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Review Article **Pediatric Emergency**

An Overview of the Updates of Management of Pulmonary Edema: Narrative Review

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Abstract

The development of abrupt respiratory failure linked to fluid buildup in the lung's alveolar spaces due to an elevated heart-filling pressure is known as pulmonary oedema. Pulmonary oedema can result from any cardiac condition marked by a rise in left ventricular pressure. Long-term high capillary pressure can potentially break down the barrier, resulting in increased fluid transfer and permeability into the alveoli and atelectasis and oedema. Numerous variables, such as dysregulated inflammation, strong leukocyte infiltration, activation of procoagulant processes, cell death, and mechanical stress, contribute to the disruption of the alveolar-epithelial barrier. In order to properly treat patients with pulmonary oedema, a thorough medical history and a physical examination are necessary to assess the condition's symptoms and possible causes. In the interim, second-level diagnostic procedures such as echocardiography, chest radiograph, natriuretic peptide level, and pulmonary ultrasonography should be performed. To determine the best course of treatment for these patients, it is imperative to identify the unique pulmonary oedema phenotype. Early in the course of treating this illness, non-invasive ventilation should be taken into consideration. For pulmonary congestion, diuretics and vasodilators are employed. Vasopressors and inotropes are sometimes needed to address hypoperfusion. Additional strategies (i.e., beta-agonists and pentoxifylline) may be beneficial for patients with diuretic resistance and chronic symptoms. The pathogenesis, clinical manifestation, and therapy of pulmonary oedema are reviewed in this publication.

Keywords: Pulmonary edema; Capillary permeability; Diagnosis; Management.

1. INTRODUCTION

The result of large fluid displacement from capillaries to interstitial tissue and the pulmonary alveolus as a result of an increase in capillary pressure and a Starling balance disruption in the pulmonary circulation is pulmonary oedema, a severe restrictive pulmonary disease. This type of severe hypoxemic respiratory failure is the most prevalent. We refer to interstitial oedema, also known as hidden (lat. oedema interstitialis), when pulmonary oedema primarily affects interstitial tissue. Alveolar edoema (also known as Oedema alveolarisi) is the most prevalent type. Most frequently, acute cardiogenic pulmonary oedema is the clinical manifestation of severe heart failure [1, 2].

The force balance between capillary and lung interstitial pressure is disrupted by cardiac failure that raises venous pulmonary pressure. Increased hydrostatic pressure and excessive fluid discharge from veins cause interstitial or, in more severe cases, alveolar oedema. Breathing discomfort and lung function are further compromised by the appearance of fluid in the pulmonary pleurae [3, 4].

Dyspnea, which is linked to bronchospasm, hyperventilation, hypoxemia, hypercapnia, and follicular oedema, is the primary symptom of pulmonary oedema. In addition, tachycardia, tach-ypnoë, and auditory symptoms (whistles, frizzs, and cracks) manifest. Pale, occasionally bruised, and covered in sticky perspiration

skin. In the so-called ortopnoë posture, patients sit up straight with their hands resting on their thighs to stabilise the shoulder girdle and provide breathing room for more exhausted muscles [3, 5].

One pathophysiologically significant factor in pulmonary edema is the redistribution of fluids into the thoracic cavity, which is brought on by an increase in left ventricular filling pressure rather than hypervolaemia as was previously thought. Therefore, rather than lowering volemia, the initial line of treatment should reverse the redistribution of fluids by lowering the left verticle's pre-load and/or after-load. Furthermore, in the pathomechanism of cardiogenic pulmonary edema, hemodynamic imbalance and disturbances of neurohormonal imbalance overlap. This has been recently linked to the development and progression of circulatory failure symptoms as well as damage to the capillary-vesicle barrier in the pulmonary circulation [3, 6].

This review comprehensively aims to demonstrate the updates on the management of pulmonary oedema.

2. Diagnostic Work-up

2.1 History and Physical Examination

The clinical characteristics of both cardiogenic and noncardiogenic pulmonary oedema are progressive increasing dyspnea, tachypnea, and rales (or crackles) on examination with concomitant hypoxia. Auscultation of an S3 gallop during a cough with pink, foamy sputum due to hypoxemia from alveolar flooding may indicate cardiogenic oedema. Likewise, peripheral oedema, increased jugular vein pressure, and murmurs may indicate a heart cause. The symptoms of infections, such as fever, coughing up expectoration, dyspnea suggesting pneumonia, recent trauma, and blood transfusions, should be closely evaluated in patients with non-cardiogenic pulmonary oedema as these patients may develop acute respiratory distress syndrome. The cornerstone of bedside evaluation for all patients exhibiting respiratory symptoms is still auscultation. More precisely, the ability to detect coarse or small crackles is essential for deciding the best course of action for the management. Cardiogenic pulmonary oedema is characterised by fine crackles. They are only audible during the inspiratory phase when the tiny airways suddenly open after closing during expiration [7].

