

Combined Pleural Fluid Cholesterol and Total Protein in Differentiation of Exudates and Transudates

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ABSTRACT

Background. The management strategy to be adopted in pleural effusion depends on whether an effusion is a transudate or exudate.

Objective. To evaluate the usefulness of pleural fluid cholesterol and/or total protein measurements for differentiating between exudates and transudates, and to compare it with Light's criteria.

Methods. In this prospective study 60 patients with pleural effusion were included. Pleural fluid total protein, lactate dehydrogenase (LDH) and cholesterol as well as serum total protein and LDH levels along with other investigations were studied. Clinical classification of transudate or exudate was done on the basis of aetiology.

Results. Based on clinical signs and symptoms, chest radiograph, other investigations and response to treatment, 49 of these effusions were classified as exudates and 11 as transudates. Using pleural fluid cholesterol levels at a cut-off point of greater than 60 mg/dL and/or total protein at a cut-off point of greater than 3 g/dL for distinguishing transudates and exudates, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), were 100 percent. Using Light's criteria for discriminating transudates and exudates, sensitivity, specificity, PPV and NPV were found to be 98%; 100%; 100% and 92%, respectively. The differences resulted from a mis-classification of one expected exudate as transudate by Light's criteria.

Conclusion. Pleural fluid cholesterol and total protein are simple, cost-effective, and useful parameters in distinguishing pleural transudates from exudates, with the advantage of requiring only two laboratory determinations and no simultaneous blood sample, compared to the use of Light's criteria. [Indian J Chest Dis Allied Sci 2013;55:21-23]

Key words: Pleural fluid total protein, Cholesterol, Light's criteria, Transudates, Exudates.

INTRODUCTION

Pleural effusion is a manifestation of several diseases, both pulmonary and extra-pulmonary, often isolated.¹ Based on the underlying pathological abnormality and mechanism of formation, effusions may be either transudates or exudates.² Analysis of pleural effusions is an important diagnostic step to guide further investigations and treatment.

The most commonly accepted criteria for differentiating exudates from transudates in pleural effusions is through the measurement of total protein and lactate dehydrogenase (LDH) levels in serum and pleural fluid. These were established by Light *et al*³ in 1972. Sensitivity and specificity, calculated from their data, were 99% and 98%, respectively. However, many workers have found Light's criteria as unsatisfactory.^{1,2,4,5}

In 1987, Hamm *et al*⁶ showed that cholesterol concentration increases in exudative pleural

effusions and, by using a cut-off point of 60 mg/dL, these correctly labeled 95% of 62 pleural fluid samples.

Since the criteria of Light *et al*³ require both pleural and blood samples, and four bio-chemical measurements, we examined whether a similar result could be obtained by combining cholesterol estimation with only one of the individual components of Light *et al*,³ thus, simplifying the diagnostic procedure and lowering the cost.

MATERIAL AND METHODS

This prospective study was carried out in the Department of TB and Respiratory Diseases, Shree M.P. Shah Medical College, Guru Gobindsingh Hospital, Jamnagar, Gujarat, India. Sixty adult patients of both sexes suffering from pleural effusion, where thoracocentesis yield a sufficient good quantity of pleural fluid for examination, were included. All patients underwent a detailed history

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and a complete clinical examination. Blood investigations (complete haemogram, total protein, glucose, cholesterol and LDH), urine examination, chest radiograph (postero-anterior view), sputum smear examination for acid-fast bacilli (AFB) were done in all patients. Additional investigations including a lateral chest radiograph, fluoroscopy, ultrasonography, computed tomography chest, pleural biopsy, bronchoscopy, 2-D echocardiogram, standard renal, liver, and thyroid profiles and other tests were done wherever indicated. Pleural fluid analysis was done for total protein, glucose, LDH, cholesterol, total cell count, differential cell count, gram stain for bacteria, Ziehl-Neelsen stain for AFB and cytology in all patients. Pleural and serum collected at the same time.

The patients were divided into three groups clinically according to expected nature of the fluid on aetiological grounds.

Group I. Patients with congestive heart failure (CHF), cirrhosis of liver and pericardial effusion. CHF was diagnosed by an enlarged heart, radiological signs of congested lungs, peripheral oedema, and response to treatment of CHF. Liver cirrhosis was diagnosed by evidence of liver cirrhosis on liver sonogram. Pericardial effusion was diagnosed by 2-D echocardiogram.

Group II. Exudates of a malignant origin confirmed by one or more means: lung biopsy or fine needle aspiration cytology, pleural biopsy, pleural fluid cytology. A case of lymphoma was diagnosed by excisional biopsy of the lymph node.

Group III. Exudates of other origin included those patients with evidence of pneumonia or tuberculosis on radiography, leukocytosis, pleural fluid for Gram's stain, fever, and response to antibiotics or anti-tuberculosis treatment.

