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REVIEW OF PULMONARY EMBOLISM

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ABSTRACT

Pulmonary embolism is a blockage of main artery or one of its branches of lung by the fat, amniotic fluid, embolisation of air or any other foreign substances. It is also due to formation of thrombus [blood clot] in the arteries of lung. Due to the pulmonary embolism the blood circulation in the body will be effected. Sometimes PE leads to death also by the lacking of breathing. In USA the annual incidence rates per 1000 persons aged 65-69 are 1.3 affected by pulmonary embolism. The diagnosis of pulmonary embolism at the earlier stage will be difficult because the symptoms like difficulty in breathing and chest pain are not easily differentiated from the other diseases like myocardial infarction. The usage of drugs like anti coagulants and thrombolytic cause bleeding problems even though they shows the antagonistic activity of pulmonary embolism at higher doses. Physician responsibility is to successfully avoid bleeding disorders are at the time of prevention of pulmonary embolism. And also by conducting of programs which should strive to coordinate care , by region wide guidelines and by implementing of care programs there is a chance to elaborate knowledge about the pulmonary embolism to the physicians and also there is a chance to bring awareness among the public which may decreases the number deaths due to pulmonary embolism annually.

KEY WORDS : **Pulmonary embolism, myocardial infraction, intra vascular co agulation, e.t.c.**

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INTRODUCTION

Pulmonary embolism [PE] is a blockage of the main artery of the lung or one of the branches by a substance. That has travels to the body through the blood stream [embolism][1]. Pulmonary embolism is a blood clot in the lung. It usually comes from smaller vessels in the leg, pelvis, arm [or] heart when a clot forms in the legs or arms it is referred to as a deep venous thrombosis [DVT][2]. Usually this is due to embolism of a thrombus [blood clot] from the deep process termed venous thrombo embolism. A small proportion is due to the embolization of air, fat or amniotic fluid. The blood flow through the lungs and the resultant pressure on the right ventricle of the heart leads to the symptoms and signs. Pulmonary embolism is increased in various situations such as cancer and prolonged bed rest[1].

ETIOLOGY

Although the blood clot is the most common cause of PE. Air, fat, bone marrow, foreign bodies, arthroplasty, cement, tumor cells also can obstruct the pulmonary vessels. Bed rest and inactivity pose the greatest risk for developing deep vein thrombosis. Certain medical conditions common among the elderly [e.g.; trauma to leg vessels, obesity, heart failure malignancy, hip fracture myelo proliferative disorders] predispose them to venous thrombosis as do smoking estrogen use, stamoxifen [synthetic, anti estrogenic compound] therapy, the presence of a femoral venous catheter surgery and immobility. Risk factors for venous thrombosis are vessel wall injury, stasis and conditions that increase the tendency of the blood to clot including rare deficiencies of anti thrombin III, protein c and proteins as well as disseminated intravascular coagulation. Polycythemia vera, the presence of a lupus anticoagulant or anti phosphor lipid antibodies. Aging is also associated with increased coagulation and products of fibrinolysis, resulting in an overall pre thrombotic state. About 90% of blood clots that cause pulmonary embolism originate in the legs. the risk that a clot will embolize the lodge in the lungs is greater if the clot is in the popliteal or iliofemoral vein [about 50%] than if it is confined to the calf veins [<5%] less common sites of thrombosis that may leads to PE are the right atrium, right ventricle, and the pelvic, renal, hepatic, subclavin and jugular veins[3].

Mainly the major risk factors for PE are of;

1. Stasis.
2. Endothelial injury.
3. Hypercoagulable states.

Most thrombi are derived from the veins of the thigh but can arise from mural [pertaining to the wall of cavity, organ [or] vessel] thrombi in the right side of the heart, surgical procedure that risk intimal injury are common causes of PE. Bedridden patients subject to long period of stasis are also at risk. Deep vein thrombosis [DVT] is not definitively associated with the occurrence of pulmonary embolism. PE also rarely results from emobilization of tumor cells or fragments, fat, amniotic fluids, foreign bodies, or air[2]. Bed rest and confinement without walking, even for a few hours, are common precipitators[4].