2.2 Evaluation

An electrocardiogram (ECG) aids in the diagnosis of cardiac ischemia or myocardial infarction in addition to a comprehensive history and physical examination. This is a simple, low-cost, and less specialised test that may be performed right at the patient's bedside. The diagnostic instruments listed below are used to identify pulmonary oedema and, more crucially, to distinguish between its many forms.

2.2.1 Laboratory

The cardiac myocytes in the left ventricles release brain-type natriuretic peptide (BNP) in reaction to ventricular blood volume or intracardiac pressure stretching. Patients with congestive heart failure may exhibit elevated BNP levels, which are correlated with both pulmonary occlusion pressure and left ventricular end-diastolic pressure. Heart failure is less likely in cases where BNP levels are less than 100 pg/ml and more likely in cases where levels exceed 500 pg/ml. Levels between 100 and 500 pg/ml are frequently observed in critically ill patients, although they are not helpful in the diagnosis of heart failure. Patients experiencing myocyte injury, such as those with acute coronary syndrome, frequently have elevated troponin levels [8].

Patients presenting with acute decompensated heart failure have an independent sign of increased in-hospital and post-discharge mortality: hypoalbuminemia (≤3.4 g/dL) [9]. Because there is a simultaneous decrease in pulmonary interstitial and plasma albumin levels, which inhibits the formation of a transpulmonary oncotic pressure gradient, low albumin levels alone do not cause pulmonary oedema.

Serum electrolyte measurements, serum osmolarity, renal function, and toxicology screening are helpful for patients who have pulmonary oedema from hazardous intake. Measuring amylase and lipase levels aids in the diagnosis of acute pancreatitis [10].

2.2.2 Radiographic Testing

Standard imaging uses both posteroanterior and lateral views, while portable imaging uses anteroposterior views. Central oedema, pleural effusions, Kerley B septal lines, peribronchial cuffing, and increased heart size are the hallmarks of cardiogenic pulmonary oedema. The oedema pattern in noncardiogenic aetiologies is usually patchy and peripheral, and air bronchograms can show the presence of ground-glass opacities and consolidations [11]. Cardiogenic-type patients are more likely to experience pleural effusions [12].

2.2.3 Echocardiography (ECG)

ECG aids in the diagnosis of valvular and left ventricular systolic dysfunction. Diastolic dysfunction can be evaluated for presence and severity using several techniques, such as tissue Doppler imaging of the mitral annulus [8].

2.2.4 Lung Ultrasound

It is a non-invasive method that does not require radiation. The most prevalent settings for its utilisation are operating rooms, emergency departments, and intensive care units. It aids in the early detection of extravascular lung water (EVLW) buildup prior to clinical symptoms [11].

2.2.5 Pulmonary Artery Catheterization

This invasive test, which is frequently regarded as the gold standard in determining the cause of pulmonary oedema, aids in the monitoring of filling pressures, cardiac output, and systemic vascular resistance. Determining whether pulmonary oedema is cardiogenic can be aided by a high pulmonary artery occlusion pressure of more than 18 mm Hg [8].

2.2.6 Transpulmonary Thermodilution

This invasive testing method is usually applied to patients having significant thoracic, cardiac, or vascular procedures. They track multiple hemodynamic indices, including cardiac index, mixed venous oxygen saturation, stroke volume index, and EVLW, and are also utilised in septic shock [11].

3. Prehospital Management

Obtaining the patient's medical history, known as the subject's examination of the patient, is a fundamental step in the diagnosis process. Since most patients have significant conditions, it might be difficult or even impossible to obtain a complete medical history. Family is frequently a poor source of honest anamnesis in stressful situations brought on by a significant relative's illness. The patient's and their spouse's advanced age contributes to their sense of confusion and powerlessness. Furthermore, there is not a straightforward diagnostic test that may support the ambulance's clinical diagnosis of pulmonary edoema. State transitioning to dyspnea should be ruled out during differentiation [4, 13].

