Diagnostic significance of pleural fluid PH and PCO2

Thesis Submitted for partial fulfillment of master degree In Chest diseases and tuberculosis

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Abstract

Pleural effusion can result from a very wide range of disease processes.
However, in about 20% of cases, the effusions remain undiagnosed after the initial evaluation. **(Light, 1998a).**

These undiagnosed pleural effusions are important clinical problem, so scientists spend much effort and time in searching for a new parameter to help in the diagnosis of etiology of different types of pleural effusions. **(Heffenr, 1995)**

Trying to evaluate the role of pH , PCO2 and WBC and its differential cells of pleural fluid in diagnosis of pleural effusion.

This study was conducted on 50 patients with pleural effusions.

Key Words :

Transudative – Empyema – tuberculour Effusion .

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LIST OF ABBREVIATIONS

ADA	Adenosine deaminase
AIDS	Acquired immune deficiency syndrome
ANA	Antinuclear antibody
CD4	complement D4
CT	Computerized tomography
DNA	Deoxyribonucleic acid
HCO3	bicarbonate
HIV	Human immune deficiency virus
IFN	interferon
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IgM	ImmunoglobulinM
LDH	Lactate dehydrogenase
MRI	Magnetic resonance images
PAF	Platelet activating factor
PCO2	Partial carbon monoxide pressure
PDGF	platelet derived growth factor
PGE	Prostaglandin E
PNL	Polymorph nuclear leucocytes
PO2	Partial oxygen pressure
PPD	Purified protein derivative
SLE	Systemic lupus erythematosus
TNF	Tumor necrotic factor
U/S	Ultrasonography
VATS	Video-assisted thoracic surgery
WBCs	White blood cells

CONTENTS

INTRODUCTION

Normally, very small amounts of pleural fluid are present in the pleural spaces and fluid is not detectable by routine methods. When certain disorders occur, excessive pleural fluid may accumulate and cause pulmonary signs and symptoms. Simply put, pleural effusions occur when the rate of fluid formation exceeds that of fluid absorption. **(Heffner ,1998a)**

In most instances, the cause of the effusion becomes apparent from the associated clinical circumstances, diagnostic thoracocentesis and or percutaneous pleural biopsies with culture, cytological and or histological examination **(Light,1998a).**

However, in about 5-10% of cases, the effusions remain undiagnosed after the initial evaluation and 20% of these effusions are later proved to be malignant **(Light,1998a).**

Biochemical examination of pleural fluid is usually done in a trial to identify the cause of pleural effusion. Distinguishing whether the effusion is an exudates or a transudate is a first step, with further investigations directed by the clinical features and these results .**Light's** criteria were published in **1972**, and since then, additional markers including cholesterol, pH, bilirubin and albumin gradient have been proposed **(Tarn and Lapworth,2001)**

Measurement of pleural fluid PH and PCo2 is useful in the diagnosis and management of pleural effusions. The effusions associated with pneumonia (parapneumonic effusions) showed the most widely varying value of PH. Apparently the pleural fluid PH has predictive value for the course of parapneumonic effusion if less than 7.20 the patient need chest tube , if greater than 7.20 resolved with antibiotic therapy without tube drainage. When the possibility of tuberculous and malignant effusion exist, PH below 7.30 is highly suggestive of tuberculosis while a PH greater than 7.40 is highly suggestive of malignancy.**(Good et al. 1980)**

PH inferior to 6.30 seemed to be characteristic of non tuberculous pleural effusion , and in these circumstances an associated PCO2 greater than 60 mmHg were present. Determination of PH and PCO_2 in pleural effusion may help to identified the etiology of this condition specially when associated to analysis of other parameters of the aspirated fluid. **(Light,1998b)**

Aim of the work

The aim of this work is to assess the role of pleural fluid pH and PCO_2 in differentiating the aetiologies of pleural effusion and to study the correlation between pleural pH and PCO2 and cellular content of the effusion.

Chapter (1)

(A) ANATOMY OF THE PLEURA

The pleural membranes are developed from the mesenchyme to line the space that will separate the lungs from the mediastinum,diaphragm and the chest wall**(sheldon and Gallagher,1981).**

The lungs are surrounded by two membranes, the pleurae. The outer pleura is attached to the chest wall and is known as the parietal pleura; the inner one is attached to the lung and is known as the visceral pleura. The two layers are continuous with one another around and below the root of the lung. In between the two is a thin space known as the pleural cavity or pleural space. It is filled with pleural fluid, a serous fluid produced by the pleura **(Siefkin and Hirasuna,1987).**

