Original Article

Pharmacology

Validity of Pleural Fluid Protein in Differentiating Tuberculouse from Malignant Pleural Effusion

1. Ghulam Nabi Khokhar 2. Muhammad Ashfaq 3. Ikram Ullah Khan 4. Muhammad Ishaq 5. Israr Ahmed

1. Prof. of Pharmacology 2. Assoc. Prof. of ENT 3. Asstt. Prof. of Pharmacology 4. Prof. of Surgery 5. Prof. of Physiology, Jinnah Medical College, Peshawar

ABSTRACT

Objective: Validity of pleural fluid protein in differentiating tuberculouse from malignant pleural effusion keeping histopathology as gold standard.

Study Design: Cross sectional study.

Place and Duration: This study was conducted in the Pulmonology department post graduate medical institute, Lady Reading Hospital Peshawar, Khyber Pakhtunkhwa (KPK) Pakistan from March 2009 to March 2010.

Materials and Methods: One hundred and seventy nine patients having clinical suspicion of pulmonary tuberculouse and malignancy and fulfilling the inclusion criteria were subjected to Abrams needle biopsy, plural tissue was examined by histopathology. Biopsy in order to know the significant difference of pleural fluid protein level between tuberculous and malignant pleural effusion, histopathology finding and protein concentration were determined their frequency and percentage.

Results: Among total number of 179 patients one hundred and fourteen (63.69%) were male and sixty five (36.32%) were female. The age limit from 15-80 years, the result shows that 60.9% were tuberculous and 39.9% were malignant pleuraleffusion, among these malignant 20 (11.2%) showed primary and 50 (27.9%) secondary malignancy. Tuberculous PE was more common in younger age group while malignant PE in older age group, 32 number of patients falling in category A, 59 in category B, and 89 in category C.A protein level in belonging to category C, there was statistically significant difference between tuberculous and malignant PE, tuberculous PE have high concentration of protein than malignant PE, The category "A" have malignant PE.

Conclusion: Plural fluid total protein level determination and differentiating is a valuable tool in reaching to the diagnosis of suspectedtuberculouse from malignant pleural effusion provided it is used in addition to the adequate clinical scenario.

Key Words: Tuberculouse pleural effusion, malignant pleural effusion, Exudates, pleural fluid protein.

INTRODUCTION

Pleural effusion (PE) is a common clinical problem both in developed and developing countries.[1] The etiological investigation of a pleural effusion is to determine whether the effusion is a transudate or exudates. Transudates reflect the presence of systemic disease with repercussion.On the mechanism of pleural fluid production and production and reabsorption.[2]In contrast, exudates reflect, the presence of primary pleural disease and require etiological investigation.[3] So in case with trandatePE, the diagnosis is usually made without any difficulty but executive PE, require careful differential diagnosis that include tuberculouse (TB) and metastatic cancers, which are often found to be the cause in a large number of patients.[4][5] Disease in any organ can cause execute PE through a variety of mechanisms including, malignancy, immunologic response, lymphatic abnormality and non-infections inflammation.[6]Tuberculouse and malignancy are the most common causes of exudative PE in our country.[7] The gold standard for diagnosis of pleural tuberculouse is theidentification of mycobacterium tuberculouse in pleural fluid or tissue[8] however in clinical practice this identification is problematic of the low identification rate of the bacillus (less than 30% in pleural fluid and approximately 50% in the pleura) and the slow growth of mycobacterium in culture (about 60 days). [9] The diagnosis of neoplastic pleural effusion is made based on the presence of malignant cells in the pleural fluid or tissue. The positivity rate of the cytological examination ranges from 40 to 87% higher than that obtained with a needle biopsy which ranges from 35 - 65 %. [13] Several tests for the diagnosis of tuberculous in pleural effusion have been used as tuberculouse identification such as Adenosine deaminase, interferon, Lysozyme, the polymerase chain reaction. [11] and specific C antibodies.[12]However these test need specific measure and expensive equipment that are not available in most laboratories particularly in developing countries, similarly in developed countries various new parameters like pleural viscosity, C- reactive protein, carcinoembryonic antigen, interleukin, interferon, vascular endothelial growth factor, tumor necrosis factor and pleural fluid T-cells are used for the determination of tuberculous and malignancy.[13] In our

country only closed pleural biopsy and pleural fluid analysis are carried out for the diagnosis of tuberculouse and malignancy.Yetkin etal. (2007)[14] have discuss the role of viscosity in the differential diagnosis of excaudate pleural effusion. The pleural fluid protein level was > 30 g/l in excaudate in the contrast of a normal serum protein level. The Lights criteria[15]indicate the concentration of protein in exudates is ratio of pleural fluid protein/serum protein >0.5.This study was aimed to explore the role of pleural fluid protein in differentiating tuberculouse from malignant pleural effusion.

