CASE REPORT

SILDENAFIL IN THE TREATMENT OF PRIMARY PULMONARY HYPERTENSION – A CASE REPORT

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Abstract: *Pulmonary arterial hypertension (PAH) is a life threatening, progressive and often fatal, debilitating disorder with a grave prgnosis. The increased pulmonary artery(PA) pressure found in PAH is due to disturbances in key vascular mediator pathways including relative deficiencies of vasodilators like nitric oxide (NO) and prostacycline, as well as increased production of vasoconstrictors like endothelin and thromoboxanes. Various vasodilators such as bosentan, eporosternol, iloprost and sildenafil have a definite role in PAH inhibitor, which is stabilization of cyclic guanosine monophosphate (C GMP), resulting in increase in NO at the tissue level thereby causing pulmonary artery vasodilatation. Sildenafil is more potent acute pulmonary vasodilator than inhalded metric oxide (NO). In addition sildenafil has been found to exert additive effects on pulmonary hemodynamics when used in combination with inhalded iloprost or NO. A case of severe pulmonary arterial hypertension managed effectively with sildenafil is being reported here.*

INTRODUCTION

Pulmonary arterial hypertension (PHA) includes primary pulmonary hypertension (PPH) with no apparent cause, PAH secondary to congenital shunt lesions, connective tissue disorders, portal hypertension, drug induced and HIV related PAH. It is a progressive disease, affects predominantly women in early life and is characterized by progressive breathlessness, exertion limitation, frequent decline and failure of right ventricle. It is estimated that PAH affects 100,00 patients worldwide. Although many treatments are available, but there is no known cure[1,2] The current therapeutic options available for PPH include calcium channel blockers anticoagulants, eporostenol (prostacycline), iloprost, bosentan and sildenafil[3]. Sildenafil a selective PDE-5 inhibitor is a potent pulmonary vasodilator and is effective in patients of moderate to severe PH[4]. Otral sildenafil has been found to be clinically effective in PPH refractory to epoprostenol[5].

CASE REPORT

A 25 years old female nondiabetic, non hypertensive presented with worsenining exertional dyspnoea being unabale to cycle for 100 yards (NYHA) class III) and increasing fatigue sisnce 5 years. There was no history of orthopnoea, syncope and hemoptysis. She complained of swelling of feet and case since last 3 months. She denied any history of exposure to chemicals, appetite suppressants or collagen vascular disease. No member of ther family had such problem. Her physical examination revealed poor body built, pulse 110/min, regular, BP 100/60 mmHg, JVP raised with prominent a and v waves with bilaterial edema. There was no cyanosis or clubbing. Cardiovascular examination revealed right ventricular heave, signs of tricuspid regurgitation (TR) and ejection systolic murmur in the pulmonary area. Right ventricular S3 gallop suggestive of right ventricular failure was audible. Her laboratory findings revealed Hb 9.2 G/d1, TLC &DLC were within normal limits. Total collagen profile was normal and HIV non reactive. ECG showed evidence of sinus tachycardia with features of right arterial enlargement with right ventricular hypertrophy with strain pattern and right axis deviation suggestive of pulmonary hypertension. X – ray chest revealed right heart enlargement with dilatioation of main pulmonary artery as well as right descending pulmonary artery. Echocardiography revealed dilated right sided chambers and main pulmonary artery. Lung functions showed only mild airflow limitation. Doppler echocardiography demonstrated evidence of TR and PAH. The estimated systolic pulmonary artery pressure was 110 mmHg and right atrial pressure of 22 mmHg. Left ventricular systolic function was preserved.

The patient was started on dioxin, diuretics, warfarin (anticoagulant) and oral sildenafil given 25 mg thrice daily. Gradually the dose of sildenafil was titrated to 150 mg/day. The patient started improving within 3 weeks of therapy and showed progressive improvement over the next three months. On a follow up at 6 months, she was able to cycle 200 yards (NYHA Class II) comfortably. Echocardiography showed a significant reduction in systolic PA pressure from previous 110 mmHg to 90 mmHg after treatment.

DISCUSSION

PPH is characterized by progressive elevation of mean pulmonary artery pressure (PAP) more than 25 mmHg at rest, right ventricular failure and death[2]. Current therapeutic options for PPH mostly include limitation of physical activity, long term anticoagulation and vasodilator therapy Calcium channel antagonists are the main stay of therapy, but only 25-30% of patients respond. Major advancement in the treatment of PPH is the development of two orally active agents bosentin (endothelin receptor antagonis) and Sildenafil which are selective pulmonary vasodilators. Sildenafil inhibits cyclin GMP specific phosphodiesterase enzyme resulting in smooth muscle relaxation via a nitric-oxide dependent increase of GMP further producing decrease in elevated PAP [3,4]. Other treatment options include epoprostenol (prostacycline) infusion and heart lung transplantation, which are limited by nonavailability in many parts of India, clinical difficulties, complications and high costs [5,6] . The dose of sildenafil for PPH remains unknown. Studies in awake limbs7 with PPH demonstrated a dose related (serial dose 12.5 mg, 25 mg and 50 mg) reduction of PAP by 21% and 43% and pulmonary vascular resistance by 18%, 23% and 45% respectively. But in a study by Malhotra S et al[8] using oral sildenafil 25 mg thrice daily titrated to 150 mg/day, there was reduction in PAP to the tune of 20 mmHg and in the present study it was again 20 mmHg. Sildenafil was tolerated without any tolerance and side effects. When administered in combination with inhaled nitric oxide (NO) augments and prolongs the pulmonary vasodilatory effect of NO and prevents the rebound pulmonary vasoconstriction which occurs after NO inhalation in the absence of sildenafil. It acts synergistically with inhalded iloprost to cause strong pulmonary vasoilattation in PPH[9].

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