International Journal of Research and Review
Vol.7; Issue: 1; January 2020
Website: www.ijrrjournal.com
Original Research Article *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

Evaluating Efficacy and Safety of Sildenafil Citrate in Pulmonary Artery Hypertension

JL Wadhwani[1], Anil Sejwar[2], Manuj Sharma[3], K Deopujari[4]

[1]Associate Professor, Department of Medicine, Gandhi Medical College Bhopal MP, India
[2]Assistant Professor, Department of Medicine, Gandhi Medical College, Bhopal, MP, India
[3]Associate Professor Endocrinology, Department of Medicine, Gandhi Medical College, Bhopal, MP, India
[4]Associate Professor Medicine, Department of Medicine, Gandhi Medical College, Bhopal, MP, India

Corresponding Author: Anil Sejwar

ABSTRACT

Background: PAH is the high blood pressure in the lungs due to the obstruction in the lung arteries. Sildenafil is an oral medication approved by WHO for the treatment of PAH.
Aims and objectives: To evaluate the efficacy and safety of sildenafil citrate in Pulmonary Artery Hypertension.
Materials and Methods: Present retrospective study was performed at Department of Medicine, Gandhi Medical College and associated Hamidia Hospital from Jun 2018 to Dec 2019. This study included 150 patients of PAH, they were given sildenafil (20 mg 3 times a day) for 16 weeks and evaluated on 6-min walk distance, WHO functional class and hemodynamic parameters.
Results: Post treatment 6-min walk distance was improved form 396.20±92.10 meters to 470.10 ± 79.80 m (P<0.001), WHO functional class improved from 0 to 15 in Class 1, from 63 to 105 Class II, from 78 to 30 in class III and from 9 to 0 in class IV and mPAP reduced from 63.52 ± 17.28 mmHg to 59.05 ± 12.99 mmHg.
Conclusion: Sildenafil is a safe, effective and inexpensive treatment option for PAH patients. Sildenafil therapy shown the improvements in exercise capacity, hemodynamic indices and overall survival of patients of PAH

Keywords: pulmonary arterial hypertension, microvasculature, sildenafil, phosphodiesterase inhibitor, ventricular.

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a rare disease characterized by the high blood pressure in the pulmonary arteries, which deliver blood from the heart to the lungs. It is gradual as the arteries become narrow, stiffen and blocked over the time. The narrowing and blockage of the pulmonary arteries causes the right side of heart to work harder to pump blood through the lungs. In PAH remodelling of the pulmonary vasculature gradually heighten the pulmonary vascular resistance and causes the right ventricular failure.[1]

Potential causes of PAH included the Heart abnormalities, such as congenital heart defects and Eisenmenger syndrome, viral infections such as HIV, connective tissue disorders, such as scleroderma and lupus, due to medication like methamphetamines, chronic liver disease, or cirrhosis, glycogen storage disorders or von gierke disease and the genetic mutations.

WHO Functional Assessment for Pulmonary Hypertension (PH) [2], Class I included the patients with PH but not resulting in limitation of physical activity. Class II includes the patients with PAH causing a slight limitation in physical activity but comfortable at rest. Ordinary physical activity causes undue fatigue and chest pain. Class III include the patients with PH resulting the limitation in physical activity but comfortable at rest. Less than ordinary activity causes undue dyspnea and

near syncope. Class IV includes the patients with PH with incapability of physical activity without symptoms, manifestation of right heart failure. Discomfort even at rest which increases with any physical activity.

The drug therapy targets the three main recognized biological signalling pathways in PAH i.e. the endothelin, nitric oxide and prostacyclin pathways. The available drugs specific to PAH are endothelin receptor antagonists, phospho-diesterase type-5 inhibitors (PDE-5), soluble guanylate cyclase stimulators and prostanoids.[3]

Sildenafil is cost effective easily available PDE-5 inhibitor that has been approved for the treatment of PAH in the USA and European Union since 2005. It acts to widen the blood vessels by blocking the PDE-5, which normally breaks down cGMP. Higher levels of cGMP increases signaling to relax and widen the blood vessels of the lungs. [4] This study is planned to assess the safety and efficacy of Sildenafil PDE-5 inhibitor.

