



A STUDY ON LEVELS OF CHOLINESTERASE IN PLEURAL FLUIDS OF DIVERSE ETIOLOGIES

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ABSTRACT

Introduction: Acetylcholinesterase, also known as true, specific, type I cholinesterase or RBC cholinesterase: It is found in nervous tissue, erythrocytes, lungs, spleen and grey matter. It is decreased in pernicious anaemia and after antimalarial therapy. **Methodology:** Patients participating in the study were explained about the procedure, technique and complications of pleural fluid aspiration. Pleural fluid aspiration was performed under strict aseptic precautions after analysing the fluid levels by percussion and chest x-rays. In few of the cases, ultrasonography-guided pleural fluid aspiration was performed. **Results:** The mean values of pleural fluid cholinesterase levels were 806.26 ± 516.28 U/L in the transudates group and 3476.11 ± 1250.17 U/L in the exudates group. The normal levels of cholinesterase varies between laboratories. The cut-off value is 1/10th of the upper limit of normal level of cholinesterase in the respective laboratory. **Conclusion:** In this study Light's criteria had a sensitivity of 91.9% and specificity of 87.3% in comparison to pleural fluid to serum cholinesterase ratio that had a sensitivity of 96.8% and specificity of 95.2%.

KEYWORDS : Acetylcholinesterase, Pleural Fluids, Diverse Etiologies

INTRODUCTION:

The term pleura refers to the thin lining layer on the outer surface of the lung (visceral pleura), the corresponding lining layer on the inner surface of the chest wall (parietal pleura), and the space between them (pleural space). Because the visceral and parietal pleural surfaces normally touch each other, the space between them usually is only a potential space. It contains a thin layer of serous fluid coating the opposing surfaces. The pleura lines not only the surfaces of the lung that are in direct contact with the chest wall but also the diaphragmatic and mediastinal borders of the lung. These surfaces are called the *diaphragmatic* and *mediastinal pleura*, respectively.¹

The pleural fluid is distributed relatively evenly throughout the pleural space. Therefore, the pleural fluid behaves as a continuous system. The pleural space is slightly narrower near the top ($18.5\mu\text{m}$) than at the bottom ($20.3\mu\text{m}$). Pleural space width in dependent recesses, such as the costo-diaphragmatic recess is 1 to 2 mm. Because the microvilli of the mesothelial cells in the visceral and parietal pleura do not interdigitate, the frictional forces between the lungs and chest wall are low. The mean white blood cell count in pleural fluid is $1,716$ cells/ mm^3 and the mean red cell count is approximately 700 cells/ mm^3 . These numbers are similar to those recorded in animals. Approximately 75% of the cells are macrophages and 25% are lymphocytes, with mesothelial cells, neutrophils, and eosinophils accounting for less than 2% each.^{2,3}

Cholinesterases are a family of enzymes that hydrolyse acetylcholine into choline and acetic acid. These are serine hydrolases that belong to the esterases family. The enzyme family of cholinesterases includes Acetylcholinesterase, also known as true, specific, type I cholinesterase or RBC cholinesterase: It is found in nervous tissue, erythrocytes, lungs, spleen and grey matter. It is decreased in pernicious anaemia and after antimalarial therapy.⁴

Butyrylcholinesterase, also known as plasma, nonspecific, type II cholinesterase or Pseudocholinesterase. It is found in plasma, liver, pancreas and intestinal mucosa, liver being the main organ. Variations occur due to liver disease, chronic inflammation, malnutrition, morphine, codeine, succinylcholine administration and hypersensitivity reactions.

BChE is normally found in plasma, liver, pancreas, intestinal mucosa and white matter of the brain. It is called so as it hydrolyzes butyrylcholine 4 times faster than AChE. It is synthesized by the liver, heart, lungs and brain but primarily by the liver. For a long time the physiological functions of BChE was vague. Now it has been found to have a role in lipoprotein metabolism, myelin maintenance, cellular adhesion, neurogenesis, as a scavenger of toxic molecules and in the processing of amyloid precursor. As an enzyme it hydrolyses acetylcholine (ACh) and other choline esters, and non-choline esters

such as a number of local anaesthetics, muscle relaxants, aspirin, and cocaine.⁵ Therefore, it may be useful for the treatment for cocaine addiction and toxicity. Its serum/plasma activity has been primarily used in clinical biochemistry to test diminished protein-synthesizing capacity of the liver and organophosphorus insecticide poisoning.⁶

METHODOLOGY:

Data was collected from the patients admitted in Hospital and Research Centre, Medical College, and were found to have pleural effusion.

INCLUSION CRITERIA-

- Patients with Age > 18yrs
- Presence of pleural effusion proved by clinical/ radiological examination.
- Patient willing to give an informed consent.

EXCLUSION CRITERIA-

- Patients having pleural effusion with suspected multiple etiologies.
- Patients having hepatic diseases.
- Patients using any of the following drugs – OCPs, anti-cancer drugs, MAO inhibitors, neostigmine, chlorpromazine.
- Pregnant patients
- Patients with OP compound poisoning.

