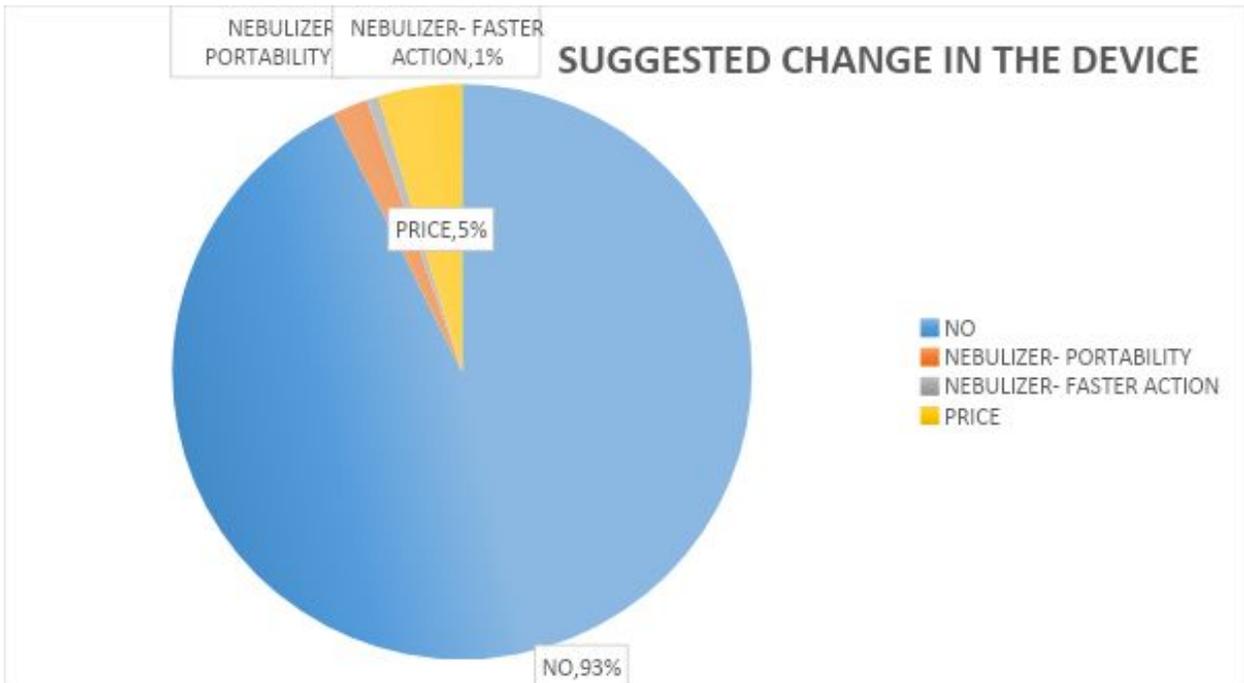


Figure 17 Suggested change in the device

The response about the efficacy of the medication and the device was found to be high. 26% of the patients were very satisfied to their medication. 69% patients was found to be in the satisfied which the highest percentage was. 5% patients (7) were doubtful about the efficacy and no patients found to be not satisfied about the efficacy of the medication and the device.