MATERIALS AND METHODS

Present retrospective study was carried out at the GMC Bhopal for a period of 18 months from Jun 2018 to Dec 2019. For this study 150 subject for this study based on the formal consent, WHO functional class II, III or IV and of age more than 18 years. Subjects who were suffering from diabetes, cardiovascular disease or on any medication at the time of enrolment were excluded from this study.

PAH for this study was defined based on the European Society of Cardiology guidelines i.e. the resting mean of pulmonary artery pressure (mPAP) >25 mm Hg.

All the subjects were given the sildenafil (20 mg orally, three times per day) and evacuated on six-min walk distance test, ECG markers, serum markers, WHO functional class and hemodynamic assessments after 16 weeks of commencement of therapy. All the observations were made at the baseline of initiation of sildenafil therapy.

Follow up was done at 16th week and every 3 months after that. The results were measured as the change in the 6-min walk distance, change in WHO functional class, ECG parameters and hemodynamic indices.

Physical examinations, laboratory tests and interviews were done to assess the adverse effect of therapy.

All the data analysis was performed using SPSS ver. 20 software. Quantitative data is expressed as mean and standard deviation whereas categorical data is expressed as number and percentage. Descriptive analysis was performed to obtain the baseline values of study population.

RESULT

Table 1: The baselines characteristics of the subjects

Factor	Count/Mean	%
Age	32 ± 15 years	
Gender		
Male	60	40%
Female	90	60%
Cause of PAH		
Idiopathic	105	70%
Connective tissue disorders	15	10%
Other	30	20%
WHO functional class		
II	63	42%
III	78	52%
IV	9	6%
Exercise capacity		
6-min walk distance	396.20±92.10 m	
Hemodynamic features		
Heart beat rate (per min)	82.10 ± 15.96	
SBP (mmHg)	106.98 ± 13.05	
DBP (mmHg)	71.01 ± 11.98	
mPAP, mmHg	64.05 ± 18.05	

All the subjects were treated with Sildenafil PDE-5 inhibitor and observed for the safety and efficacy.

As part of this study exercise capacity and WHO functional class assessments were done. At baseline the mean of 6-min walk distance was 396.20±92.10 meters, post 16 week of sildenafil therapy it improved to 470.10 ± 79.80 m (P<0.001).

Similarly post sildenafil treatment the WHO functional class of the subjects improved significantly as in Class 1 from 0 to 15, in

Class II from 63 to 105, in class III from 78 to 30 and in class IV from 9 to 0.

Heart rate improved from 82.10 ± 15.96/min to 79.98±13.00/min, systolic blood pressure (SBP) improved from 107.29±12.65 mmHg to 116.00±12.98 mmHg, diastolic blood pressure (DBP) increased from 70.54±12.03 mmHg to 73.05±10.01 and mPAP reduced from 63.52±17.28 mmHg to 59.05±12.99 mmHg.

During this study no death or adverse effects of sildenafil were recorded except the minor side effects like headache, dyspepsia and blurry vision but none of the subjects had discontinue the treatment due to these effects.

DISCUSSION

Results of the current study showed that the sildenafil PDE-5 is well tolerated and significantly improved the patient's exercise capacity, WHO functional class and hemodynamic characteristics.

In present study the 6-min walk distance at baseline was 396.20±92.10 meters, post 16 week of sildenafil therapy it improved to 470.10 ± 79.80 m (P<0.001) i.e. overall improvement of 74 m/6min. In similar study Michelakis E et recorded an increase of 128 m in 6-min walk distance post sildenafil treatment of in PAH patients. [5]

Galiè et al study observed 40 to 50 meter increase in the six-minute walk distance after the sildenafil PDE-5 treatment. [4]

Results of these studies are in consonance to our study where post sildenafil treatment an improvement of 75 m in the 6-min walk distance was recorded.

In present study post PDE-5 therapy the WHO functional class were improved significantly, before treatment there were zero subjects in class I and 9(3%) in class IV but post treatment there were 15(10%) in class I and zero were in class IV. Similar observations were made by Galiè et al who recorded that 7% of patients receiving placebo improved in at least one functional class, 28% of patients receiving 20 mg sildenafil improved in at least one functional class. [4]

Rubin LJ, et al also reported that base line, more than 90 % patients in WHO functional class III after 16 week 38% improved to class II and 3 percent and 1 percent, respectively, had improved to class I. [6]

Results of these studies evidently support our findings where WHO function class of patients increased post sildenafil therapy.

