

## Medical Management of Pulmonary Hypertension: Calcium Channel Blockers Vs Sildenafil A Systematic Review

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### ABSTRACT

**Background:** Pulmonary hypertension can be defined as incompatibility in blood pressure level into vessels and right side of heart is affected severely through this. As a result, heart failure among patients is common and reduction of blood flow affects negatively over respiratory rate. Calcium channel blockers such as Amlodipine, Nicardipine, Felodipin are potential to slow down blood pressure and accumulation of calcium ions are decreased in vessel wall. In addition, Sildenafil is an active Viagra component that also helps to regulate thickness of blood vessels for controlling pressure. This study mainly focuses on comparing medical management strategy of pulmonary hypertension by using Calcium channel blockers and Sildenafil.

**Methods:** This study is actually a systemic review to analyse the impact of Calcium channel blockers and Sildenafil on patients suffering from pulmonary hypertension. Original full research articles are selected for literature review and 63 patients are detected for easy comparison of drug usage and facilities. Both of the drugs have been applied with 0.3 mg/kg dose for each of the sample population to understand hypertension crisis. All the demographic, postoperative and preoperative variables have been discussed promptly for acquiring proper knowledge.

**Results:** The result has shown that Calcium channel blockers are better to treat pulmonary hypertension than Sildenafil by delivering no side effects on patients. On the other hand, therapeutic value of Calcium channel blockers is greater than Sildenafil and it helps to act at a limit for blood pressure lowering. In addition, a potential correlation between heart failure, pulmonary hypertension and medical management has been determined.

**Conclusion and discussion:** This study concludes that pulmonary hypertension crisis has been reduced potentially by applying Calcium channel blockers as well as Sildenafil. However, lack of accumulation of calcium in blood vessel is a more suitable approach than applying strong Viagra component named Sildenafil.

### Keywords

Pulmonary Hypertension, Calcium Channel Blockers, Medical management of disease, Sildenafil.

### Introduction

#### Rationale

Pulmonary hypertension is a problematic heart related disease by which around half of the population of UK have suffered and

the potency is almost same in case of infants and aged people. In this section, problems regarding *pulmonary hypertension* and its probable therapies are highlighted.

*Pulmonary hypertension* is one of the common heart diseases of United Kingdom and more than 7 thousand people are affected per year by its vulnerability. As per the view of Kim *et al.* [1], this heart contingency has delivered negative effect on patients and

more than 40% infants are affected badly due to this. On the other hand, it has also been shown that number of affected people in UK is increasing day by day that retains social capacity of this country inaccurately. In addition, Rademacher *et al.* [2] argued that more than 8,000 UK people are affected by pulmonary hypertension and dizziness is a common factor among them. In case of previous researches, particular age group has been selected and no concise information has been informed about necessity of modern drug therapies.

Pulmonary hypertension occurs when blood pressure becomes excessive in pulmonary veins and arteries. As a result, supply

of oxygen in different body parts face a number of problems and respiratory rate reduces potentially. In addition, Pesto *et al.* [3] pointed out that oxygen deficiencies in pulmonary vein causes dizziness and shortness of breath. However, previous articles did not explain the necessity of *Calcium chain blockers* by comparing with *Sildenafil*. On the other hand, Panopoulos *et al.* [4] suggests that proper application process of *Sildenafil* drugs is not mentioned to any previous researches. Therefore, this research would try to shed light for comparing the therapeutic effect of *Calcium chain blockers* and *Sildenafil* for medical management of *pulmonary hypertension*. [Refer to appendix 1].