Visceral and parietal division, approximately have equal surface area. Each is 1 layer of mesothelial cells (Single layer, pleomorphic with surface microvilli, more dense on the visceral side of the pleura than the parietal pleura), basement membrane , connective tissue, microvessels and lymphatics. The most interesting and unusual feature of the parietal pleura are the lymphatic stomata, holes of 2 to 10 μm in diameter that open onto the pleural space . The stomata have been demonstrated on the parietal pleural surface with scanning electron microscopy. Each stoma is formed by a gap in the otherwise continuous mesothelial cell layer, where the mesothelial cells join with the endothelial cells of the lymphatics. Each lymphatic joins others, forming a lake or lacuna**(Gray and Skandalakis,1985).**

The pleural fluid lubricates the pleural surfaces and allows the layers of pleura to slide against each other easily during respiration. It also provides the surface tension that keeps the lung surface in contact with the chest wall. During quiet breathing, the cavity normally experiences a negative pressure (compared to the atmosphere) which helps to adhere the lungs to the chest wall, so that movements of the

chest wall during breathing are coupled closely to movements of the lungs. The pleural membrane also helps to keep the two lungs away from each other and air tight, thus if one lung is punctured and collapses due to an accident, the other pleural cavity will still be air tight, and the other lung will work normally **(Last,1999).**

Different portions of the parietal pleura have received special names which indicate their position: thus, that portion which lines the inner surfaces of the ribs and intercostales is the costal pleura; that clothing the convex surface of the diaphragm is the diaphragmatic pleura; that which rises into the neck, over the summit of the lung, is the cupula of the pleura (cervical pleura); and that which is applied to the other thoracic viscera is the mediastinal pleura. The visceral pleura covers the surface of lungs, including the interlobar fissures. In humans, there is no anatomical connection between the left and the right pleural cavities so in cases of pneumothorax, the other hemithorax will still be able to function normally**(Johnston and Green,1983).**

The parietal pleura is supplied with blood from systemic circulation (intercostals , internal thoracic and musculophrenic) its veins join the systemic veins in the neighboring parts of the chest wall; it contains sensitive nerves (derived from the intercostals nerves and from the phrenic nerve) and cells with a dense cilliary layer**(Albertine et al.,1982).**

The visceral pleura is supplied with blood from bronchial artery and from the pulmonary artery which divides into a net work of very delicate capillaries. Its nerve supply is derived from the autonomic nerves innervating the lung and accompanying the bronchial vessels. It does not contain sensitive nerves (insensitive to pain) and the cells have few cilia**(Pistol, et al. 1989).**

The lymphatic drainage of parietal and visceral pleura differs from each other. The mesothelial surface of parietal pleura is permeated by stomas that connect via lacunas to a lymphatic network in the adjacent

submesothelial layers. Costal surface of the parietal pleura drains to parasternal and para vertebral nodes, while diaphragmatic surface drains to the tracheobronchial nodes.

The visceral pleura are devoid of lacunas and stomas and the underlying lymphatic vessels appear to drain the pulmonary parenchyma rather than the pleural space**(Johnston and Green,1983).**

(B) PHYSIOLOGY OF THE PLEURA

The parietal pleura has been proposed as the more important pleura for pleural liquid turnover in the normal physiologic state in absence of disease. Its microvessels are closer to the pleural surface and perfusion pressure is likely higher than the visceral pleura. It is approximately 30 to 40 μm thick. The most interesting and unusual features of the parietal pleura are the lymphatic stomata, holes of 2 to 10 μm in diameter that open onto the pleural space **(Staub et al.,1985).**

Pleural fluid is filtered across the parietal mesothelium in the top of the pleural cavity and removed by lymphatic stomatas in the more dependent mediastinal and diaphragmatic regions. The pleural lymphatics act as a feedback system that regulates pleural liquid volume and its protein composition around a low volume set point **(Heffner et al.,1998b).**

Healthy individuals have less than 15 ml of fluid in each pleural space. Normally, fluid enters the pleural space from the capillaries in the parietal pleura, from interstitial spaces of the lung via the visceral pleura, or from the peritoneal cavity through small holes in the diaphragm. This fluid is normally removed by lymphatics in the parietal pleura, which have the capacity to absorb 20 times more fluid than is normally formed. When this capacity is overwhelmed, either through

excess formation or decreased lymphatic absorption, a pleural effusion develops **(Light ,2001).**

Table(1):NORMAL COMPOSION OF PLEURAL FLUID

Volume	0.1-0.2 ml/kg
Cells / mm^3 :	1000-5000
% Mesothelial cells	3 – 7 %
% Monocytes	30 – 75 %
% Lymphocytes	20 – 30 %
% Granulocytes	10 %
Protein	1 – 2 g / dl (< 0.5 of plasma)
Albumin %	50 – 70 %
Glucose	Equal that of plasma
LDH	< 50% of plasma level
PH	> plasma

(Kinasewitz , 1999).

