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PULMONARY HYPERTENSION AND ITS MEDICAL MANAGEMENT

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Annotation. Pulmonary hypertension is a condition that affects the blood vessels in the lungs. It develops when the blood pressure in your lungs is higher than normal. About 1% of people globally have pulmonary hypertension. Pulmonary hypertension makes the heart work harder than normal to pump blood into the lungs. This can damage the heart and cause symptoms such as shortness of breath, chest pain, and lightheadedness.

Keywords: chronic thromboembolic pulmonary hypertension (CTEPH), pulmonary arterial hypertension (PAH), Calcium channel blockers.

Pulmonary hypertension (PH) is a pathophysiological disorder, which may involve multiple clinical conditions and may be associated with a variety of cardiovascular and respiratory diseases. The complexity of managing PH requires a multi-faceted, holistic, and multidisciplinary approach, with active involvement of the patients with PH in partnership with clinicians. In recent years, substantial progress has been made in detecting and managing PH, and new evidence is timely integrated in this fourth edition of the ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. These comprehensive clinical practice guidelines cover the whole spectrum of PH with an emphasis on diagnosing and treating pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH). With pulmonary hypertension, the blood vessels to the lungs develop an increased amount of muscle in the wall of the blood vessels. The heart pumps blood from the right ventricle to the lungs to get oxygen. Because the blood does not have to travel very far, the pressure in this side of the heart and in the artery taking blood from the right ventricle to the lungs is normally low—usually much lower than systolic or diastolic blood pressure. When the pressure in this artery gets too high, the arteries in the lungs can narrow and then the blood does not flow as well as it should, resulting in less oxygen in the blood.

Idiopathic Pulmonary Arterial Hypertension Medical Management

IPAH represents a significant clinical challenge, as it has debilitating symptoms and a poor prognosis if left untreated. Pharmacotherapy plays a central role in IPAH management, aiming to alleviate symptoms, improve exercise capacity, and delay disease progression. IPAH pharmacotherapy requires a personalized approach, with treatment selection guided by disease severity, patient characteristics, and therapeutic response. The drug classes used in treating this condition include CCBs, ERAs, phosphodiesterase type 5 inhibitors (PDE-5 inhibitors or PDE-5is), soluble guanylate cyclase stimulators (sGCSs), prostacyclin analogs (PCAs), and prostacyclin receptor agonists (PRAs).

Calcium channel blockers

High-dose CCBs may be used as first-line therapy in patients with IPAH, HPAH, and drug-induced PAH that test positive during vasoreactivity testing. Amlodipine or nifedipine is preferred in patients who are relatively bradycardic at baseline. Diltiazem is preferred in patients who are relatively tachycardic at baseline. Follow-up should be done 3 to 4 months after initiation of therapy. Additional PAH therapy should be started if the patient does not meet treatment goals, ie, low-risk status, classified under WHO-FC I to II, and has marked hemodynamic improvement. CCBs' common side effects include hypotension and edema.

Endothelin receptor antagonists

Endothelin-1 causes vasoconstriction and mitogenic effects via the endothelin type A receptors. Endothelin B receptors promote vasodilation by clearing endothelin-1 and accelerating prostacyclin and nitric oxide production. However, nonselective endothelin receptor or selective endothelin A receptor blockade has similar effectiveness in PAH. Ambrisentan is an endothelin receptor type A antagonist, while bosentan and macitentan are dual type A and type B ERAs. Ambrisentan can cause peripheral edema. Both ambrisentan and bosentan can produce LFT abnormalities. Bosentan can reduce warfarin, sildenafil, and tadalafil levels and negate hormonal contraceptives' effects. Macitentan can decrease hemoglobin levels. These agents are potentially teratogenic and must not be used during pregnancy.

Phosphodiesterase type 5 inhibitors and soluble guanylate cyclase stimulators

These medications primarily act on the nitric oxide pathway. PDE-5is prevent cyclic guanosine monophosphate degradation, resulting in higher nitric oxide levels and vasodilation. These drugs also have antiproliferative effects. Sildenafil, tadalafil, and vardenafil are PDE-5is studied in PAH treatment. These agents cause vasodilation-related side effects, including flushing, headache, and epistaxis.

Riociguat is an sGCS that enhances cGMP production and vasodilation. This medication exhibits antiproliferative and antiremodeling properties in animal models. Riociguat is currently approved for patients with CTEPH. The drug's most common serious adverse effect is syncope. Riociguat should not be combined with PDE-5 inhibitors, as it can precipitate hypotension.

Prostacyclin analogs and prostacyclin receptor agonists

PCAs are potent vasodilators and endogenous platelet aggregation inhibitors with cytoprotective and antiproliferative properties. The prostacyclin pathway is a common pharmacological target in PAH treatment, as it is characteristically dysregulated in this condition.

Epoprostenol is a synthetic prostacyclin analog with a half-life of 3 to 5 minutes and is administered intravenously. Dosing inconsistencies can arise from pump malfunction and catheter obstruction. Other serious adverse effects of intravenous treatment include local site infection and sepsis. Epoprostenol is usually started at a dose of 2 to 4 ng/kg/min and uptitrated based on tolerance of side effects, including flushing, headache, leg pain, and diarrhea.