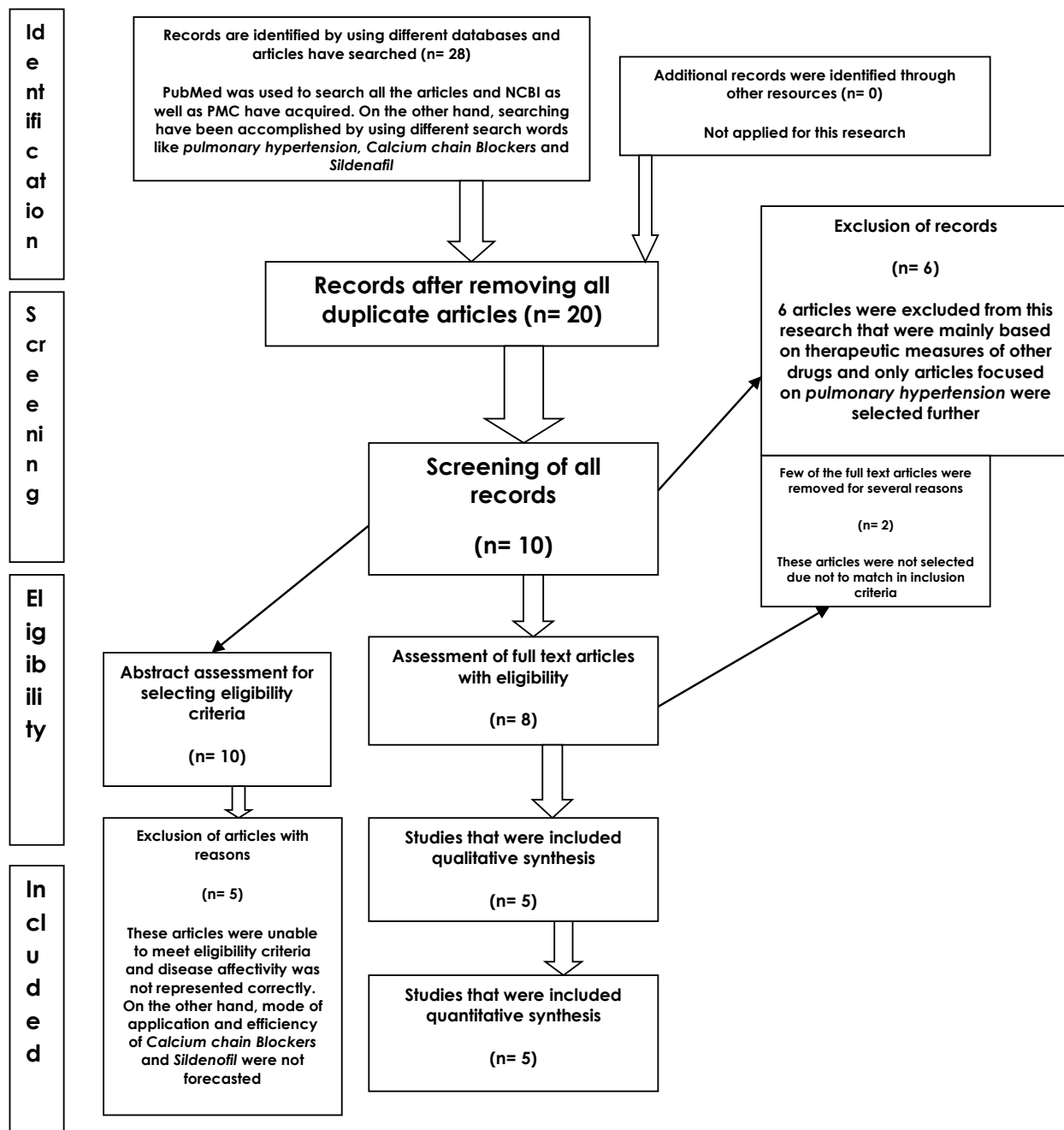


Figure 1: Flow Diagram.

## Objectives

The aim of this study is to develop knowledge about medical management of *pulmonary hypertension* by analysing effect of *Calcium chain blockers* and *Sildenafil* for its recovery.

- To develop the concept of medical management for pulmonary hypertension.
- To understand the therapeutic measures for *Calcium chain blockers* in case of *pulmonary hypertension* among UK population.
- To find out importance of *Sildenafil* as therapeutic drug to reduce vulnerability of *pulmonary hypertension* among UK population.
- To compare medical management processes of two different treatment schemes such as *Calcium chain blockers* and *Sildenafil*.

## Methods

Qualitative research method is followed for this study and various scientific journals are collected for elaborating data for this systemic review. All the articles are helpful to understand themes and concepts regarding heart disease named *pulmonary hypertension*.

