

## The management of patients with Pulmonary Hypertension- An introduction for Primary Care Physicians

Dear Doctor

As you will be aware, a patient attending your practice has been referred to the Sheffield Pulmonary Vascular Disease Unit (PVDU) at the Royal Hallamshire Hospital. This unit is one of five nationally designated specialist centres for managing patients with pulmonary hypertension in the UK. Patients with this potentially serious condition are complex and the therapies are complicated and expensive. In order ensure that patients receive the highest level of care, in a safe and cost effective manner, it is necessary for the Sheffield PVDU team to work closely with the primary care providers responsible for their routine care.

The purpose of this document is to provide an introduction for primary care practitioners outlining the nature and shared management of patients with pulmonary hypertension.

### ***Introduction.***

The primary focus of the Sheffield PVDU is to assess and co-ordinate the treatment of patients with pulmonary arterial hypertension and chronic thromboembolic disease. Pulmonary hypertension resulting from left heart dysfunction or hypoxic lung disease (eg. COPD) is treated differently and as such should be referred for review by a Cardiologist or Respiratory Physician as appropriate.

Pulmonary arterial hypertension (PAH) is a rare condition (estimated prevalence 20 to 40 per million in the UK) where is pre-capillary circulation of the lung becomes damaged and fibrosed. The disease may strike at any age and is not limited to any particular racial distribution. The underlying aetiology is quite varied, and may be idiopathic, familial, or related to connective tissue disease, congenital heart disease or viral infection. Regardless of the underlying cause, this condition is progressive in nature and results in increasing resistance to blood flow through the lungs and subsequent right heart strain and failure.

Symptoms suggestive of pulmonary hypertension are non-specific in nature, ranging from isolated exertional breathlessness and fatigue to peripheral oedema, arrhythmia, chest pain and syncope. Patient are classified using the modified New York Heart Association (NYHA) classification system (also known as the WHO Class) according to their level of function, with Class I patients being unlimited, and Class IV patients being breathless at rest. Further determination of disease severity can be made by assessing exercise capacity (by incremental shuttle walk test ), cardiac dimensions and function on imaging (CT or MRI scanning) or neuro-hormonal markers of right ventricular strain (i.e plasma BNP measurement). However, in all cases, the diagnosis and prognostic outcome can only be accurately assessed by performing invasive measurements by means of a right heart catheter study.

Chronic thromboembolic pulmonary hypertension (CTEPH) occurs when patients sustain multiple pulmonary emboli that fail to completely resolve. This results in multi-layered fibrotic tissue forming within the pulmonary arteries which obstructs blood flow. Patients develop progressive right heart dysfunction in a manner similar to PAH, although there may be more sudden deteriorations consistent with acute pulmonary emboli. However, patients with this condition do not always experience such acute events, and may not in fact have experienced a symptomatic DVT or PE.

### ***Assessment.***

All patients referred to the Sheffield PVDU will undergo a thorough assessment involving careful history taking and examination, lung function and imaging in order to confirm the aetiology and exclude other potential causes of pulmonary hypertension. Echocardiography is used as the primary screening modality. Those patients with scans consistent with pulmonary hypertension undergo right heart catheterisation for confirmation of the diagnosis. In most cases this assessment occurs as part of an inpatient admission, although patients may also be offered the possibility of day case investigations. As part of this process, every effort is made to thoroughly educate patients regarding the nature of their condition, treatment alternatives and longer term expectations in a controlled and understandable way. Patients will be offered written information regarding their condition and details of how to contact the unit after hours should they have any further concerns regarding their treatment.

### ***Available Therapies.***

Without treatment, historical data suggests that patients with either PAH or CTEPH have a poor prognosis, which is dependant on the severity of their pulmonary hypertension and level of function at the time of diagnosis. Although early assessment and initiation of therapy may significantly improve the outcome for patients, medical therapy is not curative. A unique subset of patients, those with CTEPH where the material involves the central pulmonary arteries, may be suitable of surgical intervention to remove the obstruction. In many patients who undergo this procedure of Pulmonary Endarterectomy, the improvements in function and life expectancy can be considerable. Where appropriate this procedure is considered, although for the majority of patients attending the PVDU, medical therapy will be required.

All young female patients are strongly advised to avoid pregnancy, which is associated with high maternal mortality (up to 50%). Contraceptive measures should be considered carefully, as interactions with the medical therapies mentioned below can occur.

All patients with established pulmonary hypertension are commenced on long term anticoagulation unless contraindicated. Available evidence suggests that ongoing thrombosis of damaged pulmonary vessels further contributes to the progression of the disease. Patients may also receive diuretic therapy, oxygen supplementation and anti-arrhythmic therapy to palliate symptoms and improve quality of life.

