Research Journal of Medical Sciences 3 (3): 91-94, 2009
ISSN: 1815-9346

Specific Gravity of Pleural Fluid Determined by Refractometer to Discriminate Exudates and Transudates

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Abstract: The first diagnostic step in pleural fluid analysis in patients with pleural effusion is differentiating transudates from exudates. This study was done with the objective of determining the sensitivity and specificity of pleural fluid specific gravity in differentiating transudate from exudate fluids. Hundred patients (71 males and 29 females) with pleural effusion, who were referred to the pulmonary ward of the university hospital, underwent diagnostic thoracentesis. According to Light's criteria exudates and transudates were distinguished. Then, pleural fluid specific gravities were determined by refractometer. All patients were followed, until final diagnoses were documented by invasive and/or non-invasive methods. We calculated sensitivity, specificity, positive and negative predictive values of different specific gravities to obtain the optimal cutoff value. Seventy percent patients were diagnosed as having exudative pleural effusion and 30% patients with transudative effusion. The mean (SD) specific gravity in patients with exudative and transudative pleural effusion were 1033.6 (7.05) and 1021.4 (4.45), respectively ($p<0.05$). Optimal sensitivity and specificity were achieved at a cutoff value of 1024. At this cutoff value sensitivity, specificity, positive predictive value and negative predictive value were 91.4, 66.7, 86.5 and 76.9%, respectively. Specific gravity of pleural fluid was found to be a simple and sensitive method for distinguishing between transudates and exudates.

Key words: Pleural effusion, specific gravity, exudate, transudate

INTRODUCTION

Tight control of the volume and composition of the pleural liquid is necessary to ensure an efficient mechanical coupling between lung and chest wall. The factors responsible for pleural effusion may be subdivided into 3 main categories; those changing transpleural pressure balance, those impairing lymphatic drainage and those producing increases in mesothelial and capillary endothelial permeability. Except in the first case, pleural fluid protein concentration increases above normal: This feature underlies the classification of pleural effusions into transudates and exudates (Zocchi, 2002). Thus, the initial step in the diagnostic evaluation of individuals with pleural effusion is to discriminate transudative effusions versus exudative ones (Porcel and Vives, 2003). Several studies have evaluated the discriminative properties of different pleural fluid tests for identifying exudative effusions. Established clinical practice has favored diagnostic strategies that combine pleural fluid Lactic Dehydrogenase (LDH) value, ratio of pleural fluid to serum LDH (LDH-R) and ratio of pleural fluid to serum protein combined in "or" rules (Light's criteria), in which an exudative effusion is identified if any one of the criteria is fulfilled (Heffner *et al*., 2002). More recent studies have examined the diagnostic utility of pleural fluid cholesterol (Costa *et al*., 1995), cholinesterase (Garcia-Pachon *et al*., 1996), oxidative stress concentrations (Papageorgiou *et al*., 2005), comparing the sensitivities and specificities of the new tests with the

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3 tests combination of Light's (1979) criteria. The specific gravity of a substance is a comparison of its density to that of water. Because of close correlation between specific gravity of pleural fluid and protein content, it has been used as a tool to discriminate between transudative and exudative effusions (Light, 1979).

The aim of this study, was to examine the sensitivity and specificity of pleural fluid specific gravity in differentiating between transudative and exudative pleural effusions.

MATERIALS AND METHODS

In this cross-sectional study, which was performed in the Mobasher Hospital affiliated by Hamedan University of Medical Sciences, Hamedan, Iran pleural fluids from 100 consecutive patients admitted to pulmonary ward of the university hospital were analyzed. A postero-anterior and lateral decobitus chest radiography was done in all cases. Pleural effusion was diagnosed according to >10 mm thickness of pleural fluid on the lateral decobitus radiography and underwent diagnostic thoracentesis and pleural fluid was then analyzed for LDH and protein levels. Simultaneously serum LDH and protein levels were also determined. Light's criteria (1979) were used to differentiate transudates from exudates. Pleural fluid specific gravity was estimated using refractometer (ERMA, Tokyo, Japan), calibrated for urinary specific gravity. Refractive index depends on the solid phase of a solution. It is calculated as air/solution photon velocity ratio. This ratio directly depends on the numbers of particles of the solution (Garcia-Pachon *et al*., 1996). Patients were followed by invasive and non-invasive methods and finally diagnosis was confirmed. Effusions were classified into the following diagnostic groups defined by the following predetermined criteria:

- Congestive cardiac failure was diagnosed when all of the following criteria were met: cardiomegaly, radiological evidence of congested lungs, peripheral edema and response to treatment for CHF. In all cases, there was an absence of specific clinical evidence of pulmonary embolism (e.g. hemoptysis, pleuritic chest pain) or thrombophlebitis and an absence of purulent sputum, malignancy, or pulmonary infiltrates
- Renal failure was diagnosed, when there were raised urea and creatinine levels in the presence of clinical evidence of fluid overload (e.g. pulmonary or peripheral edema) and an absence of purulent sputum, malignancy or pulmonary infiltrates
- Other transudates included the following: nephrotic syndrome, diagnosed when the patient had proteinuria, edema and hypoalbuminemia; other causes of hypo-albuminemia, determined when serum albumin level was <30 g L^{-1} in the absence of proteinuria and histologically proven liver cirrhosis (e.g. kwashiorkor, severe burns) and liver cirrhosis, diagnosed by histologic study in the presence of ascites. In all cases, there was an absence of purulent sputum, malignancy, or pulmonary infiltrates
- Neoplastic effusions were diagnosed when one of the following criteria was met: Cytologic or histologic evidence of a malignant pleural effusion, or histologic proof of a malignant tumor with exclusion of any other cause known to be associated with pleural effusions
- Tuberculous pleuritis was diagnosed by identifying the bacillis in pleural fluid or biopsy specimen cultures, or from the presence of caseous granulomas in pleural biopsy tissue. In the case of radiologic and clinical evidence of tuberculous pleurisy, followed by response to antituberculous therapy, adult patients having Mycobacterium tuberculosis in the sputum were also included; in the case of children, such patients were included when M tuberculosis was found in sputum or gastric juice, or they were found to have a positive Purified Protein Derivative (PPD) >10 mm
- Infective effusions were identified by the presence of pneumonic infections associated with acute febrile illness, pulmonary infiltrates, purulent sputum and responsiveness to antibiotic treatment, or identification of the organism in the pleural fluid; empyema, associated with the finding of frank pus in the pleural cavity; septicemia, characterized by radiologic evidence of pulmonary infiltrates and multiple organ involvement in the presence of positive blood cultures and other obvious infective conditions in the absence of any other cause associated with pleural effusions
- Pulmonary embolus or infarct was diagnosed when there was a strong clinical suspicion and high probability ventilation-perfusion (V/Q) scan, according to the revised Prospective Investigation of Pulmonary Embolism Diagnosis criteria (Gottschalk *et al*., 2007) or postmortem finding

A designed checklist was completed for each patient by residents contained variables like demographic features, clinical and laboratory findings (glucose level of fluid, differential cell count, microbiologic and cytologic studies) and the final diagnosis.

Descriptive indices such as frequency, percentage, mean and Standard Deviation (SD) were used to express data. The sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) for identification of exudates and transudates were also calculated. All analyses were done using SPSS software version 13.0 (SPSS Inc, Chicago, IL). Significance level was defined as $p<0.05$.

RESULTS

One hundred patients (71 males and 29 females) with pleural effusion were evaluated. According to Light (1979) criteria, 70% patients had exudates and 30% had transudates. The most common causes of pleural effusion were malignancies (25% patients), that all of them had exudative effusion. Table 1 presents different causes of pleural effusions. The most common exudative effusion etiology was malignancies (35.7%), which were followed by unknown causes (30%). The most common transudative effusion etiologies included congestive heart failure and unknown causes with was shown in 43.3 and 30% of patients, respectively.

The range of measured pleural fluids' specific gravities was from 1013-1050. The mean (SD) specific gravity in patients with exudative and transudative pleural effusions was 1033.6 (7.05) and 1021.4 (4.45), respectively ($p<0.05$).

