



A Study on Significance of Serum Effusion Albumin Gradient in The Differential Diagnosis of Pleural Effusion

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Abstract

To evaluate serum pleural effusion albumin gradient (SEAG) as method of differentiating pleural transudates from exudates. Cases admitted in AMCH with diagnosed pleural effusion were divided into 2 groups based on etiology. Group I (transudates): Comprising 14 patients of congestive heart failure (n=6) and nephrotic syndrome (n=3), Cirrhosis (n=4), pericardial effusion (n=1). Group II (exudates): comprising 26 cases of tuberculous (n=15), malignant (n=8) and parapneumonic effusion (n=2), rheumatoid arthritis (n=1). In all patients estimation of pleural fluid to plasma protein ratio, pleural fluid to serum LDH ratio & pleural fluid LDH level, plasma-pleural effusion gradient were evaluated. All these parameters were compared in differentiating pleural transudates from exudates. A total of 40 patients having pleural effusion were divided into 2 groups. Group I (Transudates), Group II (Exudates). Pleural fluid to serum protein of >0.5 misclassified 20%, pleural fluid LDH OF 200 U/L misclassified 17.5%, pleural fluid LDH to serum LDH misclassified 12.5%, & serum effusion albumin gradient misclassified 5% while differentiating transudates from exudates. Serum pleural effusion albumin gradient (SEAG) is a very useful parameter to differentiate between exudates and transudates esp. in cases misclassified by Light's criteria.

Key Words

Pleural Effusion, Serum Effusion Albumin Gradient

Introduction

Pleural effusion is a common complication of many disease processes either local or systemic where differentiation between transudate & exudates is necessary to assist in differential diagnosis (1-10). Presently Light's criteria (2) are used to distinguish between transudates & exudates (pleural fluid/serum protein ratio >0.5 , pleural fluid/serum LDH ratio >0.6 & absolute pleural fluid LDH >200 U denote an exudates). But many pleural effusions, misclassified as transudates or as exudates have been reported using these criteria (11-12). Recently, many new parameters have been reported to distinguish transudates from exudates, like pleural fluid cholesterol (11-12), pleural fluid to serum bilirubin ratio (13), pleural fluid cholinesterase (14), alkaline phosphatase (15), creatinine kinase, uric acid (16) and pleural fluid malondialdehyde (MDA) (17). But none have

better sensitivity and specificity than Light's criteria. Recently, serum-pleural effusion albumin gradient (SEAG) has been reported as a good parameter with sensitivity and specificity of 95% and 100% respectively (18). The present study was planned to evaluate (SEAG) for differentiating pleural transudates from exudates.

Material and Methods

A total of 40 patients having pleural effusion of diverse etiology were divided into 2 groups: Group I (transudates): Comprising 14 patients of congestive heart failure (n=6) and nephrotic syndrome (n=3), Cirrhosis (n=4), pericardial effusion (n=1). Group II (exudates): comprising 26 cases of tuberculous (n=15), malignant (n=8) and parapneumonic effusion (n=2), rheumatoid arthritis (n=1). Cases, in which either no cause was definitely diagnosed

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or more than one cause was present, were excluded from the study. After detailed history taking, thorough clinical examination and investigation, each patient was evaluated for the following: Blood: Serum LDH, total plasma protein and plasma albumin levels. Pleural fluid: Total proteins, LDH and albumin levels

Estimations

A). Protein estimation: Plasma and pleural fluid total protein levels were estimated by the method described by Reinhold (19).

B). LDH estimation: LDH level was estimated by UV kinetic method recommended by the Scandinavian Society for clinical Chemistry and was expressed as IU/L (20).

C). Albumin estimation: Determination of plasma and pleural fluid albumin was done using manual method of Doumas *et al* (21) and modified Spencer and Price method (22).

Statistical Analysis

The mean and S.D. were calculated for each parameter both for exudates and transudates, and unpaired “t” test was used to compare them with respect to various parameters.