PREVALENCE

PE affects an estimated 117 people per 100,000 persons yearly, resulting in about 350,000 cases yearly and causes up to 85,000 deaths yearly. PE affects mainly adults. In USA pulmonary emboli and its primary cause deep vein thrombosis are estimated to lead to 110,000 hospitalizations annually in patients more than 65 years. Annual incidence rates per 1000 persons aged 65-69 are 1.3 and 1.8 for pulmonary emboli and deep vein thrombi respectively. Both rates increase with age. Pulmonary embolism is highly fatal and 32% of cases, they are not diagnosed until after they cause death[4]. If untreated pulmonary embolism has a high mortality and accounts for 55-10% all in hospital deaths[4,5]. Registry data shows an overall 3 months mortality of 17.4%[6] of these deaths 45% were ascribed to PE and 755 occurred during the initial hospital admission for PE [7].

SYMPTOMS

Symptoms of PE are sudden onset dyspnea [shortness of breath], tachypnea [rapid breathing], chest pain of a worsened by breathing, cough, hemoptysis, [coughing up blood] more severe cases can include signs such as discoloration, usually of the lips and fingers[1]. Patients who have small thrombo emboli may be asymptomatic or have atypical symptoms. Non specific symptoms suggestive of pulmonary emboli in the elderly include persistent low-grade fever, change in mental status, or a clinical picture that mimics air way infection. Patients with PE usually present with one of the following symptoms patterns

1. Diagnostically confusing syndromes [confusion, unexplained fever, wheezing, resistant. .heart failure, unexplained arrhythmias].
2. Transient shortness of breath and tachypnea.
3. Pulmonary infraction [pleuritic pain, cough, hemoptysis, pleural infusion, pulmonary …..Infiltrate].
4. Right side heart failure along with shortness of breath and tachypnea secondary to ….pulmonary embolism [or]
5. Cardiovascular collapse with hypotension and syncope.

The most common physical findings are leg edema, tenderness cyanosis, and pleural friction rub, ,increased warmth, Oman's sign[3].

CAUSES

Causes for PE are multifractorial and are as follows

1. Venous stasis: Venous stasis leads to accumulation of platelets and thrombin in veins.

2. Hypercoagulable states: The complex and delicate balance between coagulation and anti coagulation is altered by many diseases, by obesity, after surgery, or by trauma.

Hypercoagulable states may be acquired or congenital. Factor-V Leiden mutation causing resistance to activated protein c is most common risk factor. And is most common cause of familial thromboembolism.

3. Immobilization: Leads to local venous stasis by accumulation of clotting factors and fibrin resulting in thrombus formation.

4. Surgery and trauma: Both surgical accidental trauma predispose patients to venous thrombo embolism by activating clotting factors and causing immobility. Severe burns carry a high risk of DVP or PE.

5. Pregnancy: The incidence of thrombo embolic disease in pregnancy has been reported to range from 1 case in 2oo deliveries to 1 case in 1400 deliveries.

6. Oral contraceptives and estrogen replacement: Estrogen containing birth control pills have increased the occurrence of venous thrombo embolism in healthy women.

7. Malignancy: The neoplasm's most commonly associated with PE, in descending order of frequency, are pancreatic carcinoma bronchogenic carcinoma, carcinomas of the genitourinary tract, colon, stomach and breast.

Travel of 4 hours or more in the past month, surgery within the last 3 months, current or past history of thrombo phlebitis, central venous instrumentation with in past 3 months , paralysis, varicose veins , inflammatory bowel disease.

PATHOPHYSIOLOGY

Once DVT develops, clots may dislodge and travel through the venous system and right side of the heart to lodge in the pulmonary arteries, where they partially or completely occlude one or more vessels. The consequence depend on the size and number of emboli, the pulmonary reaction, the under laying condition of the lungs, and the ability of the body's intrinsic thrombolytic system to dissolve clots. Small emboli may have no acute physiologic effects; many begin to lyses immediately and resolve within hours or days. Larger emboli can cause a reflex increase in ventilation [tachypnea], hypoxemia from ventilation/perfusion [V/Q] mismatch, shunting, and low mixed venous oxygen content as a result low cardiac output, telecasts from alveolar hypomania and abnormalities in surfactant, and an increase in pulmonary vascular resistance caused by mechanical obstruction and