Currently available advanced medical therapies attempt to influence that pathways involved in regulating the repair of pulmonary blood vessels. This may involve supplementing pathways that promote vascular repair (eg. prostacyclin or nitric oxide), or blocking those pathways that promote abnormal growth (eg. endothelin). The choice of therapies is tailored to the individual patients based on the severity of the patient's condition, the complexity of the treatment and the available scientific evidence to support its use. At present, three main drug classes are available:

1. *Endothelin receptor antagonists-* (e.g Bosentan)

The agents block the deleterious effects of endothelin and thus prevent vasoconstriction and fibrosis. Long term data suggests these agents improve function, exercise capacity and survival. These are oral treatments and are generally well tolerated, although may be associated with peripheral oedema and deranged liver function, and therefore require regular long term monitoring.. Interactions with other medications are common, most notably with anticoagulants and advice should be sought when co-prescribing new therapies.

2. *Phosphodiesterase Type 5 Inhibitors* (e.g Sildenafil)

These agents selectively augment the vaso-dilative effect of nitric oxide in the pulmonary circulation. They are also orally administered, well tolerated and have been shown to improve function and exercise capacity. Longer term survival data is limited at this time. Reported adverse effects include nasal congestion, epistaxis, peripheral oedema and dyspepsia. Drug interactions are uncommon, although co-administration of nitrate based compounds is contra-indicated.

3. Prostacyclin analogues- (e.g Iloprost, Treprostinil)

These agents promote vasodilation and vascular repair. They are potent agents which may significantly improve function and outcome. They are currently available as nebulised and continuous sub-cutaneous or intravenous infusion forms. They are usually reserved for the most severe patients, or those failing to respond to other therapies. Systemic adverse effects are common, particularly following initiation or alteration of the dose of these agents. These include headache, flushing, nausea, diarrhoea, generalised bone pain and hypotension, although these effects usually diminish over time. Drug interactions are uncommon.

Advanced medical therapies for pulmonary hypertension are expensive, with the complicated intravenous or subcutaneous therapies costing up to £37,000 per year. In all cases, approval for funding for such therapies will be sought from the patient's local Primary Care Trust or Specialist Commissioning Group, and the responsibility for ongoing prescribing such therapies will rest with the Sheffield PVDU. All patients are encouraged to maintain regular contact with their primary care physician, and to discuss any concerns or adverse effects that they may be experiencing. Although you may not be familiar with these medications, we ask for your assistance in organising the long term monitoring of the patients' condition and potential adverse events attributable to the therapy.

Pulmonary hypertension is a rapidly evolving field, and many new agents are currently undergoing clinical evaluation. Your patient may be invited to participate in clinical trials of such agents and you will be provided with information regarding the nature of the agents your patient may be offered.

***Social and Psychological support.***

The diagnosis of pulmonary hypertension can be devastating for some patients. Each patient receives written information regarding their diagnosis and potential therapies, and is given the full contact details of the unit. Sheffield PVDU also works closely with Supportive and Palliative Care Nurses and Social Services. Where appropriate, patients may be referred for assistance with a variety of social and psychological problems, many of which will require co-ordination with local services. In addition, patients are given information regarding local and national patient support organisations that can provide additional information, support and assistance.

***Summary***

The Sheffield PVDU team acknowledges that managing patients with this potentially life threatening condition is often challenging. The diagnosis and follow-up of these patients can be complicated and demanding. We are available for advice and assistance when required, and will be happy to provide you with additional literature regarding pulmonary hypertension. We endeavour to ensure that primary care physicians are informed of all changes in patient condition and treatment in timely and appropriate manner.

For advanced medical therapies, drug prescribing and funding arrangements are the responsibility of Sheffield PVDU. The assistance of primary care physicians will be requested to monitor the adverse effects of therapy, facilitate changes in anticoagulation (particularly when invasive procedures are required) and to co-ordinate the management of associated medical conditions. Although patients attend the unit on a regular basis, in no way is this intended to replace the holistic care that is provided their primary care team.

Through an integrated shared care management strategy it is hoped that your patient will be offered effective therapeutic options that improve function, quality of life and survival in a safe and cost-effective manner.

***Contact numbers:***

If you require further information regarding the investigations or therapies outlined above or the service itself, please do not hesitate to contact Dr David Kiely, Dr Rodney Hughes, Dr Charlie Elliot or Iain Armstrong:

Phone number: **0114 271 2590**

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