Results

The mean age of the 40 patients was 45 years. Male to female ratio was approximately 3:2, the ratio of smokers to non-smokers was 1:1, the ratio of vegetarian and non-vegetarian was 2:1 and the ratio of alcoholic to nonalcoholic was 2:1. pleural fluid examination results were analyzed on the basis of Light’s criteria and compared with SEAG parameter.

Table 1 shows exudates and transudates separated by pleural fluid protein to serum protein of .5 in comparison to the established diagnosis of transudates and exudates. The pleural fluid to serum protein ratio of .5 separated 23 cases (57.5%) as exudates & 17 (42.5%)

as transudates. When etiology was reviewed 5 of the exudates & 3 transudates were falsely classified. Total misclassification of 20% occurred. ‘P’ value is significant.

Table 2 shows exudates and transudates separated by pleural fluid LDH of 200 U/L. ‘P’ value is significant. Pleural fluid LDH of 200 U/L separated 24 (60%) as exudates & 16 (40%) as transudates. When etiology was reviewed 4 of exudates & 3 of transudates were falsely classified. Total misclassification of 17.5% occurred. ‘P’ value is significant.

Table 3 shows exudates and transudates separated by pleural fluid LDH to serum LDH of 0.6 in comparison to the established diagnosis of exudates and transudates. Pleural fluid LDH to serum LDH of .6 separated 27 (67.5%) as exudates & 13 (32.5%) as transudates. When the etiology was reviewed 3 of the exudates & 2 transudates were falsely classified. Total misclassification of 12.5% occurred. ‘P’ value is highly significant.

Table 4 shows number of cases separated by serum-effusion albumin gradient of 1.2 g/dl in comparison to the established diagnosis of exudates and transudates. Serum-Effusion Albumin gradient of 1.2 g/dl separated 26 (65%) cases as exudates & 14 (35%) as transudates when etiology was reviewed only one exudates & 1 transudate was falsely classified. Total misclassification of 5% occurred. ‘P’ value is highly significant.

Table 5 shows comparative analysis of the parameters used in the study of 40 cases of pleural effusion. It is seen that misclassification of only 5% occurred with the serum effusion albumin gradient in comparison to higher misclassification rate that was seen with other parameters used in the study.

Table 6 shows sensitivity, specificity of various parameters studied. Sensitivity and specificity of 96.1% and 93.0% was seen with serum effusion albumin gradient

Table 1. Cases Differentiated by Pleural Fluid to Serum Protein Ratio of 0.5

Types of Pleural Fluid	Etiologically Diagnosed (N = 40)	No. of Cases Differentiated by P/S Protein of 0.5	No. of Cases Truly Classified	No. of Cases Falsely Classified	‘P’ Value
Exudate	26	23	18	5	<. 01 (S*)
Transudate	14	17	14	3	

Table 2. Cases Separated by Pleural Fluid LDH of 200 U/L

Types of Pleural Fluid	Etiologically Diagnosed (N = 40)	No. of Cases Differentiated by Pleural Fluid LDH of 200 U/L	No. of Cases Truly Classified	No. of Cases Falsely Classified	‘P’ Value
Exudate	26	24	20	4	<. 01 (*S)
Transudate	14	16	13	3	



Table 3. Cases Separated by Pleural Fluid LDH to Serum LDH of 0.6

Types of Pleural Fluid	Etiologically Diagnosed (N = 40)	No. of Cases Differentiated by P/S LDH OF 0.6	No. of Cases Truly Classified	No. of Cases Falsely Classified	'P' Value
Exudate	26	27	24	3	<.001 (H.S.**)
Transudate	14	13	11	2	

Table 4. Cases Separated by Serum - Effusion albumin Gradient of 1.2g/dl

Type of Pleural Fluid	Etiological Diagnosis (N = 40)	No of Cases Differentiated by SEAG of 1.2 G/DL	No. of Cases Truly Classified	No. of Cases Falsely Classified	'P' Value
Exudate	26	26	25	1	<.001 (H.S.**)
Transudate	14	14	13	1	