Treprostinil is often administered via intravenous and subcutaneous routes. Oral and inhaled treprostinil formulations are also available. The drug can be administered via an infusion pump and subcutaneous catheter, but the intravenous route is used only for those who cannot tolerate subcutaneous infusion. Infusion site pain is the most common side effect. Subcutaneous treprostinil is started at a dose of 1 to 2 ng/kg/min, and doses are escalated based on tolerance of side effects, including local site pain, flushing, and headache.

Iloprost is another analog with intravenous formulations available. Selexipag is a PRA and is administered orally.

Idiopathic pulmonary arterial hypertension treatment approach

The medications discussed above target 3 distinct pathways implicated in disease improvement: antagonism of the endothelin system, agonism of the prostacyclin pathway, and agonism of the nitric oxide pathway. Recent updates in hemodynamic definitions for pulmonary hypertension have revised the abnormal mPAP cutoff values from at least 25 to greater than 20 mm Hg and abnormal PVR from greater than 3 to greater than 2 Wood units. While these drugs' efficacy has been studied in patients with mPAP greater than 25 mm Hg and PVR greater than 3 Wood units, their effectiveness in patients with mPAP between 21 to 24 mm Hg and PVR between 2 to 3 Wood units remains uncertain.

Drawing from global experience and randomized controlled trials, the latest ESC/ERS guidelines recommend specific treatment strategies, which include the following:

- General and supportive measures should be provided to all patients.
- The 3-strata risk stratification system (low, intermediate, and high risk) must be used during the initial evaluation, while the 4-strata system (low, intermediate-low, intermediate-high, and high risk) is

recommended for subsequent visits.

• Initial triple therapy with an ERA, PDE-5i, and intravenous or subcutaneous PCA should be started in patients without cardiopulmonary comorbidities classified as high-risk. Lung transplant evaluation should be initiated if the patient remains at high-risk on follow-up.

• Initial therapy should include an ERA and PDE5i in people without cardiopulmonary comorbidities classified as low-to-intermediate risk. A PRA may be added or the PDE5i switched to an sGCS if the patients remain in the intermediate-low risk status. Intravenous or subcutaneous PCA should be added if the patient deteriorates and acquires a high-risk status.

• Initial therapy should include either a PDE5i or ERA in individuals with cardiopulmonary comorbidities. Patients should receive regular follow-up and individualized therapy thereafter.

• Cardiac comorbidities are defined in this context as conditions associated with an increased left ventricular diastolic dysfunction risk, such as obesity, hypertension, diabetes mellitus, and coronary heart disease. Pulmonary comorbidities include parenchymal lung diseases and are often associated with low DLCO (<45% predicted value).

Interventional idiopathic pulmonary arterial hypertension therapy

Balloon atrial septostomy and Potts shunt (a shunt between a left pulmonary artery and descending aorta) can decompress the right heart, improving systemic blood flow and oxygen transportation despite causing desaturation. These complex treatments are rarely performed and have substantial mortality. Thus, these procedures must only be considered in centers with expert providers. Pulmonary artery denervation using intravascular ultrasound catheters and radiofrequency ablation is still in the experimental stages. The technique aims to reduce sympathetic overdrive associated with vasoconstriction and vascular remodeling mediated through the baroreceptors at the pulmonary artery bifurcation.

All in all, except for CTEPH, which sometimes can be reversed by surgery, pulmonary hypertension often cannot be fully cured, but there are several treatments that can improve quality of life for people who have the condition. Research indicates that people who are diagnosed early tend to have better outcomes, making early detection and treatment important.

Reference:

1. Boburjon, M., & Ziyomiddinovich, N. M. (2024). BOLALARDAGI YASSI OYOQLIKNING PROFILAKTIKASI VA UNI DAVOLASHDA ORTOPEDIK POYABZALNING AHAMIYATI. TADQIQOTLAR, 29(2), 109-111.

2. Boburjon, M., & Ziyomiddinovich, N. M. (2024). DIABET KASALLIGI, UNING TURLARI VA UNI DAVOLASH USULLARI. TADQIQOTLAR, 29(2), 112-115.

3. Jumakulovich, E. N., Ziyomiddinovich, N. M., Parmonovich, I. S., Shukrulloevich, O. A., & Ermatovna, K. K. (2023). EVALUATION OF THE EFFECTIVENESS OF THE DAILY DIET OF SCHOOLCHILDREN SUFFERING FROM IRON DEFICIENCY ANEMIA FROM ENRICHED LOCAL PROTEIN-CONTAINING PRODUCTS. JOURNAL OF BIOMEDICINE AND PRACTICE, 8(4).

4. Jumakulovich, E. N., Umarovich, A. I., Najmiddinovich, S. A., Ziyomiddinovich, N. M., & Ermatovna, K. K. (2023). ҚАНДЛИ ДИАБЕТ КАСАЛЛИГИ ОЛДИНИ ОЛИШНИНГ ГИГИЕНИК ХУСУСИЯТЛАРИ. JOURNAL OF BIOMEDICINE AND PRACTICE, 8(4).

5. Nasirdinov, M., Ermatov, N., & Khajiev, D. (2022). HYGIENIC ANALYSIS OF THE RESULTS OF TREATMENT OF SCHOOLCHILDREN WITH IRON DEFICIENCY ANEMIA WITH LOCAL BEAN MEAL IN DAILY RATION. In Современная наука и молодые учёные (pp. 128-130).

6. Nasridinov, M., Ermatov, N., & Akhunova, M. Hygienic Analysis of Micronutrients Consumption Degree in Daily Diet of the Pupils that Live in Rural Conditions of Fergana Valley.