MATERIALS AND METHODS

The study was conducted at pulmonary department Post Graduate Medical Institute Lady Reading Hospital Peshawar, KPK, from March 2009 to March 2010.179 patients were selected in this study, attending to pulmonology unit OPD, Emergency department and private clinics were evaluated. Patient's unit exudate pleural effusion was subjected to Abrams needle biopsy after taken informed written consent. The specimen was sent from Histopathological examination and pleural fluid for biochemical examination. The biopsy and laboratory analysis reposts were collected and recorded in Proforma designed for this study, one standard laboratory was used for plural fluid analysis and pleural tissue was examined by well experience histopathologist to the diagnosis of malignant pleural effusion is based on the finding of neoplastic cells in pleural fluid or pleural tissue obtained by Abrams needle biopsy.Lymphocytic exudative pleural effusion, sign and symptoms consistent with Tuberculous Pleural Effusion, sign and symptom consistent with malignant pleural effusion all the patients male and female from 15-80 years of age.Transudative pleural effusion, cases of in conclusion pleural biopsy, polymorphic exudative pleural effusion/ emphyema, those patients who were uncooperative or not willing for pleural biopsy.Sample size was 179, using 9% prevalence, 95% confidence level and 4.2% margin of error, under W.H.O formula of sample size determination.In order to know the significant difference of pleural fluid level between tuberculouse and malignant pleural effusion three categories were made is category "A" having from 4-5 g/dl and category C, having protein concentration higher than 5 g/dl.Data was analyzed using statistical package for social sciences (SPSS) version 10.0. Mean ± standard deviation was calculated for age and pleural fluid protein level. Qualitative variables such as gender, pleural biopsy histopathology result were calculated in frequencies and percentages. Chi- square test was calculated for total plural fluid protein level for tuberculouse and malignant pleural effusion and P valve was significant it found < 0.05.

RESULTS

Total no of patients were 179. There were 114 (63.69%) male and 65(36.32%) were female. Age limit was from 15-80 years, age wise distribution and result of TPE & MPE are given. Table (1). Age range was as follows the no of patients with age range 15-20 years was 12 (6.7%), 20 to 40 years 72 (40.2%), 41-60 years 67 (37.4%) and the patients age range of 61-80 years old were 28 (15.6%).TPE and MPE in various age groups was analyzed as that TPE was more common in age groups of < 20 years and 20-40 years, while in age groups of 41-60 years the tuberculous pleural effusion (TPE) cases were 22(20.9%) the mean age in tuberculouse pleural effusion was 35.8+15.435D similarly in age groups of 61-80 years, the MPE was common than TPE. The mean age for malignant pleural effusion groups was 57+ 13.13 SD. TPE was common in younger age groups whole malignant, in older age group. Table (2).The pleural fluid protein were analyzed as n=32(17.9%) of patients were having PfP level of category A, n=59(33%) were in the category B, and n=88 (49.2%) of the patients were having protein level in category C, Table [3].

Table No 1: Age – wise distribution of Tuberculous and malignant pleural effusion

Age Groups in Years	Diagnosis		Total
	TPE	MPE	
< 20 Years	11 10.1%	1 1.4%	12 6.7%
20-40 Years	67 61.5%	5 7.1%	72 40.2%
41-60 Years	22 20.2%	45 64.37%	67 37.4%
61-80 Years	9 8.3%	19 27.1%	28 15.6%
Total	109 100%	70 100%	179 100%

Table No. 2: Sex-wise distribution of Tuberculous and Malignant Pleural Effusion

Sex	Biopsy Result		Total
	TPE	MPE	
Male	76 69.7%	38 56.3%	114 63.7
Female	33 30.3%	32 45.7%	65 36.3
Total	109 100%	70 100%	179 100%