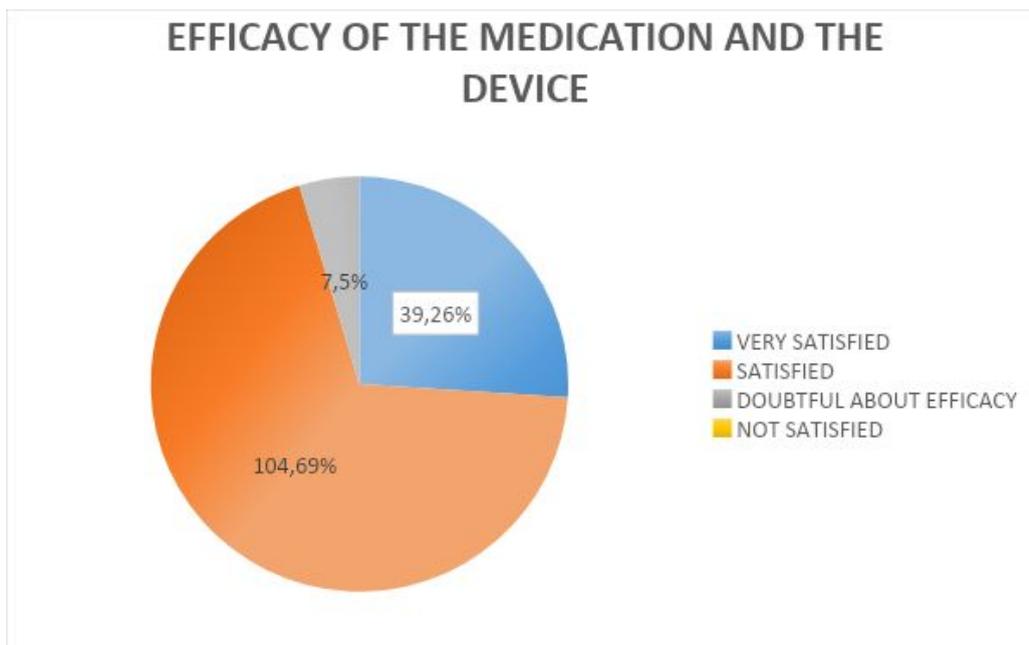


Figure 18 Efficacy of the medication and the device

Almost half of the patients (49.34%) were found to be satisfied with the cost of the medication. 12% patients were very satisfied with the medication currently they are prescribed by the doctor. 12% (18) patients were doubtful about the cost. A higher number was found to be not satisfied which is 27% of the total patients as some of the drugs and device are not cheap.

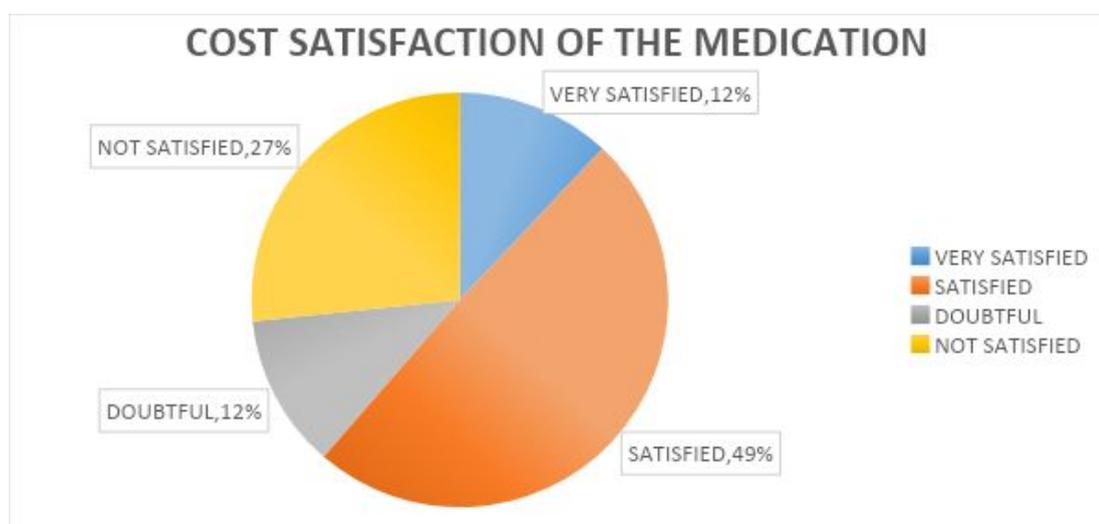


Figure 19 Cost satisfaction of the medication

In this study, we tried to find the best dosage form based on the cost effectiveness. According to the patients, MDI is the best dosage form (61%) in the pulmonary drug delivery system, followed by DPI, which is 33%, and only 6% patients chose nebulizers (Figure 20).