vasoconstriction. Endogenous lyses reduce most emboli, even those of modulate size, without treatment and physiologic attritions decrease over hours or days, some emboli resist lyses and may organize and persist occasionally, chronic residual obstruction leads to pulmonary hypertension [chronic thrombo embolic hypertension] that may develop over years and result in chronic right heart failure. When large emboli occlude major arteries, or when many small emboli occlude >50% of the distal arterial system, right ventricular system increases, causing acute right ventricular failure, failure with shock [massive PE] or sudden death in severe cases. Risk factors for death include age >70 years, cancer and COPD. The risk of death depends on the degree and rate of rise of right sided pressures and on the patients underlying cardiopulmonary status higher pressures more healthy patients with pre existing cardio pulmonary disease. Otherwise healthy patients may survive a PE that occludes >50% of pulmonary vascular bed. Pulmonary infraction occurs in<10% of patients diagnosed with PE. This low rate has been attributed to the dual blood supply to the lungs [i.e.; bronchial and pulmonary.

A thrombus that has separated from its site of origin travels through the circulation to the inferior vena cava. The right ventricle pumps this thrombus to the pulmonary arteries, the thrombus finally lodges' may occur singly or multiply. They can be microscopic in size or be big enough to occlude the major branches of the pulmonary artery. PE sometimes may leads to corpulmonale. The most important patho physiological consequence of PE is V/Q mismatch in which there is **"**DEAD SPACE**"** ventilation in some parts of the lung and over perfusion in others. "dead space" ventilation refers to ventilation of lung segments that have obstructed vascular supply and thus no perfusion on the other hand. Over perfusion and decreased vascular resistance in other part of the lung leads to right-to-left intra pulmonary shunting with insufficient oxygenation of a large portion of per fused blood[2].

DIAGNOSIS

Diagnosis of PE is based primarily on validated clinical criteria combined with selective testing because the typical cleanliness of breath, chest pain cannot be definitively differentiated from other causes of chief pain and shortness of breath. Clinical imaging is usually based on clinical grounds i.e.; the medical history, symptoms and findings on physical examination assessment of clinical probability[1].

BLOOD TEST

Early primary research has shown that in low/moderate suspicion of PE a normal D-dimmer level (shown in blood test) is the possibility of thrombotic PE[8]. PE is being suspected a number of blood test is done, in order to exclude important secondary cause of PE. This blood count, clotting status (PT,APTT,TT), and some screening tests (erythrocyte sedimentation rate, renal function if one of this is abnormal, further investigation be warranted. Standard test for diagnosing pulmonary embolism is pulmonary angiography[9]. Specific appearance of the right ventricle on echocardiography is referred as the mc Connelly's sign. This is the finding the free wall but normal motion of the apex. This phenomenon has 77% sensitivity and 94% specificity for the diagnosis of embolism[10].

Electrocardiogram (ECG) is routinely done on patients with chest pain to quickly diagnose myocardial infractions. Heart may show signs of right heart strain or acute corpulmonale in cases of large PE. the classic signs are large S wave in lead-III and an inverted T wave in lead-III ("SIQ3T3") [11]. This is occasionally (up to 20%) present, but may also lung conditions and has therefore limited diagnostic value. The most commonly seen signs in the ECG are sinus axis deviation and right bundle branch block[12].

TREATMENT

Drugs used to treat pulmonary embolism are of ;

1.Anticoagulants

2.Thrombolytics

1. Anticoagulants

These drugs show mechanism of action by preventing the coagulation formation [or] by dissolving the already formed coagulations. The drugs under this category are mainly

A. Heparin

B. Warfarin

A. Heparin: Mainly two forms of heparin are used they are

1. Unfractioned heparin

2. Low molecular weight heparin.

1. Unfractioned heparin

It is administered in the hospital only, to the patients is given continuously through I.V but can also be given as an injection under skin. Frequent blood tests [usually 6 hours] are required to monitor the clotting effects of this medicine.

Mechanism of action:

It shows mechanism of action by in activating the thrombin and activated factor X [factor Xa] through an antithrombin [AT] dependent mechanism. Heparin binds to the AT through a high affinity polysaccharide, which present on about a third of heparin molecule. For inhibition of thrombin, heparin must bind to the coagulation enzyme antithrombin, where as binding to the enzyme is not required for inhibition of factor Xa. Molecules of heparin with fewer than 18 sachharides lack the chain length of bridge between thrombin & AT, therefore are unable to inhibit thrombin. in contrast, very small heparin fragments containing the polysaccharide sequence inhibit factor Xa via AT by inactivating thrombin heparin not only prevents thrombin but also inhibits thrombin induced activation of platelets factors V and VIII[14].