Sample size-

Sample size require for per group for unpaired comparison = 61. Hence sample size is $61 \times 2 = 122 = 125$.

Patients were divided into two groups

- Group I consisted of 62 patients with transudative effusions and
- Group II consisted of 63 patients with exudative pleural effusion

Patients participating in the study were explained about the procedure, technique and complications of pleural fluid aspiration. Pleural fluid aspiration was performed under strict aseptic precautions after analysing the fluid levels by percussion and chest x-rays. In few of the cases, ultrasonography-guided pleural fluid aspiration was performed.

RESULTS:

The study population comprised of total 125 patients. Out of them 78 (62.4%) were males and 47 (37.6%) were females.

Table 1- showing gender distribution of the cases

Sex	Frequency	Percent
Male	78	62.4
Female	47	37.6
Total	125	100.0

In this study the majority of the cases belonged to the age group of 31-40 years (21.6%) followed by 41-50 years of age group (17.6%). The youngest patient was 18 years old and the eldest patient was aged 93 years old.

The most common cause of pleural effusion was tuberculosis in this study (41.6%) among the exudates and congestive cardiac failure among the transudates (24%). Other significant causes included Dengue fever and Cirrhotic portal hypertension 7.2% and 8% respectively.

Table-2: Showing Etiological distribution of the cases

Diagnosis	Frequency	Percent
Acute Pancreatitis	1	0.8
CCF	30	24.0
CKD	8	6.4
CPH	10	8.0
Dengue fever	9	7.2
Malignancy	3	2.4
NS	5	4.0
SE	7	5.6
TB	52	41.6
Total	125	100.0

The mean values of pleural fluid cholinesterase levels were 806.26 ± 516.28 U/L in the transudates group and 3476.11 ± 1250.17 U/L in the exudates group. The normal levels of cholinesterase varies between laboratories. The cut-off value is 1/10th of the upper limit of normal level of cholinesterase in the respective laboratory. The cut off value was 1600 U/L to differentiate between transudates and exudates. This criteria misdiagnosed 4 (6.5%) cases of transudates as exudates and 5 (7.9%) cases of exudates as transudates. This ratio was found to be statistically significant in this study (p-value <0.001).

Table-3: Predictive value of pleural fluid cholinesterase levels

	Observed	
	Transudate	Exudate
Transudate	58	5
	93.5%	7.9%
Exudate	4	58
	6.5%	92.1%
Total	62	63
	100.0%	100.0%

In this study the most number of misdiagnosed cases were due to the pleural fluid to serum LDH ratio that misclassified 16 cases. Pleural fluid to serum cholinesterase ratio misclassified 5 cases in the total cases. In this study Light's criteria had a sensitivity of 91.9% and specificity of 87.3% in comparison to pleural fluid to serum cholinesterase ratio that had a sensitivity of 96.8% and specificity of 95.2% and hence was the most efficient parameter.

DISCUSSION:

Pleural fluid is one of the most common presentations of a wide variety of the cases. The first step in the management of pleural effusion is its differentiation into a transudate or exudate. The most popular method used is the Light's criteria. But various studies have concluded that pleural effusions are misclassified by Light's criteria in a substantial number of patients. Hence, better and newer parameters with higher sensitivity and specificity are needed. In this study, a new parameter i.e. pleural fluid to serum pseudocholesterase ratio was compared with the Light's criteria in terms of efficacy.

In the original study by Light et al⁷, in a series of 150 patients, the authors correctly classified all but two of the pleural effusions, one transudate and one exudate. In this study Light's criteria misclassified 13 cases in total, whereas the new parameter misclassified only 5 cases. In the study done by Garcia-Pachon et al⁸, Light's criteria misclassified 12 cases (9 transudate and 3 exudate) with a sensitivity of 97.4% and specificity of 74.29%.

In the study by Naveen M et al⁹, the levels of cholinesterase in the pleural fluids was found to be effective to differentiate between transudates and exudates. Among the 50 patients included in the above study, Light's criteria misdiagnosed 10% of the cases. And pleural fluid cholinesterase levels misdiagnosed 2 cases. However in the present study pleural fluid cholinesterase levels misdiagnosed 9 of the total cases.

Table-5: Efficacy of Light's criteria in different studies

Study	Sensitivity	Specificity
Light et al ⁷	99%	97.8%
Garcia-Pachon et al ⁸	97.4%	74.29%
Sharma et al ¹⁰	91.25%	90%
Gowdaiah PK et al ¹¹	93%	96%
Present study	91.9%	87.3%

In this study pleural fluid to serum cholinesterase ratio misdiagnosed 5 cases. The observed sensitivity and specificity in this study was 96.8% and 95.2% respectively. In a study done in 2014 by Gowdaiah PK et al the ratio of pleural fluid to serum cholinesterase ratio misclassified only one case. Similar findings were obtained in the study done by Garcia-Pachon et al and Sharma et al. Thus such a consistent observation can be considered as a significant parameter for evaluation of pleural effusion.¹²

CONCLUSION:

Among the 125 patients, 62 had transudative effusions and 63 had exudative effusions. The average values of pleural fluid pseudocholesterase was significantly higher in exudates than in transudates.

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