For the laboratory classification of pleural fluids, a cut-off point of >3 g/dL for total protein and a cut-off point of >60 mg/dL was adopted for cholesterol.

Laboratory classification was also made by using Light's criteria. According to this criteria if any one of the following is present then the fluid was classified as an exudate: (1) pleural fluid to serum total protein ratio greater than 0.5, (2) pleural fluid to serum LDH ratio greater than 0.6, and/or (3) pleural fluid LDH greater than 200 IU/L.

Statistical Analysis

The statistical analysis was performed using Microsoft Excel. The sensitivities, specificities, positive predictive values and negative predictive values were obtained. The aetiological classification according to the criteria of Light *et al*³ was used as the "Gold Standard".

RESULTS

The aetiological classification of the 60 effusions is shown in table 1. According to the causal disease, 11 pleural fluid samples were labelled as transudates and 49 were labelled as exudates. One of the 49 exudates was mis-classified as transudate (sensitivity 98%) while there was no mis-classification of the 11 transudates (specificity 100%).

Table 1. Causes of pleural effusion

| Transudates (Group I) | |
|--------------------------------------|----|
| CHF | 5 |
| Cirrhosis | 2 |
| Pericardial effusion | 2 |
| Constrictive pericarditis | 1 |
| Post operative | 1 |
| Malignant effusion (Group II) | |
| Lung | 8 |
| Epiglottitis | 1 |
| Lymphoma | 1 |
| Other Exudates (Group III) | |
| Tuberculosis | 30 |
| Pneumonia | 8 |
| Liver abscess | 1 |

CHF=Congestive heart failure

When pleural fluid cholesterol alone was used at a cut-off point of >60 mg/dL, one (tuberculous pleural effusion) of the 49 exudates was mis-classified as transudate (sensitivity 98%) while there was no mis-classification of the 11 transudates (specificity 100%). When the pleural fluid cholesterol with a cut-off point of >60 mg/dL in combination with a pleural fluid total protein with a cut-off point of >3 g/dL was used for classification, all exudates and transudates were correctly labelled (sensitivity and specificity both were 100%). The exudate that was erroneously classified by the criteria of Light *et al*³ was correctly identified using cholesterol level, while the exudate that was mis-classified by cholesterol was correctly identified by the pleural fluid total protein level.

Table 2 shows the sensitivity, specificity, PPV and NPV calculated for the criteria of Light *et al*³, for cholesterol alone, for total protein alone and for combination of cholesterol and total protein.

DISCUSSION

The initial step in the management of pleural effusions is to distinguish transudates from exudates.

Table 2. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for different parameters

| | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|--|-----------------|-----------------|---------|---------|
| Pleural fluid protein | 98 | 100 | 100 | 92 |
| Light's criteria | 98 | 100 | 100 | 92 |
| Pleural fluid cholesterol | 98 | 100 | 100 | 92 |
| Pleural fluid protein and/or pleural fluid cholesterol | 100 | 100 | 100 | 100 |

The criteria often used to do so are based on biochemical parameters proposed by Light *et al.*³ Since no single test has yet proved to be completely satisfactory, the search for improved methods continues.

The cholesterol levels are elevated in exudative pleural effusions of much shorter duration.⁷ The cause of the increased cholesterol concentration in pleural exudates is unknown. Increased pleural permeability leading to accumulation of cholesterol in pleural exudates due to "serum leakage" may be a reasonable explanation. Cholesterol is found in all tissues and is uniformly found in all pleural effusions.⁸

Our results show that an increased concentration of cholesterol greater than 60 mg/dL and/or total protein levels greater than 3 g/dL in pleural fluid constitute useful measurements for separating exudates from transudates. The diagnostic yield of this combination is superior to that obtained by Light *et al.*³ in their original investigation and to those reported by other authors^{2,4-6} and what is observed in the present study using the same diagnostic criteria in similar patients. Romero *et al.*,⁹ propose a modification of the cut-off points of Light *et al.*³ that increase specificity to 93% with a slight decrease of sensitivity to 94%. Despite the improvement, these values are lower than those obtained with the combined use of cholesterol and total protein.

CONCLUSIONS

Combined pleural fluid cholesterol and total protein are simple, cost effective, and useful parameters for differentiation of transudates from exudates. Simultaneous measurement of total protein and cholesterol in pleural fluid permits the identification of exudates through the elevation of either one or both of these indicators, with an accuracy superior to the best that has been reported with the criteria of Light *et al.*³ The proposed combination has the advantages that a simultaneous blood sample is not required and that chemical tests are reduced from four to two, thereby, lowering the cost of the diagnostic procedure.

The major limitations of the present study are the small numbers of patients, especially one patient out of 60 patients was mis-classified. The results of the present study need to be confirmed in further studies with large sample size of the patients.

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