## Definition of research question

The research question for this study is about developing the concept of medical management for pulmonary hypertension. Random human models beyond age group, sex and race were considered to understand the effectivity of these drugs for human. On the other hand, this research topic was selected based on past literatures and prosper was used to formulate systemic review question.

## Protocol

Agreement of *PRISMA* protocol was used for developing researchers understanding about this topic and data collection process was acquired. All the data were extracted by following *PRISMA* flow chart and checklist and ethical approval has been registered to reduce future contingencies [5].

Figure 2 shows flow diagram of this research and all the exclusion and inclusion criteria are selected based on particular topic. In case of this study, mainly keywords like *Calcium chain blockers*, *Sildenafil* and *pulmonary hypertension* were searched for data collection. Primarily, 28 articles were selected for meeting study category and 20 articles were selected further after removing duplicates. On the other hand, six records were excluded from this study and 10 articles were screened afterwards for better data proficiency. In addition, abstract of 10 articles were analysed previously based on study topic and finally 5 were identified for meeting all criteria. Therefore, quality-checking measures have been done to retrieve all the data regarding above-mentioned disease and its treatment processes.

## Eligibility criteria

All the inclusion criteria for this review are enlisted below to deliver proper information about this topic.

**Table 1:** PICOS to select eligibility criteria.

Parameter	Description
Population (P)	Human populations were selected to research on medical management scheme of <i>pulmonary hypertension</i>
Intervention and Exposure (I)	The intervention was set to compare medicinal effect of <i>Calcium Chain Blockers</i> and <i>Sildenafil</i>
Control Group (C)	The control group was human beyond gender, age, sex and race
Outcome (O)	The outcome was that <i>Calcium Chain Blockers</i> were common remedy process from <i>pulmonary hypertension</i> but <i>Sildenafil</i> has shown quick action
Study Design (S)	Both the randomised controlled trails and clinical trials were accommodated for accomplishing this study

More than 20 full text articles were selected previously for conduction of this study and the type were selected based on randomised controlled trails, pre-clinical trials and clinical trials. As per the opinion of Kim *et al.* [1], there is a huge difference between mode of action and side effects of *Calcium Chain Blockers* and *Sildenafil*.

## Inclusion criteria

Human population has been selected for this research to find out effect of *Calcium Chain Blockers* and *Sildenafil* to treat *pulmonary hypertension*. Along with this, UK based data are selected for study purpose and journals on medical management are included. Therefore, all the papers were selected by reminding this theme and both the male and female participants were included for understanding medicinal value.

## Exclusion criteria

Paper regarding potential heart diseases for animals other than human are excluded and therapies by using materials other *Calcium chain blockers* and *Sildenafil* are excluded. However, people who have used other drugs were excluded from this study as the theme lies to deliver importance of *Calcium chain blockers* and *Sildenafil* drugs for remedy purpose.

## Information sources

The whole study was accomplished with the help of the articles retrieved from NCBI, PubMed and PMC websites. The researchers considered no unpublished articles during study progress and collection of data and their analysis.

## Search Strategy

Last 5 years' articles were selected and different phrases were searched to gain accurate article with high proficiency. The search was started from March 2020 and the date was 15<sup>th</sup> March for acquiring information from articles. In addition, *Boolean operators* were used to search authentic articles for this study purpose.

## Study selection

Selecting, sorting and organising of data have been acquired after primary and secondary screening and duplicates were removed for

each article. Along with this, all the articles were selected after reading abstracts and screening has been done if abstracts were met the eligibility criteria.

### Data collection process

Data has been collected from Google scholar, NCBI and other medical portal with the help of supervisor suggestions. On the other hand, selection of qualitative data was included population, control group, exposure group, and article year and exposure rate has been acquired.

### Data items

All the data items were based on *Calcium Chain Blockers* and *Sildenafil* and mean scores is decided promptly for decision-making.

### Risk of bias

Risk of bias was major for this research as individual researchers have focused on particular type of medicines whether *Calcium Chain Blockers* or *Sildenafil*. On the other hand, there was conflict between randomised control trials and clinical trials before reporting properly. In addition, articles with positive results were highlighted and underrated articles were not chosen for this review process.