Adverse effect:

Thrombocytopenia, osteopenia, hemorrhage, thrombosis, osteoporosis, hypo aldosteronism and hypersensitivity reactions[14].

2. Low Molecular Weight Heparin [LMWH]

They increase the action of anti thrombin III on factor Xa but not its action on thrombin, because the molecules are too small to bind to both enzyme and inhibitor.essential for inhibition of thrombin but not for that of factorXa. The LMWH is more affective more than the UFH. The LMWH is usually.preferred because it can be given as an injection once or twice per a day and is given at home itself. Blood tests are not need to monitor LMWH clotting effects[14].

Mechanism of action

Compared with UFH, LMWH's have reduced ability to inactivate thrombin because the smaller fragments cannot bind simultaneously to antithrombin. In.contrast because bridging between antithrombin and Xa factor is less critical for antifactor Xa activity, the smaller fragments inactivate factor Xa almost as well as do large molecules. because virtually all heparin molecules contains at least 18 polysaccharide units UFH has an antifactor Xa, anti factor II a ratio of 1:1.in contrast commercial LMWH's have anti factor Xa to anti factor II a ratio between 2:1 and 4:1 depending on their molecular size distribution. Reduced binding to plasma to plasma proteins and cells is responsible for the more predictable dose response relationship of LMWH, longer plasma half life [compared with UFH] the lower risk of heparin induced thrombocytopenia and octopenia. LMWH's are cleared principally by the renal route[16].

Treatment of venous thrombo embolism

LMWH's re administered in weight adjusted doses by S.C injection and are not moniterd. Depending on the LMWH agent, a dose of 100 antifactor Xa units per Kg twice daily or of 150-200 antifactor Xa units per Kg daily is given. Although laboratory monitoring is not usually required, the antifactor Xa level should be checked in patients with renal insufficiency, morbid obesity, and pregnancy because the pharmacokinetic properties, efficacy and safety of LMWH are not well established in these situations. LMWH preparations are at least as affective as and safe as intravenous heparin for the treatment of DVT and PE, and the rates of recurrent thrombo embolism and major bleeding are similar with all of the LMWH preparations that have been evaluated out of hospital administration of LMWH to eligible patients with DVT is as affective and safe as

intravenous heparin administered in hospital ones daily administration of two different LMWH preparations is as safe as twice daily dosing. The risk of bleeding with LMWH is small and comparable to that with low-dose UFH. Low doses of LMWH administered S.C ones daily are at least as affective and safe as low dose UFH administered S.C 2 or 3 times daily[16].

B. Warfarin

Warfarin is taken in pill form. When the warfarin is at a proper level heparin is discontinued and treatment with warfarin continues. warfarin reduces the risk of another blood clot [after PE 3 or 6 months] warfarin is also be known as vitamin K antagonists [reflecting the structural between warfarin and vitamin K] their effects several days to develop because of the time taken for degradation of performed carboxylated clotting factors. Their onset of action thus depends on the elimination half lives of the relevant factors. Factor VII with a half life of 6 hours is effected first then IX, X and II with half lives of 24, 40 and 60 hours respectively[13].

Adverse effect

Hemorrhage [especially into the bowel [or] the brain]. The warfarin shows the activity lately after administration than the heparin. Heparin shows the clotting removal action immediately. Warfarin takes longer to start working. And also warfafin has more.severe adverse effects than heparin so warfarin is used in emergency treatment only[13].

2. Thrombolytics

Mainly used thrombolytics are of

A. Streptokinase

B. Urokinase

Clot dissolving medicines are not commonly used to treat PE .although they can quickly dissolve a clot. Thrombolytics also greatly increase the risk of serious bleeding. so they are occasionally used to treat a life threatening PE.

A. Streptokinase

It is also named as kabikinase streptase. Acts to convert.plasminogen to plasmin. Plasmin degrades fibrin clots, fibrinogen and other plasma proteins.Increase in fibrinolytic activity that degrades fibrinogen levels for 24-36.hours takes place with IV in fusion of streptokinase.

Adverse effect

Chills, fever, skin rashes are frequent [20%]. Complications may include purpurea, respiratory di stress syndrome, serum sick ness, vasculities, renal [or]..hepatic dysfunction[14].