Table 1: Causes of transudative and exudative pleural effusion

Causes	Exudative (%)	Transudative (%)	Total (%)
Malignancies	25 (35.7)	-	25 (25)
Unknown	21 (30.0)	9 (30.0)	30 (30)
Congestive heart failure	-	13 (43.3)	13 (13)
Empyema	9 (12.9)	-	9 (9)
Tuberculosis	7 (10.0)	-	7 (7)
Pulmonary tromboembolism	1 (1.4)	4 (13.3)	5 (5)
Eosinophilic pneumonia (Leofler's syn)	2 (2.9)	-	2 (2)
End stage renal disease	-	2 (6.7)	2 (2)
Parapneumonic effusion	2 (2.9)	-	2 (2)
Nephrotic syndrome	-	1 (3.3)	1 (1%)
Lupus erythematosus	-	1 (3.3)	1 (1)
Rheumatoid arthritis	1 (1.4)	-	1 (1)
Viral pneumonia	1 (1.4)	-	1 (1)
Drug effusion (nitrofurantoin)	1 (1.4)	-	1 (1)

Table 2: Sensitivity, specificity, positive and negative predictive values at different specific gravity cutoff values

Specific gravity	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1020	95.7	33.3	77.0	76.9
1021	95.7	46.7	80.7	82.4
1022	94.3	46.7	80.5	77.8
1023	91.4	56.7	83.1	73.9
1024	91.4	66.7	86.5	76.9
1025	90.0	66.7	86.3	74.1
1026	87.1	80.0	91.0	72.7
1027	85.7	86.7	93.8	72.2
1028	84.3	93.3	96.7	71.8
1029	77.1	96.7	98.2	64.4
1030	75.7	96.7	98.1	63.0

The sensitivity, specificity, PPV, NPV of specific gravity in different cutoff points are presented in Table 2. The optimal accuracy of the sensitivity and specificity was achieved at a cutoff value of specific gravity at 1024. Therefore, sensitivity, specificity, PPV and NPV were 91.4, 66.7, 86.5 and 76.9%, respectively. Exudates were classified having a specific gravity >1024 and transudates <1024.

DISCUSSION

A transudative effusion results from an imbalance of Starling's forces ending to the movement of fluid into the pleural space, whereas inflammation of the pleural surface by increased vascular permeability forms exudative pleural effusions (Yetkin *et al*., 2006). Light (1979) criteria are the standard method for distinguishing between transudates and exudates, due to its high sensitivity in identifying exudates (Gonlugur and Gonlugur, 2005). According to our results, specific gravity of pleural fluid in patients with exudative effusions was significantly greater than that of patients with transudative pleural effusion. The least cutoff point, tested in this study was 1020. Using this cutoff level yielded sensitivity, specificity, PPV and NPV (for exudates) of 95.7, 33.3, 77 and 76.9%, respectively. Although, 1020 had a good sensitivity in identifying pleural exudates, but its specificity was low and therefore, the false positive cases were high, which was not optimal. From 1024-1030, specificity increased and sensitivity decreased. Using a cut of point of 1030 yielded a sensitivity of 75.7% and specificity of 96.7% (for exudates). Base on the researchers opinion, a cut off point of 1024 yielded the best results in differentiating exudates from transudates.

According to Light (1979), refractometer gave falsely high level for the specific gravity of the pleural fluid. A reading for 1019 (rather than 1016) corresponded of protein of 3.0 g/100 mL and each deviation of 0.005 (rather than 0.003) corresponded to a concentration of 1 g/100 mL; however, determinations of protein in the pleural fluid directly from the refractometer's scale for protein (calibrated for serum) was rapid and accurate (Light, 1979). Separation of exudates from transudates remains a useful step in determining the etiology of a pleural effusion and the decision as to whether further and often more invasive investigations should be carried out on the patients.

CONCLUSION

Pleural fluid specific gravity determination was found to be a simple and time saving method with an acceptable sensitivity for distinguishing between transudates and exudates.

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