4. Management

Since pulmonary oedema is a potentially fatal emergency, prompt and coordinated diagnostic and treatment actions are required. The precise cause will influence the treatment in part. Infection, acidemia, and renal failure are common comorbid and/or secondary diseases that also need immediate attention. Treatment of the underlying pathologic illness and symptom relief are the goals of therapy for patients with pulmonary oedema.

4.1 Support of oxygenation and ventilation

It is critical to make sure there is enough oxygen. In order to have practically full saturation of red blood cells, the objective should be quickly reaching an oxygen saturation of 95% and/or an arterial partial pressure of oxygen of greater than 70 mmHg. Clearance of alveolar oedema fluid may be hampered by hypoxia. However, extremely high oxygen concentrations are also harmful. Using a face mask, nasal cannula, or nonrebreathing reservoir mask, oxygen can be administered without the need for positive pressure or intubation. Compared to face mask oxygen or bi-level positive airway pressure mask ventilation (Bi-PAP), high-flow nasal cannula oxygen improves mortality and intubation rates for patients with acute hypoxic respiratory failure without hypercapnia [22].

4.2 Diuretic therapy

Since diuresis reduces lung extravascular water and increases oxygenation, it has been a cornerstone of treatment for patients with pulmonary oedema, especially those with decompensated heart failure. It is advised to start intravenous loop diuretics as soon as possible, as this reduces mortality. Whether a patient is naiive to diuretics or has had prolonged exposure should determine the first dosage. Recently, diuretic combination therapy and continuous infusion of loop diuretics have become more popular. Nonetheless, there were no appreciable differences in the symptoms or blood creatinine levels of patients receiving continuous infusion or a 12-hour bolus of furosemide in a sizable clinical trial, including patients with acute decompensated heart failure [15].

Continuous diuretic infusion was linked to increased weight loss but did not differ in urine output, electrolyte imbalances, ototoxicity, or cardiac or all-cause mortality, according to a meta-analysis of 10 randomised controlled studies. A Cochrane analysis indicated that continuous diuretic infusions produced more pee and caused less ototoxicity than intermittent high-dose bolus injections despite the fact that the benefits of continuous infusion are unclear. Most heart failure recommendations urge weight loss and significant net diuresis as critical early treatments, and these goals are feasible. It makes sense to use combination therapy or infusions if necessary to accomplish these interim goals [16].

4.3 Vasodilator

In acute heart failure with cardiogenic oedema, nitrates are frequently utilised because they lessen preload and, with the exception of nitroprusside, afterload to a lesser degree. Patients with pulmonary oedema and hypertension benefit most from nitrates. There is a chance of hypotension; thus, blood pressure needs to be closely watched. Sublingual nitrates should be administered as a first treatment before intravenous access is established, according to certain authorities who advise high-dose intravenous nitrates administered often [17]. Others believe that the benefits of the outcome have not been shown, and they will keep using intravenous nitrates as an adjuvant therapy until the enhanced outcome is proven [18, 19].

4.4 Morphin and opiates

The usual course of treatment for acute cardiogenic pulmonary oedema has been intravenous morphine. It lowers heart rate and preload, as well as afterload, to some extent. Additionally, it lowers serum catecholamine levels, sympathetic hyperactivity, and anxiety, which lowers afterload and myocardial oxygen consumption. Opioids should be administered with caution in the emergency room since they may increase the requirement for mechanical ventilation and/or ICU admission. Opioids can, however, lower the ventilatory drive [20].

4.5 Angiotensin-converting enzyme inhibitors

In patients with hypertension and pulmonary oedema, angiotensin-converting enzyme inhibitors can lower preload and afterload. Low intravenous doses of short-acting medications are frequently used as initial therapy. Oral and longer-acting medications may be utilised if well tolerated. For individuals with heart failure and acute myocardial infarction, long-term therapy lowers mortality [20].

4.6 Inotropic and inodilator drugs

Positive inotropes like dopamine and dobutamine raise the risk of arrhythmias and the oxygen demand of the heart. Improved results have not been demonstrated by clinical trials. Phosphodiesterase-3 inhibitor milrinone vasodilates the pulmonary and systemic vascular beds while also increasing myocardial contractility. In patients with severe left ventricular failure and limited cardiac output who have pulmonary oedema, indicators may theoretically be beneficial, albeit efficacy has not been demonstrated [21].