Table 5. Comparative Analysis of The Parameters

Parameter	Exudates Classified Correctly [%]	Transudates Classified Correctly [%]	Mis -Classification Rate [%]
PF Protein [3gm/dl]	72.70	77.70	25.00
P/S Protein [0.5]	78.26	82.35	20.00
PF LDH [200IU/L]	83.30	81.25	17.50
P/S LDH [0.6]	88.80	84.60	12.50
SEAG of 1.2 gm/dl	96.15	93.60	5.00

Table 6. Sensitivity and Specificity of the Parameters

Parameters	%age	
	Sensitivity	Specificity
PF Protein	80.0%	70.0%
Pleural fluid to plasma protein ratio	85.0%	73.7%
Pleural fluid LDH level (IU/L)	86.0%	77.0%
Pleural fluid to serum LDH ratio	92.0%	73.3%
Serum-effusion albumin gradient	96.1%	93.0%

Discussion

In the evaluation of a pleural effusion the first step is to distinguish between transudates and exudates (1-10). The criteria used for the purpose was suggested by Light *et al* (12) with misclassifications varying from 2% to 40% (23-25). Later, many more parameters like pleural fluid cholesterol, pleural fluid to serum cholesterol ratio, pleural fluid to serum bilirubin ratio, pleural fluid to serum cholinesterase ratio were suggested, but no parameter has yet been proved to be satisfactory.

Keeping all these factors in mind the present study was undertaken in Assam Medical College, Dibrugarh between 2003-2004 to study the significance of serum-effusion albumin gradient in differential diagnosis of pleural effusion and compared with already established Light's criteria.

In the present study of 40 cases of pleural effusions, pleural fluid protein of 3gm/dl separated 55% as exudates

and 45% as transudates with a total misclassification of only 25% occurs. The sensitivity and specificity of this parameter is 80% and 70%. Pleural fluid to serum protein ratio of 0.5 separated 57.5% as exudates and 42.5% as transudates with a misclassification rate of 20% with a sensitivity and specificity of 85% and 73.7%. Pleural fluid LDH of 200 U/L separated 60% as exudates and 40% as transudates with a misclassification rate of 17.5% and with a sensitivity and specificity 86% and 77%.

Pleural fluid LDH to serum LDH of .6 separated 67.5% as exudates and 32.5% as transudates with a misclassification rate of 12.5% with a sensitivity and specificity of 92% and 73.3%.

Lastly serum effusion albumin gradient of 1.2g/dl separated 65% as exudates and 35% as transudates with a total misclassification of only 5% with a sensitivity and specificity of 96.1% and 93%.



The study revealed that even though the parameter of pleural fluid protein of 3gm/dl, pleural fluid to serum protein of 0.5, pleural fluid LDH level of 200 U/L and pleural fluid LDH to serum LDH of 0.6 are useful in differentiating the exudates and transudates. The greater differential value is found with SEAG value of 1.2gm/dl, which correctly classified 96.15% of exudates and 93.6% of transudates with a total misclassification of only 5% with a sensitivity, and specificity of 96.1% and 93%.

Conclusion

Hence, serum-effusion albumin gradient is found to be better criteria for rightly classifying transudate and exudate in misclassified effusion.