Table No. 3: The Categories of Pleural Fluid Protein Sensitivity and Specificity

Category	Frequency	%age	Sensitivity	Specificity
A	32	17.9	100.00	0
B	59	33.0	97.20	41.43
C	88	49.2	73.30	90.60

The sensitivity and specificity of pleural fluid protein of various categories was analyzed that at category A, the sensitivity was reaching to 100% but the specific was having the lowest value. At category "B" the sensitivity was 97.2% and specificity was 41.43% in category "C"

the sensitivity was the lowest of three having value 73.39% while the specificity was highest reaching to 90.6%.the positive (PPV) and negative predictive (NPV) values were analyzed for the three categories of plural fluid protein as that PPV was lowest for category C having value of 2.7 while NPV was 58.57 for category B, the PPV was 26.6 while the NPV was having value of 52.87. The PPV was highest for category "A" reading to the value 73.4 similarly the PPV was also highest in this category reading to the value of 88.57.

DISCUSSION

The distinction between tuberculous and malignant pleural effusion poses a diagnostic challenge to the physician. This is mainly due to the large proportion of cases in which no confirmatory diagnosis of pleural tuberculouse is achieved by microbiological methods, and the sensitivity of cytological studies for malignancy is inadequate[16]. Tuberculouse and malignancy are the most important and commonest causes of lymphocytic exudative pleural effusion. But the ratio is different in developed and developing countries. In areas were the tuberculouse is not prevent MPE is more common than TPE. In a study, conducted in Spain (2003) on 392 patients 73% cases were MPE and 27% were TPE.[17]Our study also showed that fact that TPE was commoner than MPE, accounting for 60.9% of total classes. Rest of cases (39.1 %) was malignant PE. Age has also been an important complementary variable while deciding about tuberculous or malignant PE. In our study the TPE was commoner in younger age group than MPE, Which was more in older age group. The mean age for TPE was 35.8 + 15.43 SD while 57 + 13.13 SF was the mean age for MPE. Our findings were comparable with the international studies.Porcel JM et al (2003) reported in their study, the mean age of 30 years (range 22-40) in TPE while the mean age was 68(58-76) years in MPE cases.[18]In our study we showed that pleural fluid protein level was higher in TPE than MPE and the difference was statistically significant at > 5g/dl (category "C") at < 4g/dl(category "A"). The MPE was commoner than TPE and the difference was significant. These finding were consistent with international data.Porcel- Perez JM et al (2004) reported that 73% of TPE were having pleural fluid protein level > 5g/dl.This value was the cutoff point for considering tuberculous etiology of the lymphocytic educative PE[14]. In another Spanish study conducted on 105 patients of TPE, 57% of patients showed plural fluid protein level above 5g/dl.[19]Antonangelo et al (2007) reported higher protein level in TPE than MPE. The protein level was 5.3+0.8g/dl in tuberculous PE while 4.2+1 was the level in MPE. The difference was statically significant.[23] Along with other laboratory parameters, protein level was utilized for discrimination between tuberculous and malignant PE. The same findings were found in the study conducted by Liam et al (2000) on patients having tuberculous or malignant PE [20]. Melo et al proposed 4.5g/dl as cutoff value for diagnostic presumption of TPE [21]. Porcel JM et al (2003) reported protein level of 5.4g/dl in tuberculous while the level was 4.2g/dl in malignant pleural effusion. The difference was statistically significant. [18]The study recommended two scoring models for differentiation between tuberculous and malignant PE. It also revealed that in areas where ADA facility is unavailable, plural fluid total protein level can be used for differentiation between tuberculous and malignant PE as used in one of the scoring model lacking ADA. The pleural fluid protein showed sensitivity of 77% and specificity of 80%. These results are comparable with those of our study which showed 73.30% sensitivity and 90.60% specificity at pleural fluid protein level of > 5g/dl.

CONCLUSION

Plural fluid total protein level determination and differentiating is a valuable tool in reaching to the diagnosis of suspectedtuberculouse from malignant pleural effusion provided it is used in addition to the adequate clinical scenario.

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Address for Corresponding Author:
Prof. Dr. Muhammad Ishaq
Chairman & Founder
Jinnah Medical College
Warsak Road Peshawar
Cell: +92-333-9152060
Email: Ishaq@Jmcp.Edu.Pk : Faizimrd@Gmail.Com