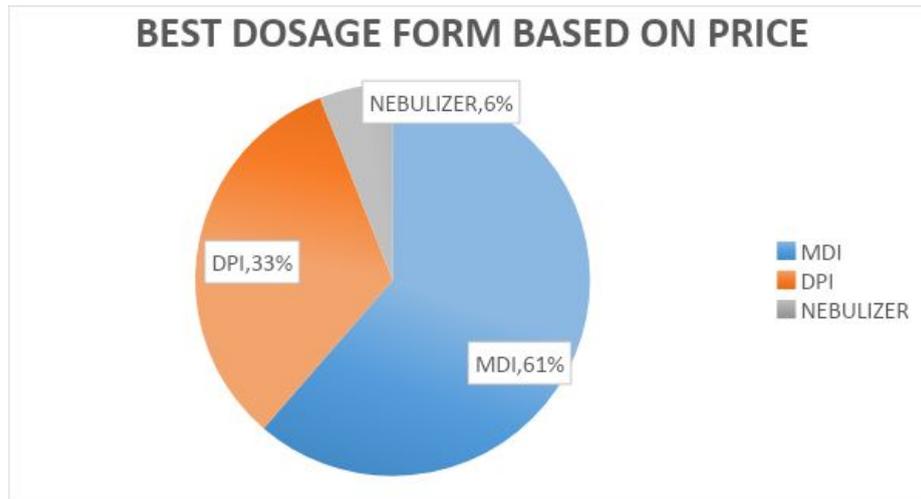


Figure 20 Best dosage form based on price

Chapter 5 DISCUSSION

52% male and 48% female patients participated in this study where only 12% patients were below age 18 and 88% of the patients were above 18 years old. This study demonstrates that majority of the patients (62%) patients are using pulmonary drug more than 12 months. 19% patients are using pulmonary drug 6-12 months and 19% patients are using pulmonary drugs less than 6 months.

Here in this study we can see that majority of the people in Mirpur are using the MDI (34%) as their current device. Although significant amount of the patients are using MDI with the combination of other types of device. 30% of the patients (45) are using MDI. Here, there is no patient using the DPI and nebulizer combination although DPI and nebulizer combination could be possible in higher population. 1% population was found to be using all the three types of devices. This type of combination is possible when the patients are prescribed large number medication due to severity or the complexity of their disease.

Based on the comfort patients preferred MDI over DPI (MDI- 53% whereas DPI-24%) due to the fact that patients are more familiar with the MDI and availability. Although other studies

showed that patients are more likely to choose DPI for being more economical compared to MDI or nebulizers. (Arora et al., 2014) Moreover, lack of knowledge could affect the device preference as we can see on figure 7 that lack of knowledge about different device was higher (32%).

Although 93% patients were instructed by either the doctor or the pharmacist, tendency to follow to the instructions was significantly low. This could be due to negligence of the patients or could be long-term behavior which can directly affect the therapeutic outcome of the medication. There is 9% patients who do not know about the method and steps to inhale the drug. Patients who were not instructed properly usually are self-educated which can result in the outcome of the medication.

We observed drug and device related difficulties in this study. Most of the problem were based on the drug related. One of the patients were suffering from muscle contraction after using salbutamol and fluticasone in irregular cases. Note that, muscle contraction is a common side effect of using salbutamol and fluticasone. Therefore, the doctor might prescribe different medication for the patient if it is possible. Another patient was facing dizziness after administration of the drugs. This as well could be possible side effect of his current medication as he only feels dizziness after administration of the drug. Moreover, 2% of the patients were forgetful about taking their medication on time even though they knew about their medication time and the dosage. This can happen when there are many drugs prescribed and physical similarities in the prescribed drugs.

The majority of the patients were either very satisfied or satisfied based on the efficacy of the drug and the device. Only 7 patients out of 150 (5%) were doubtful about the efficacy. No

patients were found to be unsatisfied about their medication. The doubtfulness might arise in the case of the cure of their disease. As all of the patients were either asthma or COPD, those diseases are not curable currently. Although with correct medication, dose and maintenance patients may find greater relief from those diseases. The continuous medication might arise some doubt about their medication.