### Summary Measures

Summary of this study has been plotted in result section through flow diagram and graphs of subgroup analysis have been shown in a potential manner. All the statistical data was gathered properly by analysing graphs and confidential interval was supported correctly.

### Synthesis of result

Ms-Excel was used for data synthesis, analysis, and all the data were documented authentically in a confidential software drive. On the other hand, all the data would forest plot to deliver proper information about medical management scheme of *pulmonary hypertension* by using *Calcium Chain Blockers* and *Sildenafil*.

### Results

Table 2 has shown all the articles were focused on different study population and controlling of *pulmonary hypertension* was developed in a proper manner. Most of the articles were shown positive results and application of *Calcium Chain Blockers* and *Sildenafil* in order to reduce *pulmonary hypertension*. On the other hand, exposure and control group have been forecasted proficiently to develop better knowledge on this topic.

The above table 3 shows the demographic and health related data of the patients and the results from diagnostic tests are evaluated in a correct order.

**Table 2:** Studies use for systemic review.

Article name	Year	Author	Population size	Medications	Results
The role of preoperative sildenafil therapy in controlling of postoperative pulmonary hypertension in children with ventricular septal defects	2017	Bigdelian and Sedighi	63	Sildenafil	Positive Result
Management of pulmonary arterial hypertension in patients with systemic sclerosis	2020	Almaaitah et al.	Patient population	Calcium chain Blockers	More than 2% population are cured
Pulmonary Arterial Hypertension and Pregnancy	2018	Chhabra et al.	Pregnant women	Calcium chain Blockers	Negative results have shown
Evaluation and management of pulmonary hypertension in children with bronchopulmonary dysplasia	2017	Krishnan et al.	Infants and children	Sildenafil	Positive result has been shown
Pulmonary arterial hypertension: pathophysiology and treatment	2018	Lan et al.	All populations are considered	Both Calcium chain Blockers and Sildenafil	Positive result by treatment

**Table 3:** Demographic data of 63 patients.

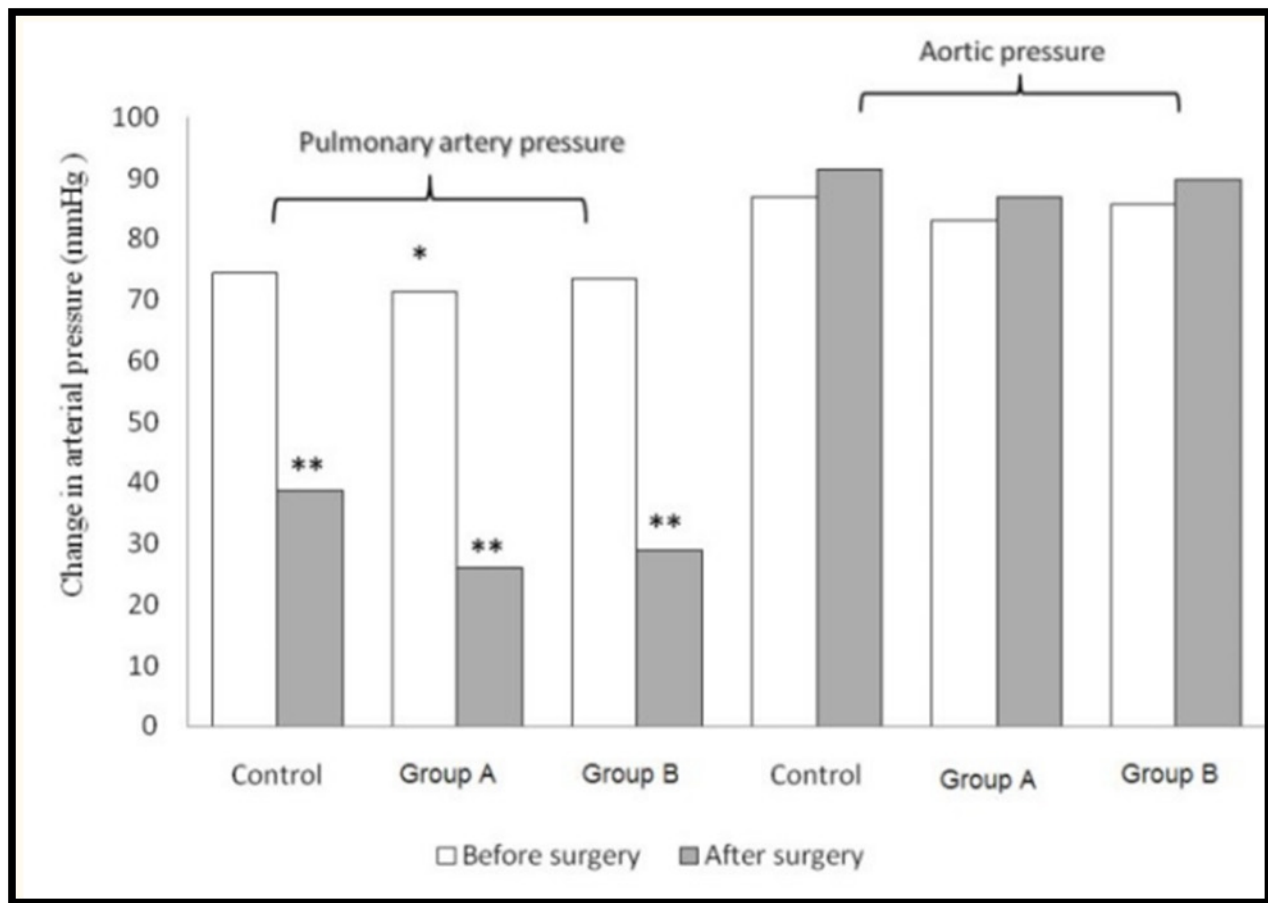
Variables	(n = 63)	Percent
Gender		
Male	39	62
Female	24	38
VSD type		
Per membranous	60	95
Muscular	3	5
Diagnosis defect		
VSD	10	15
VSD+PDA	47	75
VSD+ASD	6	10

