PULMONARY HYPERTENSION (PH)

Pulmonary hypertension (PH) is a disorder of the pulmonary circulation in which elevated pressure in the pulmonary vascular circuit can, when severe, lead to right heart failure and eventually cause death. Pulmonary arterial hypertension (PAH) is a subtype of PH.

Current recommendations suggest that screening should be performed only on persons at increased risk for developing PAH.

The diagnosis of PAH is usually made during the process of evaluating symptoms such as dyspnoea, exercise intolerance, chest pain, or syncope. Electrocardiographic changes, elevated brain natriuretic peptide (BNP) levels, and echocardiographic changes may suggest the diagnosis; however, current recommendations state that a right-heart catheterization (RHC) is “strongly advised” to formally make the diagnosis of PH. A ventilation-perfusion (V/Q) scan should be performed to evaluate for chronic thromboembolic disease. Other tests include thyroid function tests, liver function tests (LFT), antiphospholipid antibodies, testing for collagen vascular diseases, and testing to detect the human immunodeficiency virus (HIV). A baseline BNP. All patients with PH should undergo baseline pulmonary function testing including spirometry, determination of lung volumes, and evaluation of the diffusion limitation for carbon monoxide (DLCO). Quantification of exercise tolerance is often performed by measuring the distance that a patient can walk in 6 minutes (6MWD).

General Management-Related Issues include supplemental oxygen, anticoagulation with warfarin, therapy with prostacyclin analogs (prostanoids) including epoprostenol, treprostinil, iloprost etc., endothelin receptor antagonists (bosentan), Phosphodiesterase type 5 (PDE5) inhibitors such as sildenafil or tadalafil; and Atrial septostomy (AS), pulmonary thromboendarterectomy and finally lung transplantation.

The prognosis of untreated PAH is poor; however, with therapy the expected survival and quality of life have improved dramatically.

QUESTIONS

Select an answer for each question.

1. **Current recommendations** suggest that screening should be performed only on the following persons:
   A. Those at increased risk for developing pulmonary arterial hypertension (PAH)
   B. All males over the age of 50
   C. African American males over the age of 50
   D. Patients with a known history of renal disease who have undergone coronary artery bypass graft (CABG)
2. Prenatal testing is also available for screening in cases where FPAH has been identified in family members; however, because of the low occurrence of the disease, even when the test is positive, _____% will go on to develop PAH.
   A. 3% to 5%
   B. 5% to 10%
   C. 10% to 20%
   D. 20% to 30%

3. The initial evaluation of patients with PH should consist of:
   A. Testing to confirm the diagnosis
   B. A search for causative disorders and complications from the disease
   C. A determination of the severity of the disease
   D. All of the above

4. If right-heart catheterization confirms the diagnosis of PH:
   A. The patient should be considered for transplantation immediately
   B. A vasodilator should be given to determine the degree of pulmonary arterial vasoactivity
   C. Home oxygen therapy is recommended
   D. Right heart catheterization cannot confirm a diagnosis of PH

5. A ventilation-perfusion (V/Q) scan should be performed to evaluate for:
   A. PaO₂ variations
   B. Chronic thromboembolic disease
   C. FEV₁ > 75%
   D. Percent of peripheral vascular involvement

6. Epoprostenol must be given in the following manner:
   A. Through continuous intravenous administration
   B. Orally, twice a day
   C. Via subcutaneous injection
   D. Either orally or through q4 hour injections depending on the patients severity

7. The two receptors for endothlin-1 that have been identified as playing a role in PAH are:
   A. ET₁ and ET₂
   B. ET₁ and ET₄
   C. ET₆ and ET₈
   D. ET₁ and ET₉

8. The presence of a _____ has been shown to confer a survival advantage in patients with severe IPAH awaiting lung transplantation.
   A. Decreased stroke volume
   B. Polycythaeemia
   C. Increased functional residual capacity
   D. Patent foramen ovale
ANSWERS

1. **Those at increased risk for developing pulmonary arterial hypertension (PAH)**
   Current recommendations suggest that screening should be performed only on persons at increased risk for developing PAH. Those with first-degree relatives with idiopathic PAH (IPAH), those with a known genetic mutation that has been associated with the development of familial PAH (FPAH), those with the scleroderma spectrum of diseases, patients with portal hypertension undergoing evaluation for liver transplantation, and patients with congenital heart disease and systemic-to-pulmonary shunts should undergo screening for occult pulmonary hypertension.

2. **10% to 20%**
   Prenatal testing is also available for screening in cases where FPAH has been identified in family members; however, because of the low occurrence of the disease, even when the test is positive, only 10% to 20% will go on to develop PAH. For this reason, the role of prenatal screening has been questioned, particularly if it is being performed for the purpose of pregnancy termination.

3. **All of the above**
   The initial evaluation of patients with PH should consist of testing to confirm the diagnosis, a search for causative disorders and complications from the disease, and a determination of the severity of the disease.

4. **A vasodilator should be given to determine the degree of pulmonary arterial vasoreactivity**
   If right-heart catheterization confirms the diagnosis of PH, a vasodilator should be given to determine the degree of pulmonary arterial vasoreactivity.

5. **Chronic thromboembolic disease**
   A ventilation-perfusion (V/Q) scan should be performed to evaluate for chronic thromboembolic disease.

6. **Through continuous intravenous administration**
   Epoprostenol was the first studied prostanoid, and its introduction some 10 years ago revolutionized the treatment of patients with PAH. Epoprostenol is unstable at room temperature and must be kept cold prior to and during infusion. Because of its short half-life in the bloodstream (only about 3-5 minutes), epoprostenol requires continuous intravenous administration; usually via a tunneled catheter into a central vein.

7. **ET\textsubscript{A} and ET\textsubscript{B}**
   Two receptors for endothelin-1 have been identified, ET\textsubscript{A} and ET\textsubscript{B}, with the former mediating vasoconstriction and remodeling and the latter involved in the clearance of endothelin-1 and perhaps also in vasodilatation and NO release. Many endothelin receptor antagonists, including sitaxsentan and ambrisentan, are being studied in PH; however, only bosentan is currently available for use in the United States.

8. **Patent foramen ovale**
   The presence of a patent foramen ovale has been shown to confer a survival advantage in patients with severe IPAH awaiting lung transplantation. Atrial septostomy, by creating a right-to-left intra-atrial shunt, decompresses the right ventricle and has been shown to immediately improve symptoms of right ventricular function and exercise capacity, and has been shown to increase cardiac index anywhere from 15% to 58%.