B. Urokinase

It is also be named as abbokinase. Direct plasminogen activator produced by human fetal kidney cells grown in culture. It acts on the endogenous fibrinolytic system and convert plasminogen to the enzyme plasmin which in turn degrades fibrin clots, fibrinogen and other plasma proteins. The advantage of this agent is, a non antigenic. Urokinase is more expensive than streptokinase thus it is limitedly used one[14].

Other treatment

Inferior vena cava [IVC] filters are placed endovascular, meaning that they are inserted via the blood vessels. The choice of rate depends mainly on the amount of location of the blood clot within the venous system. To place the filter, a catheter is guided into the IVC using fluoroscopic guidance, then the filter is pushed through the catheter and developed into the desired location, usually just below the junction of the IVC and the lowest renal vein[16,17,18].

Adverse effect

Contrast allergy, renal insufficiency[16,17,18].

ACUTE PULMONARY EMBOLISM

Right ventricular dilation in the setting of acute PE is associated with an adverse prognosis. The effect of epoprostenol was evaluated on the right ventricular diameter and function in patients with acute pulmonary embolism and right ventriculation dilatation. Pulmonary embolism is a frequent and potentially fat disorder[19,20] an acute increase in right ventricular after load is the hallmark of severe pulmonary embolism, and is responsible for many of its clinical manifestations and complications. The

traditional view is that mechanical obstruction by thrombus mass causes pulmonary hypertension[21]. Apart from mechanical obstruction, vasoconstriction of the pulmonary vasculature plays a pivotal in the acute rise in pulmonary arteries pressure in patients with pulmonary embolism[22]. Studies in experimental animal models support a critical role for pulmonary vasoconstriction in acute pulmonary embolism[23,24]. In animal models of acute pulmonary embolism prostacyclin, a relatively selective pulmonary vasodilator, prevented or partially reversed the rise in pulmonary vascular resistance and pressure[25,26]. However the potentially beneficial role of pulmonary vasodilator therapy in acute pulmonary embolism has never been studied in a systematic way,

A total 82 patients with pulmonary embolism as diagnosed by spiral CT, were screened for eligibility

Adverse effect

Two patients showed facial fleshing during infusion with epoprostenal, however this was transient and did not influence infusion rate[26].

CONCLUSION

Pulmonary embolism is the occlusion of one or more pulmonary arteries by thrombi that originate else where, typically in the large veins of the lower extremities or pelvis. Pulmonary embolism is frequent and potentially fatal disorder. The Risk factor and the condition that impair venous return, The condition that cause endothelial injury or dysfunction, and underlying hyper coagualable states. Symptoms and signs are nonseptic include dyspena, pleuritic chest pain, cough syncope or cardio respiratory arrests tachypnea, tachhycardria, hypertension and a loud pulmonic component of the 2nd heart sound.PE can be diagnosed by CT angiogram, ventilation/perfusion.scan,pulmonary arteriogram, electrocardiogram(ECG),echocardiograph, ultrasonography, computed tomography lung scintigraphy. Treatment is with anticoagulants and sometimes clots dissolution with thrombolytics or surgical removal. Preventive measures include anticoagulants and sometimes insertion of an inferior vena cava fitter. The use of anticoagulants and thrombolytics cause bleeding disorder. Anticoagulants used for primary treatment and thrombolytics are used in the life threatening causes only. Results of animal experiments studying the presence of pulmonary emboli are difficult to apply to humans. PE may account for 15% of all post operative deaths. leg amputation and hip, pelvic and spinal surgery are associated with highest risk. Fatal events may occurs rarely,1-2 cases per 100,000 pregnancies PE increases with prolonged bed rest paralysis increase the risk.

Further research should be performed on the contribution of process of care and hospital volume and physician volume, as well as on the longitudinal trend of volume out comes correlations for patients with PE. Anticoagulation's control can be improved when care is centralized at anticoagulation's clinic. Programs should strive to coordinate care, adopt institution and region wide guidelines and develop and implement appropriate quality of care programs. Patients who are suspected of having pulmonary embolism begin their radio logic work up with spiral CT; assuming contrast injection is not contraindicated. if the spiral CT is negative then PE is excluded if the spiral CT is positive then the patient should be treated There are no data for the period following hospital discharge, so there may have been patients in group who developed PE Subsequently.

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