**Table 4:** Comparison of variables after applying *Sildenafil*.

Variables <sup>a</sup>	Control group (n = 20)	Group A (n = 22)	Group B (n = 21)	P value
Age (month)	5.4 ± 0.6	5.4 ± 0.5	5.7 ± 0.3	0.123
Weight (kg)	6.4 ± 0.6	6.6 ± 0.6	6.8 ± 0.5	0.206
BSA(m <sup>2</sup> )	0.3 ± 0.1	0.3 ± 0.07	0.3 ± 0.1	0.433
CI (L/min/m <sup>2</sup> )	4.1 ± 1.1	3.7 ± 0.9	3.6 ± 1.1	0.381
mPAP (mm Hg)	75.4 ± 3.0	71.3 ± 2.9	73.3 ± 3.2	0.001*
mAOP (mm Hg)	86.7 ± 6.2	83 ± 7.6	85.5 ± 8.2	0.254
PA/AO pressure ratio	0.86 ± 0.6	0.85 ± 0.6	0.85 ± 0.7	0.862
PVR (dynes-sec-cm <sup>-5</sup> )	1161.8 ± 53.2	1088.5 ± 53.3	1125.1 ± 57.1	0.001*
SVR (dynes-sec-cm <sup>-5</sup> )	4362.4 ± 334	4135.4 ± 414	4294.3 ± 440	0.175
Oxygen saturation (%)	86.9 ± 1.1	86.6 ± 1.1	87 ± 2.04	0.764

**Table 5:** Comparison between control group and test population.

Variables <sup>a</sup>	Control group (n=20)	Group A (n=22)	Group B (n=21)	P value
ACC time (min)	61.9 ± 8.9	66.8 ± 11.1	68.1 ± 12.3	0.169
CPB time (min)	105.6 ± 18.5	93.1 ± 13.3	97.1 ± 16.7	0.049*
mPAP (mm Hg)	38.6 ± 0.9	25.98 ± 0.86	28.84 ± 0.38	0.001*
mAOP (mm Hg)	91.4 ± 7.9	86.90 ± 7.6	89.71 ± 8.2	0.184
PA/AO pressure ratio	0.42 ± 0.03	0.29 ± 0.02	0.32 ± 0.03	0.001*
Oxygen saturation (%)	95.7 ± 0.73	96.2 ± 0.75	96.1 ± 1.03	0.094
PVR (dynes-sec-cm <sup>-5</sup> )	508.6 ± 16.8	282.9 ± 15.4	334.1 ± 6.8	0.001*
SVR (dynes-sec-cm <sup>-5</sup> )	4553.2 ± 298	4363.2 ± 399	4505 ± 421	0.242
Intubation time (hours)	12.3 ± 1.0	8.4 ± 0.9	9.07 ± 1.3	0.001*
ICU stay (hours)	75.3 ± 3.0	70.09 ± 4.7	70.71 ± 2.0	0.001*