4.7 Ultrafiltiration

Fluid removal, or UF, is especially helpful for patients who have diuretic resistance and renal impairment. In hypervolemic patients with HF, UF was shown in a randomised trial to be more effective than IV diuretics in reducing net fluid loss and rehospitalization. According to these results, patients with volume overload and CPE who have not responded well to moderate to high doses of diuretic therapy or whose side effects (such as renal dysfunction) prevent them from starting diuretics or render them ineffective should have UF taken into consideration [22].

4.8 Management of arrhythmias

Especially in individuals with heart failure (HF), atrial fibrillation (AF) is a prevalent arrhythmia. It is frequently challenging to identify if HF is caused by or results from AF. Because acute HF raises left atrial pressure and wall stress, it can cause AF. Acute heart failure can result from AF, especially if the ventricular response is quick. Conversely, AF could be persistent and unrelated to acute heart failure decompensation. Whether or not AF is thought to be the cause of HF decompensation and whether or not it is linked to substantial hemodynamic instability determine how the condition is treated. Rate control and prompt decision-making about the necessity of cardioversion are the first steps in managing AF. We must take into account the possibility of a thromboembolic event before performing emergency cardioversion. There seems to be very little chance of thromboembolism if cardioversion takes place within 48 hours of the onset of AF. Patients in whom cardioversion will occur more than 48 hours after the beginning of AF or in whom the duration is unclear must receive anticoagulation prior to cardioversion (e.g., intravenous heparin) [22, 23].

4.9 Additional management stratigies

Acute breakdown of the barrier, which can result in increased fluid generation and alveolar collapse, can prompt the use of pentoxifylline and beta-agonists as supplementary management techniques [24]. Elevated levels of surfactant protein B in the bloodstream may aid in the identification of CPE patients who may not respond well to medication because of mechanical damage to the alveoli–capillary barrier [25].

Pentoxifylline given after HF diagnosis resulted in a 4-fold reduction in all-cause mortality, from 18.3% to 5.4%, according to a recent meta-analysis [26]. Originally, the drug's beneficial effects on patient outcomes were attributed to its ability to suppress TNF-alpha generation. However, a more recent assessment suggests that the drug's other immunomodulatory qualities may be the reason for its benefits [27].

SGLT2i, or sodium-glucose co-transporter 2 inhibitors, have recently been used to treat heart failure. Empagliflozin and dapagliflozin lower the risk of cardiovascular (CV) death and hospitalisation in heart failure (HF). Their exact mode of action in HF is still unknown. Together with evidence-based beta-blockers, mineralocorticoid receptor antagonists, and sacubitril-valsartan, SGLT2i have earned a spot as the fourth pillar of HF medical therapy. They ought to be taken into account for the management of all HF patients who exhibit symptoms, regardless of their HF phenotype, including those who are hospitalised. High-risk individuals whose HF clinical picture is deteriorating benefit from vericiguat. The majority of HF hospitalised patients can be up-titrated to high doses of GDMT in a matter of weeks, and this strategy lowers the risk of unfavourable HF outcomes [27, 28].

5. Prognosis

Acutely decompensated pulmonary oedema can arise from noncardiac or cardiac aetiologies. Supplemental oxygenation, diuretics, nitrates, and morphine are examples of temporary treatments for dyspnea and hypoxemia. Nevertheless, to stop its recurrences, effective treatment of the underlying reasons is required. Because there are so many different cardiogenic and non-cardiogenic causes of pulmonary oedema, as well as distinct mortality data for each, it is challenging to quantify prognostic predictions. The advanced stage of pulmonary oedema in ARDS has gradually improved the prognosis. Hospital mortality dropped in the 1990s, from 60% in 1967–1981 to between 30% and 40% [29]. Moreover, an examination of ARDS mortality studies showed that between 1994 and 2006, total mortality decreased by almost 1.1% per year. The prognosis based on mortality data is highly dependent on the ARDS triggering procedure [30].

6. CONCLUSION

Pulmonary edoema patients are a diverse group of people. It is necessary to accurately identify the

particular pulmonary edoema phenotype in these patients as well as any probable causes or precipitants in order to provide appropriate therapy. Early consideration of diuretics and non-invasive ventillation is recommended. Vasopressors and inotropes are sometimes needed to address hypoperfusion. Patients who have diuretic resistance and chronic symptoms may benefit from beta-agonists and other forms of supplementary medication in addition to vasodilators. There is a need for more research on how medicinal therapy helps people with pulmonary edoema reduce lung damage.

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