Expenditure plays an important role in the treatment of any kind of disease. If the cost of the medication and the device is too high, patients might be non-compliant which significantly affects the therapeutic outcome of the medication. Based on the cost satisfaction, only 12% of the patients were very satisfied about their drug and device incorporated with. 49% patients were satisfied about their medication. Here, majority of the patients were either very satisfied or satisfied. However, 12% patients were doubtful and 27% of the patients were not satisfied at all. As we have discussed previously, most of the patients were using MDI as their current inhaler. On an average DPIs are more cost effective and patients tend to prefer DPI for being more economical. In this case, most of the patients were using MDI, so cost satisfaction was expected to be lower.

Most of the patients preferred MDI over DPI which is 61% and 33% respectively based on the price. This outcome may rise due to lack of knowledge (33% patients did not know about different type of dosage forms) of different types of devices. In addition, most of the patients were using MDI; they might prefer their own current device as the best based on cost effectiveness.

Chapter 6 CONCLUSION

Although being so advanced in technology and medical science people millions of people die from different disease. Asthma and COPD are some of the major leading cause of mortality all over the world. Although there is no medication to cure, the asthma and COPD but there are many different types of drugs, which can reduce the severity and mortality. We have observed that 63% of the patients are using pulmonary drugs more than 1 year and many are the patients are long-term users. Most of those patients are using MDI and almost 30% of the patients are using DPI. Although almost one-third (32%) of those patients have little to no knowledge of different type of pulmonary drug delivery devices, they prefer the MDI over DPI or nebulizer based on ease of use and cost effectiveness.

6.1 Recommendations

We have seen in the dada that a vast number of people are unaware about different types of drugs, which are consumed by them almost in regular basis. Patients' awareness should be increased in Mirpur about the drugs they are consuming. Doctors/physicians and the

pharmacists can play an active role by demonstrating the use of the drug and the device. Moreover, patients should show demonstrations how they use the device at home to the doctor/ physician or the pharmacist to avoid any kind of misinformation and confusion. The physician or the pharmacist must show the correct way to use the drug and the device to the patients and other basic information about the drug and the device. In this way, patients should be more aware and more cautious about taking the medication, which will increase higher acceptance, and compliance thus increased positive therapeutic outcome.

Secondly, we have seen that many patients are not satisfied about the cost of their medication. The price of the drugs and the devices should be reduced if possible to increase the compliance among the patients.

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Appendix A.

Questionnaires

Patients Compliance in Pulmonary Drug delivery systems in Mirpur

Name:

Age: 0-18

18- Above

Gender: Male

Female

Prefer not to say

Name of the Disease:

Name of the Drug:

1. Did you take any drugs for any pulmonary disease before?

Yes

No

2. How long you have been using pulmonary drug delivery systems?

< 6 months

6-12 Months

> 12 months

3. Inhalation Dosage form/Technique: Metered Dose Inhaler (MDI)

Dry Powder Inhaler (DPI)

Nebulizer

4. Do you know about all the pulmonary dosage forms available in the market?

Yes

No

5. If yes, which form of drug you prefer/ are comfortable with compared to others?

Metered Dose Inhaler (MDI)

Dry Powder Inhaler (DPI)

Nebulizer

6. How long you are taking the current drug?

7. How often do you take the current drug?

8. If you are taking the current drug daily, how many times do you take the drug in a day?

9. Did the physician/pharmacist show instructions before taking the current medication?

Yes, I understood every point.

Yes, but I did not understand the instructions

No

10. Do follow every steps to take the drug?

- Yes
- No
- Maybe

11. Can you take the drug all by yourself?

- Yes
- No

12. Are you facing any kind of difficulties using current medication regarding the device or the drug itself?

- Yes
- No

13. If you do, what kind of difficulties you are facing?

14. Do you want to change anything in your current inhalation system?

- Yes
- No

15. If yes, what is the change you would like make to overcome your difficulties?

16. Are you satisfied with the efficacy of the medication?

- Very satisfied
- Satisfied
- Doubtful about efficacy
- Not satisfied

17. Are you satisfied with the costs of the medication?

- Very satisfied
- Satisfied

Doubtful about efficacy

Not satisfied

18. Based on cost effectiveness which pulmonary dosage form is better?

Metered Dose Inhaler (MDI)

Dry Powder Inhaler (DPI)

Nebulizer