Pressures control fluid formation and absorption

Normally the pleural space contains only a small amount of fluid (less than 15 ml) and no air. Because of the elastic recoil of the lungs and chest wall, the normal intrapleural pressure is subatmospheric (average, - 5 cm H_20). Because of the additional gravitational forces of the weight of the lung in the pleural space, the intrapleural pressure is

more negative at the apex (-10 cm H_20) compared with the base (-2 cm H_20) at functional residual capacity. At maximal inspiration (total lung capacity), the pressure in the pleural space becomes more negative (decreasing to - 20 to - 60 cm H_20) **(Sahn , 1988).**

The decrease in pleural pressure, created primarily by the downward movement of the diaphragm results in a pressure gradient drawing air into the upper airway. Under normal circumstances fluid is continually leaving the parietal pleural surface into the pleural space and being reabsorbed through the parietal lymphatics **(Siefkin and Hirasuna , 1987).**

Pleural fluid formation is governed by the Starling law of capillary-interstitial fluid exchange, which states that the rate of fluid movement is related to the permeability of the pleural membrane and the balance of hydrostatic and oncotic pressures in the pulmonary capillary bed and pleural space. In the following equation, Q_f is fluid movement, L_p and A are the filtration coefficient and surface area of the pleura, $sigma_d$ is the reflection coefficient for protein movement across the pleura, and P and pi are the hydrostatic and oncotic pressures of the pulmonary capillary bed and pleural space, respectively.

$$\mathbf{Q_f = L_p \, X \, A[(P_{cap} - P_{pl}) - sigma_d(pi_{cap} - pi_{pl})]}$$

In persons with healthy cardiorespiratory systems, most pleural fluid is believed to originate in the capillary bed of the parietal pleura. The primary mechanism in humans for resorption of fluid from the pleural space is lymphatic drainage through the parietal pleura. This route is strong and capable of clearing several hundred milliliters of pleural fluid from each hemithorax daily. Fluid accumulates in the pleural space when the rate of formation exceeds the rate of clearance **(Johnson,2000).**

Accumulation of pleural fluid results when the forces that determine fluid movement are changed. When fluid accumulates as a result of

increased capillary permeability, a leakage of high-protein fluid occurs. A block of lymphatic drainage will also result in increased protein content in the pleural fluid. In both of these mechanisms an exudate is produced **(Mehta and Dweik , 2000).**

When fluid accumulation is due to an increased capillary hydrostatic pressure or decreased oncotic pressure, the relative protein concentration compared with that in the serum is low and this fluid is called a transudate. Capillary hydrostatic pressure can be increased by increasing the pressure within the capillary or decreasing the pressure surrounding the capillary since the transvascular pressure produces the net effect. Therefore, decreases in pleural pressure (i.e., more negative) can result in a pleural effusion **(Murray et al,1994).**

Fluid resorption is also enhanced by the greater surface area of the visceral pleura made up by the interlobar fissures and by the microvilli on the visceral pleural mesothelial cells. Since the visceral pleura is supplied over most of its surface by the bronchial circulation, either alone or together with the pulmonary arterial circulation ,the capillary hydrostatic forces in the visceral pleural in humans may be closer to those of the systemic capillaries**(Beach and Manthey,1998).**

Sahn,(1988) studied the rate of formation and lymphatic removal of fluid in pleural effusion in 11 patients(congestive heart failure, carcinoma, and nephrotic syndrome).He injected a radioactive material (Technetium-99) into the pleural space and found an average lymphatic flow of 36 ml / kg / hr. and an average net flow of fluid entery of 0.40 ml / kg / hr. Thus, the volume of pleural fluid was increasing in these patients. The rate of lymphatic flow was decreased at night, which thought to be related to decreased intercostals and diaphragmatic activity.

Agostoni and Zocchi,(1998)studied albumin turnover in pleural effusion in different diseases. They used radio-iodinated human serum albumin injected into the pleural space as a marker and found that protein removal from the pleural space was decreased in many diseases as with inflammatory pleural effusions. The protein concenterates of the

Chapter (2)

PLEURAL EFFUSION

DEFINITION

The pleural cavity contains a relatively small amount of fluid approximately 10 mL on each side. Pleural fluid volume is maintained by a balance between fluid production and removal, and changes in the rates of either can potentially result in the presence of excess fluid, traditionally known as a pleural effusion**(Blackmore et al,1996).**

The accumulation of pleural fluid can usually be explained by one or more of the following factors: 1. Increased pleural fluid formation:

a. Elevation of hydrostatic pressure (eg, congestive heart failure)
b. Decreased colloid osmotic pressure (eg, cirrhosis,nephrotic syndrome)
c. Increased capillary permeability (eg, infection, neoplasm)
d. Passage of fluid through openings in diaphragm (eg, cirrhosis with ascites)
e. Reduction of pleural space pressures (eg, atelectasis)

2. Decreased pleural fluid absorption:

a. Lymphatic obstruction
b. Elevation of systemic venous pressures resulting in impaired lymphatic drainage [eg, superior vena cava (SVC) syndrome] **(Mehta and Dweik ,2000).**