**Figure 2:** Comparison between preoperative and post-operative pressure.



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This table 4 has shown change in physical health after application of *Sildenafil* and clear comparison about control group and study group is given.

This table 5 shows the differentiation about various groups after using drugs potential to *pulmonary hypertension recovery*.

## Discussion

### Interpretation of data

The aim of discussion of the study is to deliver accurate information by summarising the data from all selected papers. This section mainly focuses to develop better understanding why it is important to consider *Calcium chain blockers* and *Sildenafil* as modern therapeutic alternative of *pulmonary hypertension*.

This study has investigated the comparison between *Calcium chain blockers* and *Sildenafil* for reducing viability of *pulmonary hypertension*. On the other hand, several medical management schemes and opportunities have been elaborated from this study. Medical management is a process to insert modern therapeutics for reducing the probability of any potential disease. This study informs that *Calcium chain blockers* provide no side effect for patients suffering from pulmonary disorder. In addition, lack of calcium accumulation in blood vessel is an effective therapy to manage vulnerability of *pulmonary hypertension*. On the contrary, Goldstein *et al.* [6] commented that *Sildenafil* delivers number of negative side effects for patient's body and disease management becomes difficult. In addition, congenital heart surgery can help to reduce negative impact of *pulmonary hypertension* among infants. Along with this, Arora *et al.* [7] pointed out that pulmonary crisis can be managed potentially and rate of morbidity and mortality can be managed accurately. Therefore, proper choice of treatment is necessary to decrease viability of this heart related contingencies and ventricular dysfunction has been controlled.

### Summary of findings

This section of the study provides a clear overview about findings of selected journal articles by which importance of medical management can be understood. On the other hand, most of the part of this section is focused on deliverance of drugs name and its uses for better health condition.

This review has highlighted that mode of action of *Calcium chain blockers* and *Sildenafil* are very different but both of them are effective to reduce negative viability of *pulmonary hypertension*. On the other hand, data has been gathered from this research that oral consumption of *Sildenafil* is better for preoperative use to reduce rate of mortality among infants. As per the opinion of Farhat *et al.* [8], *Calcium chain blockers* are probably the first therapeutic subsidy to reduce vulnerability of *pulmonary hypertension*. Primarily, doctors have prescribed few common medicines such as *Amlodipine*, *Nicardipine*, *Felodipin* to control angina and blood pressure. In addition, Hoepfer *et al.* [9] pointed out that, *Calcium chain blockers* helps to manage calcium accumulation in blood vessels. On the other hand, open up of blood vessels are important

to supply sufficient amount of oxygen throughout the body. In addition, this vasodilator is a proficient one to deliver positive impact for idiopathic pulmonary hypertension therapy.

*Calcium chain blockers* are not suitable option for pregnant women due to some potential side effects. As pointed out by Perros *et al.* [10], thick uterus wall is needed for pregnant women but toxicity of *Calcium chain blockers* affects negatively on blood supply for foetus. Therefore, these long acting tablets are prohibited for pregnant women and doctors have restricted to prescribe medications for would be mothers. On the other hand, Zhang *et al.* [11] mentioned that headache, dizziness, flushing and swallowing ankle are the common disorders of *Calcium chain blockers*. By analysing 5 relevant articles and accomplishing in field study with 63 patients, data has been gathered that providing of proper dose is needed for these drugs. Apart from this, Lancaster and Zeid [12] suggested to take minimum dose twice a day for reducing viability of *pulmonary hypertension*. Both the tablets and capsules are helpful to manage *pulmonary hypertension* and heart rate can be controlled properly.