References

- Sahn SA. The pleura. *Am Rev Respir Dis* 1988; 138:184
- Light RW, MacGregor MI, Luchsinger PC, Ball WC. Pleural effusion. The diagnostic separation of transudates and exudates. *Ann Intern Med* 1972; 77:507
- Light RW. Pleural effusion. *Med Clin North Am* 1977; 61:1339
- Romero S, Chandela AMC *et al.* Evaluation of different criteria for the separation of pleural transudates from exudates. *Chest* 1993; 104:399.
- Barter T, Santarelli R, Askers SM *et al.* The evaluation of pleural effusion. *Chest* 1994; 106:1209.
- Valdes L, Pose A, Alvarez D *et al.* Biochemical discrimination of transudate and exudate. *Chest* 1994; 106:1634.
- Vives M, Porcel JM, Devera MV, Ribelles E, Rubio M A Study of Light's criteria and possible modifications for distinguishing exudative from transudative pleural effusion. *Chest* 1996; 109:1503.
- Lakhotia M, Shah PK, Yadav A, Gupta A, Modi RK. Comparison of biochemical parameters in pleural effusion. *J Assoc Phys India* 1996; 44(9): 612
- Padilla NI. Pleural effusion: criteria for distinguishing between transudates and exudates. *An Internal Med* 1996; 13(9): 460
- Garquez I, Porcel JM, Vives M, Rubio M, Rivas MC. Comparative analysis of Light's criteria and other biochemical parameters for distinguishing transudates and exudates. *Respir Med* 1998; 92(5): 762
- Hamm H, Brohan VB, Bohmer R *et al.* Cholesterol in pleuraleffusion: a diagnostic aid. *Chest* 1987; 92:296
- Gupta KB, Tandon S, Singh GP, Dhania OP, Janmeja AK. Pleural fluid cholesterol and serum cholesterol ratio as a parameter to differentiate between pleural transudates and exudate. *Ind J Tub* 1999; 46:255.
- Meisel S, Shamiss A, Thaler M *et al.* Pleural fluid to serum bilirubin concentration ratio for separation of transudates from exudates. *Chest* 1990; 98(1): 141
- Gracia PE, Padilla Navas I, Sanchez JF *et al.* Pleural Fluid to serum cholinesterase ratio for the separation of transudates and exudates. *Chest* 1996; 110:97
- Thaglu K, Kizkin O, Remziye EL. Alkaline phosphate: distinguishing between pleural exudates and transudates. *Chest* 1994; 107:1912
- Metintas M, Alatas O, Alatas F, Colak O, Ozdemir N. Comparative analysis of biochemical parameters for differentiation of pleural exudates from transudates: Light's criteria, cholesterol, bilirubin, albumin gradient, alkaline phosphatase, creatinine kinase and uric acid. *Clin Chem Acta* 1997; 29:264(2): 149
- Hammouda RMA, Khaid MM, Salem A. Lipid peroxidation products in pleural fluid for separation of transudates and exudates. *Clin Chem* 1995; 41(9): 1314
- Reinhold JG. In: Reiner M, (editor) Standard Methods of clinical chemistry. New York: Academic Press, 1953
- Chandrashekhar AJ, Palatao A, Dubin A *et al.* Pleural fluid lactic dehydrogenase activity and protein content. *Arch Intern Med* 1989; 123:48
- Doumas BT, Watson WA, Biggs HG. Albumin standards and the Measurement of serum albumin with Bromcresol. *Green Clin Chem Acta* 1971; 31:87
- Spencer K, Price CP. Influence of reagent quality and reaction conditions on the determination of serum albumin by the Bromcresol Green Dye-binding Method. *Ann Clin Biochem* 1977; 14:105
- Burges LJ, Martiz RJ, Talijard JF. Comparative analysis of the biochemical parameter used to distinguish between pleural transudates and exudates. *Chest* 1995; 107(6): 1604
- Akriviadis EA, Kapnias D, Hadjigavriel M *et al.* Serum/ascites albumin gradient: its value as a rational approach to the differential diagnosis of ascites. *Scand J Gastroenterol* 1996; 31(8): 814
- Light RW. Diagnostic principles of pleural disease. *Eur Resp J* 1997; 10(2): 476
- Light RW. Useful tests on the pleural fluid in the management of patients with pleural effusions. *Curr Opin Pulm Med* 1999; 5(4) :245-49

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