Present study observed the decrease in heart rate from 82.10 ± 15.96/min to 79.98 ± 13.00/min, in similar study Richalet JP, et al examined the effects of sildenafil and observed that the sildenafil group have significantly lower heart rate, higher oxygen saturation, and lower PASP compared to the placebo group. [7]

Current study shows that the post sildenafil therapy SBP increases from 107.29±12.65 mmHg to 116.00 ± 12.98 mmHg, DBP increased from 70.54±12.03 mmHg to 73.05 ± 10.01. which is in contrast to the results of Kloner et al, who reported that sildenafil leads to a small, usually clinically insignificant drop in blood pressure, this variation could be due to the sample selection as current study only enrolled the PAH patients in their study they have enrolled normal healthy subjects as well. [8]

Present study observed that post sildenafil treatment mPAP reduced from 63.52 ± 17.28 mmHg to 59.05 ± 12.99 mmHg. Kothari SS et al observed similarly i.e. mPAP decreased from 62 mmHg to 47 mmHg after a mean of 7 months of sildenafil treatment. [9]

Michelakis et al also observed the similar reduction of mPAP in subjects treated with sildenafil. [10] Above discussion show that results of current study are in agreement with previously done studies and trails.

CONCLUSION

Present study conclude that the oral sildenafil (PDE-5) is an inexpensive, safe and effective method to achieve the

pulmonary vasodilatation PAH patients. We observed that sildenafil improved the 6-min walk distance, WHO functional class, hemodynamics and overall survival of subjects.

REFERENCES

1. Seferian A, Simonneau G. Therapies for pulmonary arterial hypertension: where are we today, where do we go tomorrow? Eur Respir Rev 2013; **22**: 217–226.
2. Hsu CH, Glassner C, Foreman AJ, et al. Treadmill testing improves survival prediction models in pulmonary arterial hypertension. Am Heart J 2011; 162: 1011–1017.
3. Humbert M, Sitbon O, Simonneau G. Treatment of pulmonary arterial hypertension. N Engl J Med 2004; 351: 1425–1436.
4. Galie` N, Ghofrani HA, Torbicki A, Barst RJ, Rubin LJ, Badesch D, Fleming T, Parpia T, Burgess G, Branzi A, Grimminger F, Kurzyna M, Simonneau G. Sildenafil citrate therapy for pulmonary hypertension. N Engl J Med 2005; 353: 2148–2157.
5. Michelakis E, Tymchak W, Lien D, Webster L, Hashimoto K, Archer S. Oral sildenafil is an effective and specific pulmonary vasodilator in patients with pulmonary arterial hypertension. Circulation 2002; 105: 2398–2403.
6. Rubin LJ, Badesch DB, Barst RJ, et al. Bosentan therapy for pulmonary arterial hypertension. N Engl J Med 2002;346:896-903.
7. Richalet J-P, Gratadour P, Robach P, et al. Sildenafil inhibits altitude-induced hypoxemia and pulmonary hypertension. Am J Respir Crit Care Med. 2005;171:275–81.
8. Kloner RA. Cardiovascular effects of the 3 phosphodiesterase-5 inhibitors approved for the treatment of erectile dysfunction. Circulation. 2004;110:3149–55.
9. Kothari SS, Duggal B. Chronic oral sildenafil therapy in severe pulmonary artery hypertension. Indian Heart J. 2002; 54(4):404-9.
10. Michelakis ED, Tymchak W, Noga M, Webster L, Wu XC, Lien D, Wang SH, Modry D, Archer SL. Long term treatment with oral sildenafil is safe and improves functional capacity and hemodynamics in patients with pulmonary arterial hypertension. Circulation 2003; 108: 2066–2069.

How to cite this article: Wadhwani JL, Sejwar A, Sharma M et.al. Evaluating efficacy and safety of sildenafil citrate in pulmonary artery hypertension. International Journal of Research and Review. 2020; 7(1): 498-501.

******