*Sildenafil* is an effective drug to control negative impact of *pulmonary hypertension* among infants. This drug shows quick action for disease reduction and a patient can be cured within 60 minutes to 4 hours. As per the opinion of Arora *et al.* [13], *Sildenafil* can be used as post-operative drug for the children suffering from complex heart diseases. On the other hand, sensitivity of right ventricle is increased by applying this drug orally for helping easy movement of blood from heart to lungs. Along with this, Krishnan *et al.* [14] commented that PDE5 activity is decreased by supplying *Sildenafil* and more cyclic GMP is produced within lungs. On the other hand, pulmonary blood pressure is decreased potentially for improving heart function and body balance can be controlled. Apart from this excessive breakdown of cGMP becomes facilitative for patients to acquire better stimulation and physical development can be acquired properly.

Previous researchers have informed that daily consumption of *Sildenafil* can deliver negative effect for human body and other organs have been affected badly. On the other hand, it is also reported by Almaaitah *et al.* [15], prolonged consumption of *Sildenafil* causes chronic disease. Painful erection at about 4 hours is dangerous for any human being and it becomes immediate to contact with doctors. Apart from this, *Sildenafil* affects negatively on gonatrophic hormones and development of body parts has been ceased inaccurately. Along with this, Rosenzweig *et al.* [16] pointed out that, permanent eye blindness and vision decrement are common vulnerable side effects of *Sildenafil*. On the other hand, Viagra is an active component of this drug and this impact negatively on nervous system and body weakness can be occurred as a result. Apart from this, consumption of *Sildenafil* in high doses is vulnerable for metabolism and regular digestion of human being are affected potentially [17]. Therefore, use of *Sildenafil* as drug for *pulmonary hypertension* is still under trial for numerous side effects.

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*Calcium channel blockers* and *Sildenafil*, both are vital drugs to reduce viability of *pulmonary hypertension* among human population. However, there is some major differences between applications and doses of these above-mentioned drugs. As per the opinion of Desai and Desouza [18], *Sildenafil* acts on molecular level and blood pressure level of an individual can be managed through this. On the other hand, *Calcium channel blockers* generally work over normal physiological functions and reduce calcium accumulation in blood vessels. In addition, Lan *et al.* [19] argued that *Sildenafil* acts quickly for reducing negative impact of *pulmonary hypertension* among patients. However, critical patients are generally operated by using *Sildenafil* as regular drug for reducing affectivity of *pulmonary hypertension*. On the other hand, viability of oxygen deficiency can be fixed in a correct manner by applying *Sildenafil* in hospitals. Therefore, morbidity rate for this body dysfunction can be reduced in a potential manner by applying this drug on a daily basis in proper dose.

*Pulmonary hypertension* therapy follows use of anticoagulant medicines in UK and doctors mainly try to prevent blood clots. As per the opinion of Solaimanzadeh [20], *medical centres of UK to remove excess fluid from body generally use diuretics tablets* and imbalance of oxygen can be maintained accurately. On the other hand, normal oxygen treatment is also accomplished to reduce potency of heart failures among patients. In addition, Fukuda *et al.* [21] pointed out that *endothelin receptor antagonist* is effective to treat vulnerability of *pulmonary hypertension*. On the other hand, molecular level treatment is also accepted for infants suffered by *pulmonary hypertension*. Apart from this, *soluble cyclase stimulators* are also used for regulating blood pressure of individual person and oxygen deficiency in lungs can be controlled. In addition, *Calcium channel blockers* are effective to control angina and accumulation of calcium ion in blood vessels can be reduced correctly.

### Study limitation

This research has several limitations due to the small sample size and time limit of this study is not accurate in order [22]. As per the opinion of Bigdelian and Sedighi [23], money is important for any research to improve clarity and viability. In case of this research, money was a bigger problem and researchers became unable to extract actual data of this medical issue and disease management schemes. Along with this, review of all the articles have not accomplished properly because of time congestion and interpretation of all data became bias in nature. On the other hand, proper keywords have not been searched to gather information from relevant previous articles. Apart from this, Tamura *et al.* [24] mentioned that analysis of medical history of sample populations is necessary to adapt before continuing study with a particular set of participants. However, in case of this research, no relevant information about past medical factors of populations has been developed to acquire real field information.

### Conclusion

Medical management of *pulmonary hypertension* is generally accomplished by using *Calcium channel blockers* and *Sildenafil*.

On the other hand, doctors have prescribed to use *Calcium channel blockers* on a daily basis rather than *Sildenafil* due to vulnerable side effects. However, *Calcium channel blockers* are not suggested for pregnant women as lack of calcium in blood vessels becomes problematic for foetus. Apart from this, critical patients suffering from *pulmonary hypertension* are treated by using *Sildenafil* as it provides quick actions. In addition, the above-mentioned drug becomes helpful to act in molecular level by using dose at about 0.3 mg/kg body weight. Left to right shunt of human ventricle is necessary to manage blood pressure level of a patient affected by *pulmonary hypertension*. Moreover, systemic review of articles and in field survey has shown result that optimal dosing of both the medicines help to obtain efficacy of disease and management of this chronic disorder becomes easy.

### Ethical approval

This research has been accomplished under proper ethical regulations and rules of *NLM* and *NHS* have been maintained accurately. On the other hand, all the articles have acknowledged properly for reducing conflict of interest. Along with this, names and medical data of the patients are stored with high confidentiality and no information is shared with third party without the members of research team.

### Completing interests

This systematic review is more relevant than any previous researches on this topic because researchers have compared action of major type of medicines using for *pulmonary hypertension* reduction. In addition, side effects for each of the drug are enlisted promptly in this review to forecast their usage and affectivity for patients. On the other hand, this study is a unique one to compare mode of actions of *Calcium channel Blockers* and *Sildenafil*. Researchers have fetched out data from various literatures to demonstrate clearly about drug application and its potency for medical management of *pulmonary hypertension*.

### Acknowledgement

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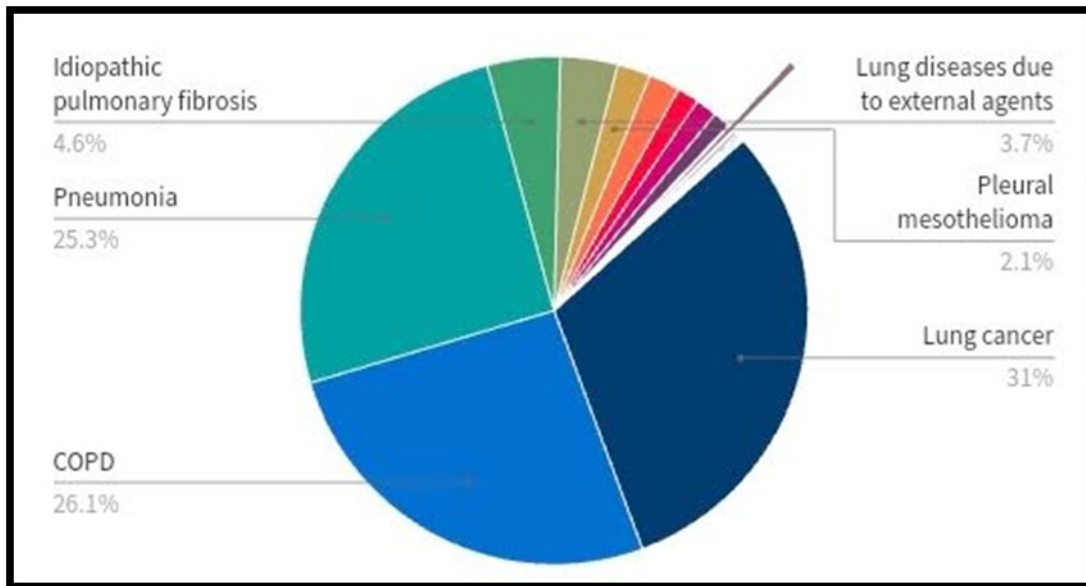
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## Appendices



**Appendix 1:** Effect of pulmonary hypertension on UK population.  
(Source: Panopoulos *et al.* 2020)